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(54) **MULTIPLE SPECIFICITY BINDERS OF CXC CHEMOKINES AND USES THEREOF**

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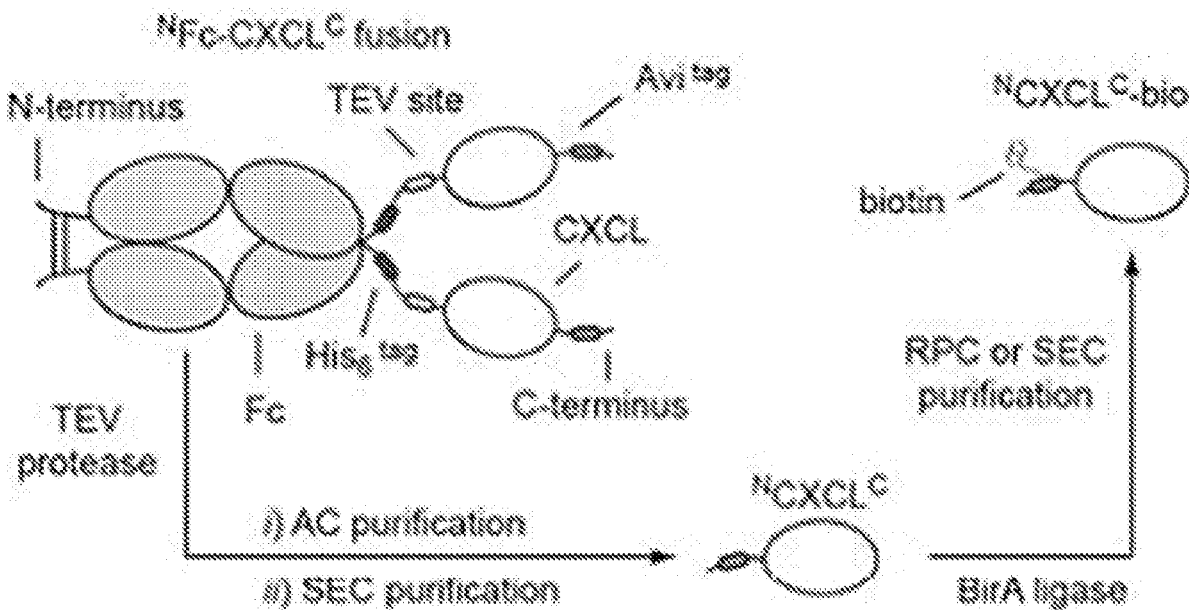
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(57) **ABSTRACT**

The present disclosure provides for fusion proteins comprising multispecific variable regions that bind more than one ELR+ CXC chemokine. The disclosure also provides methods of treating or preventing a condition associated with an abnormal immune response.

**Specification includes a Sequence Listing.**



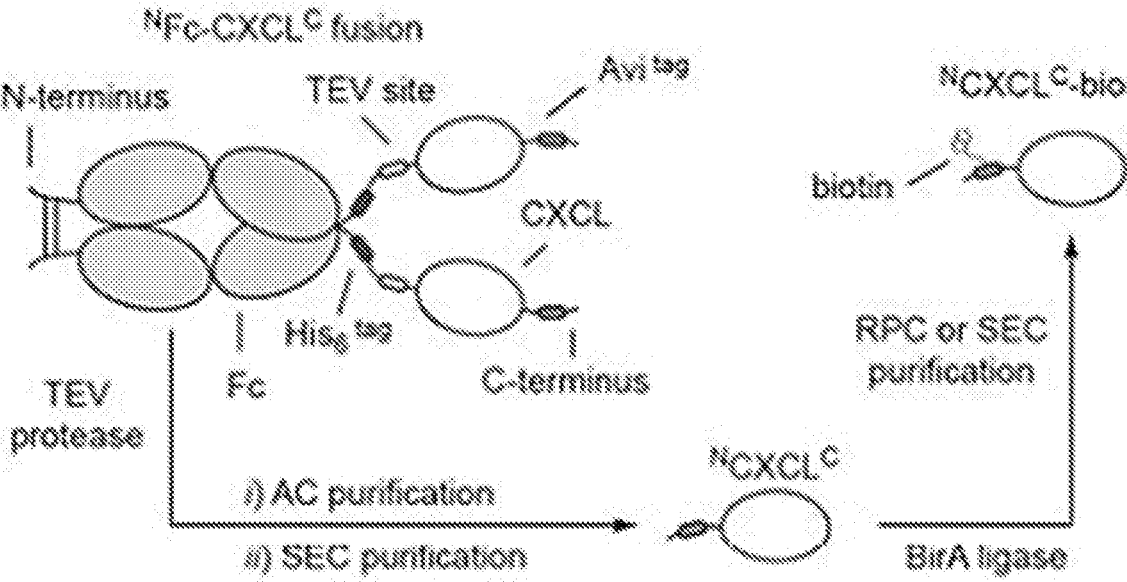


FIG. 1

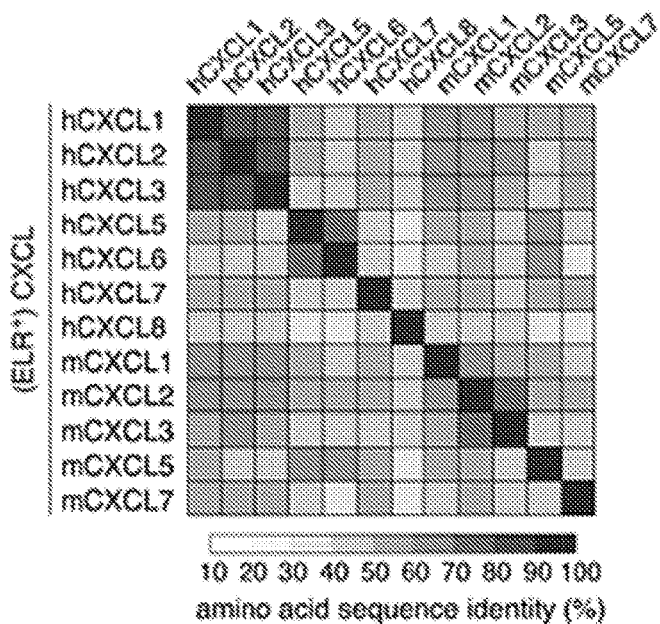


FIG. 2A

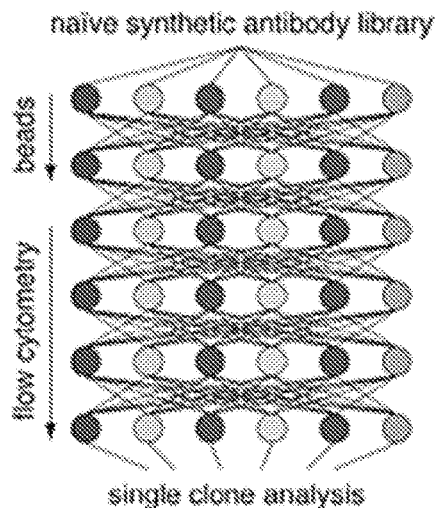


FIG. 2B

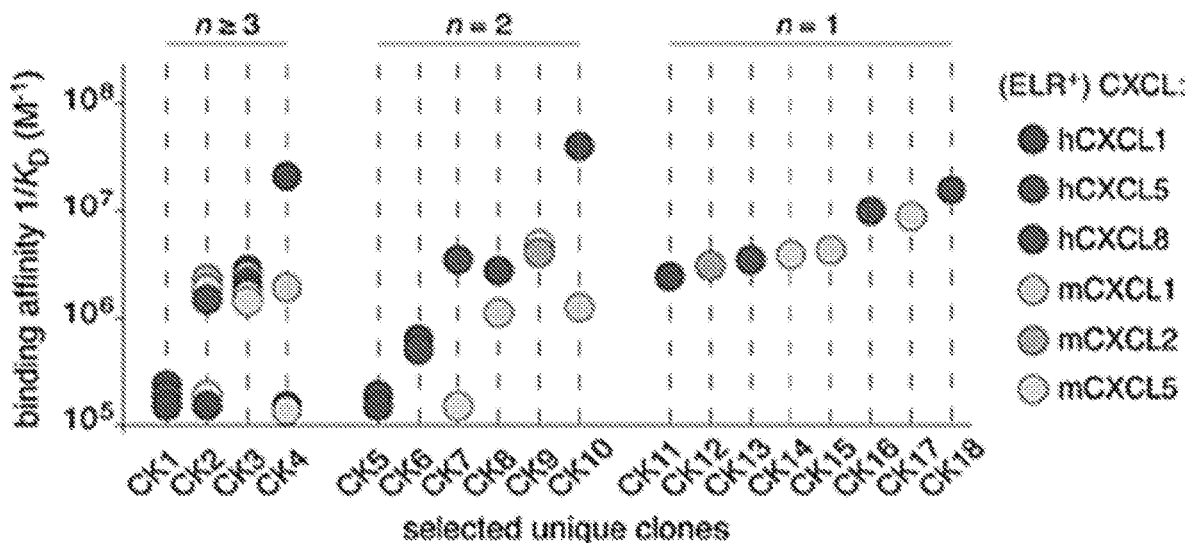


FIG. 2C

FIG. 2D

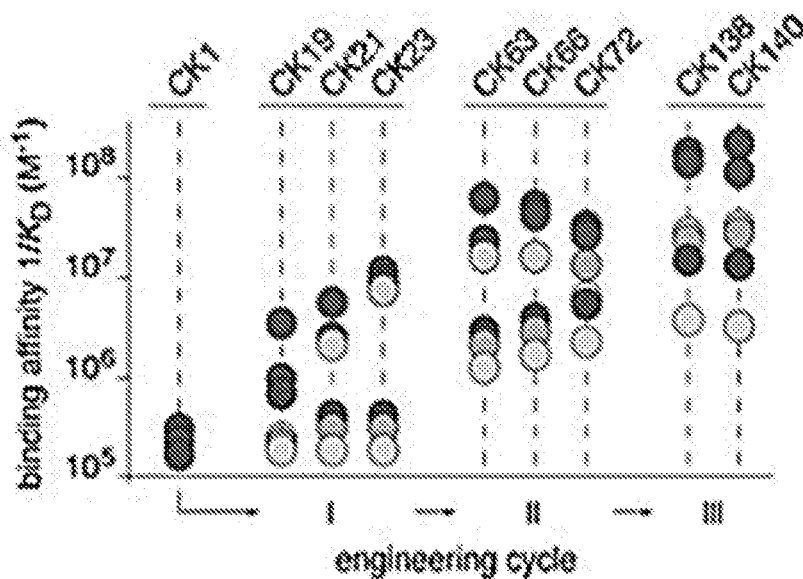


FIG. 2E

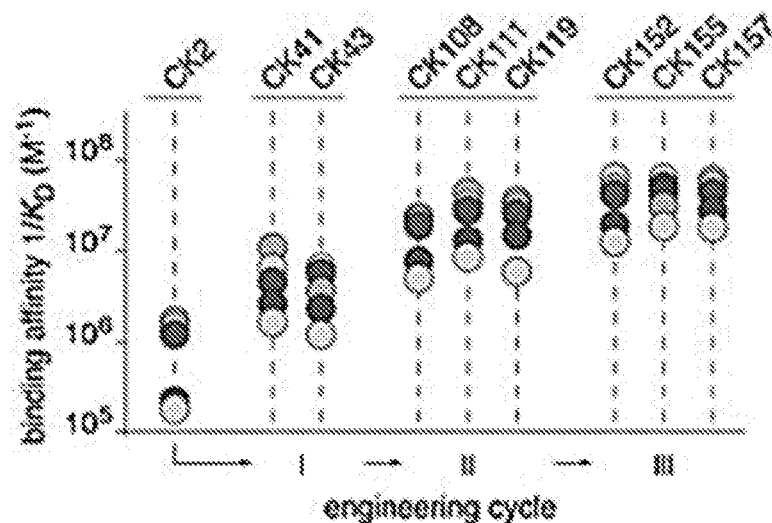
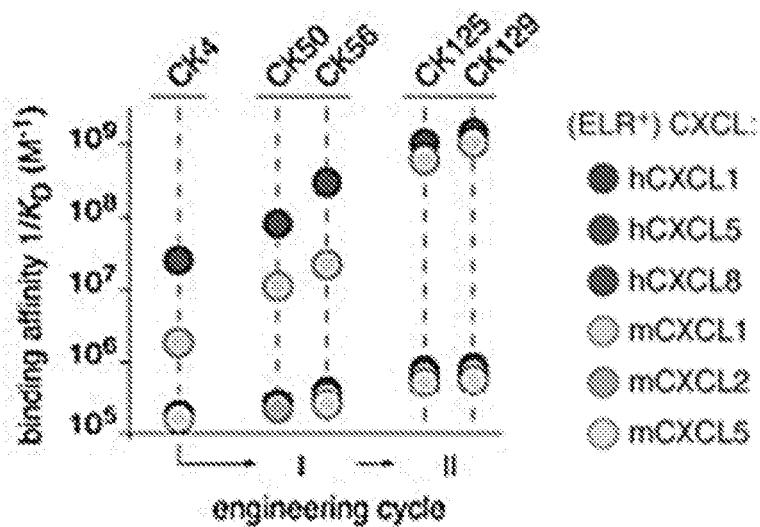


FIG. 2F





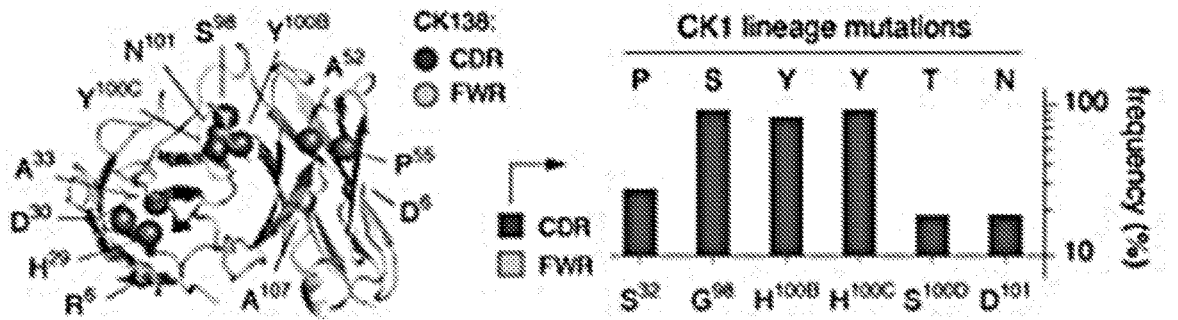


FIG. 2G

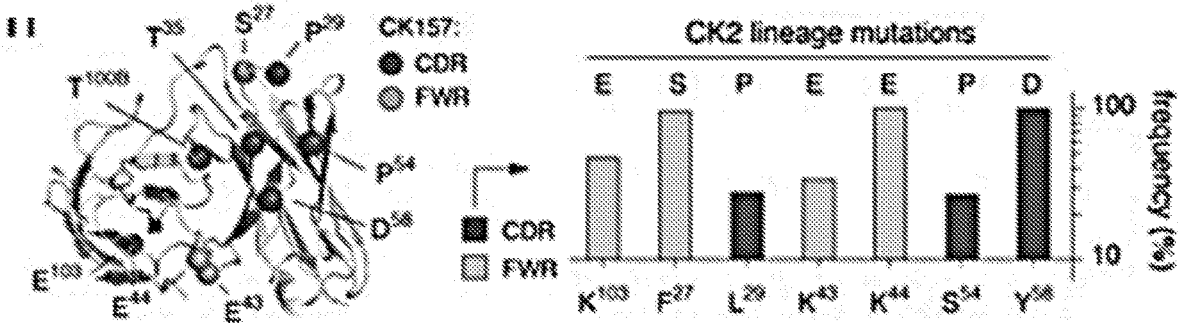


FIG. 2H

FIG. 3A

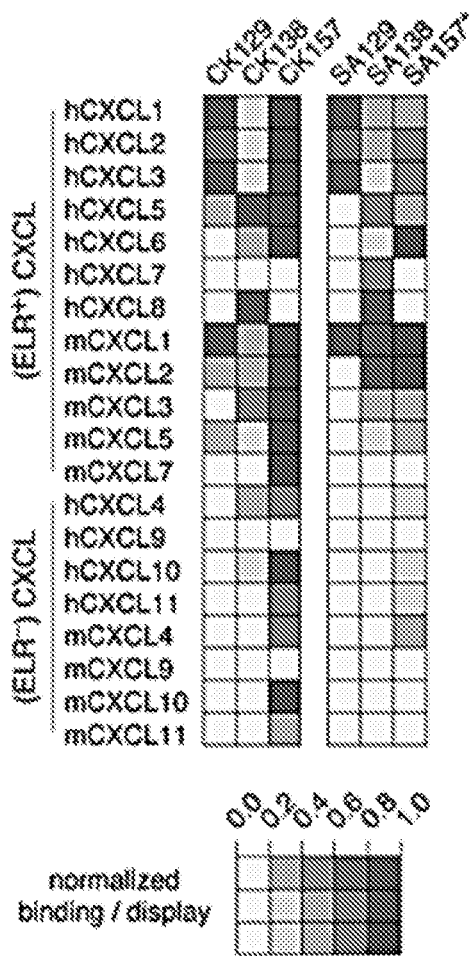


FIG. 3B

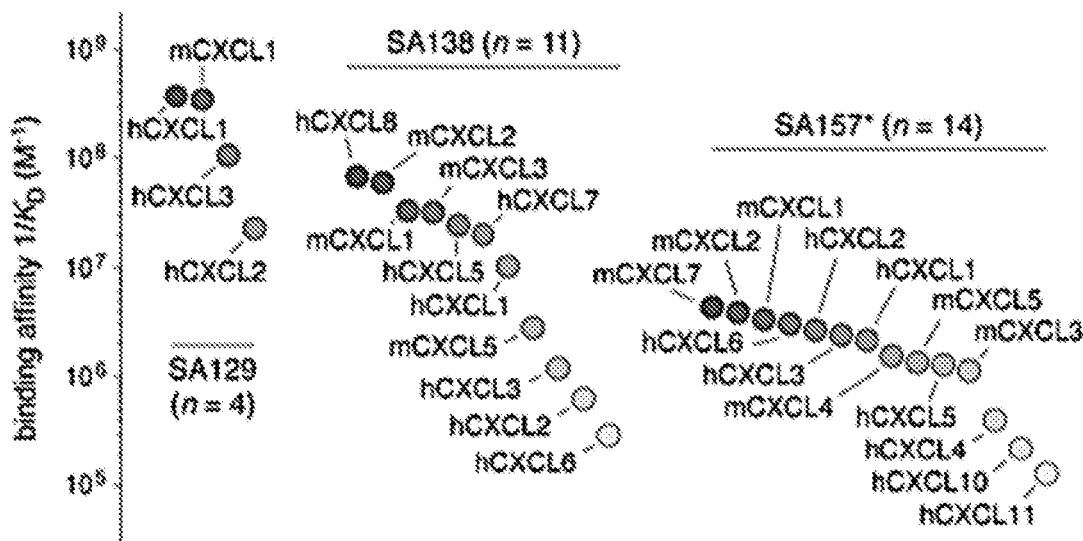
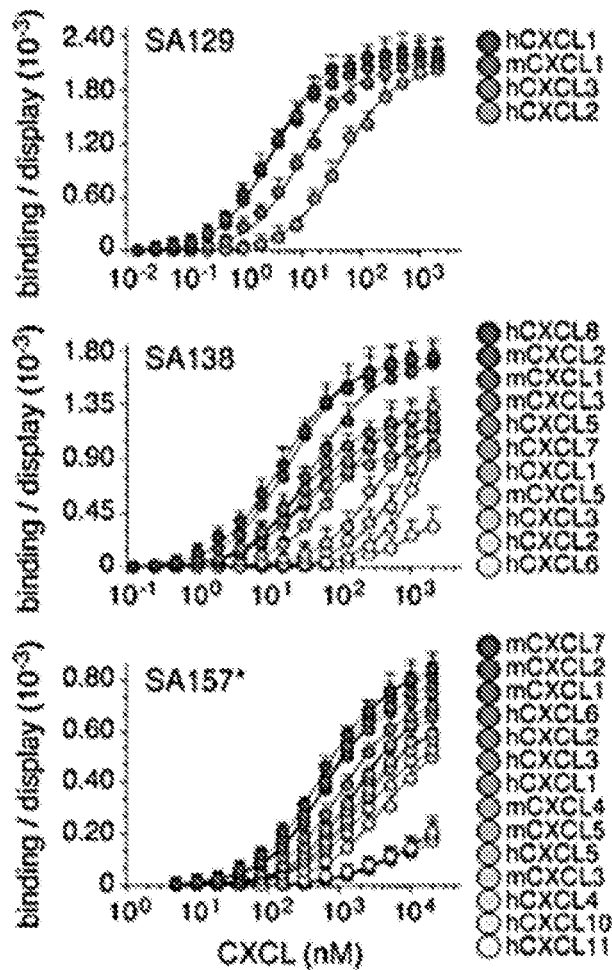


FIG. 3C

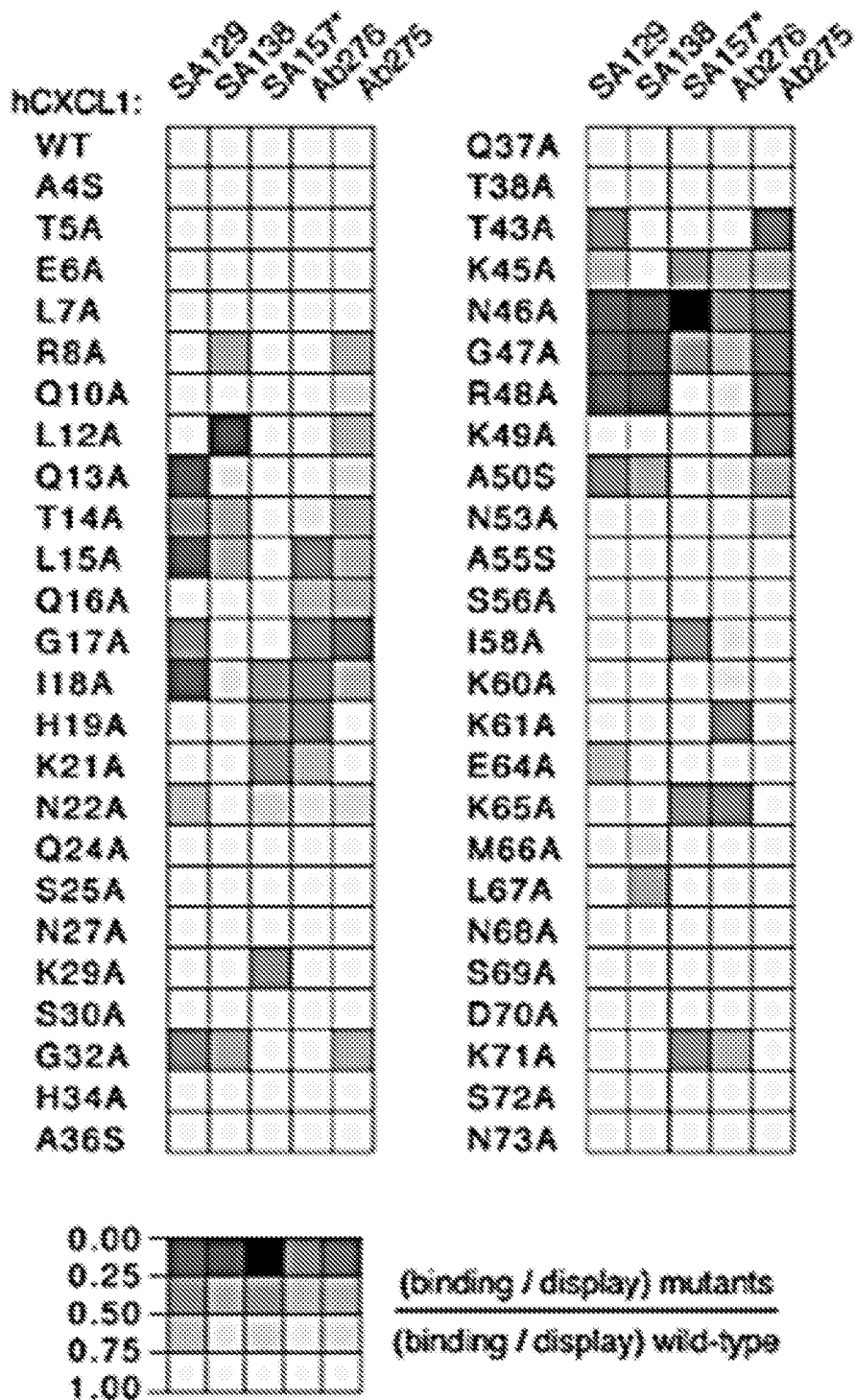


FIG. 4A

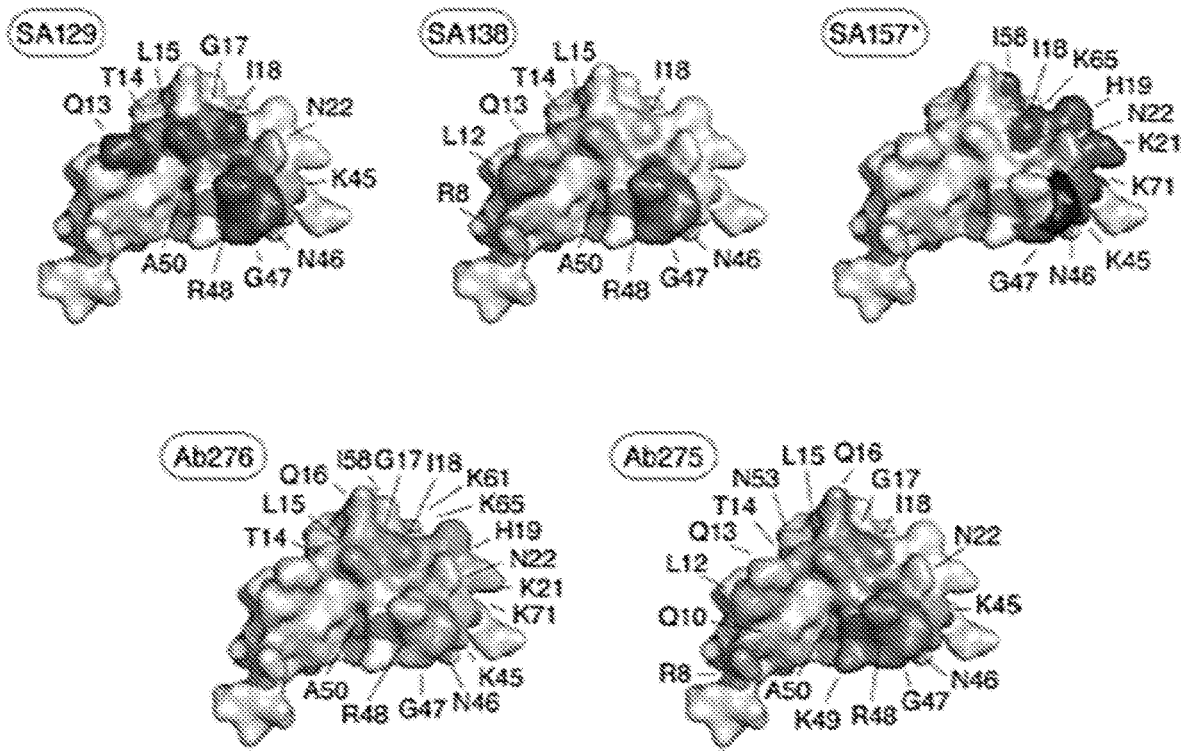


FIG. 4B

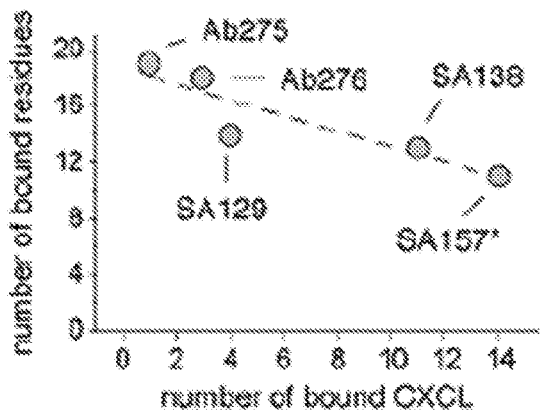


FIG. 4C

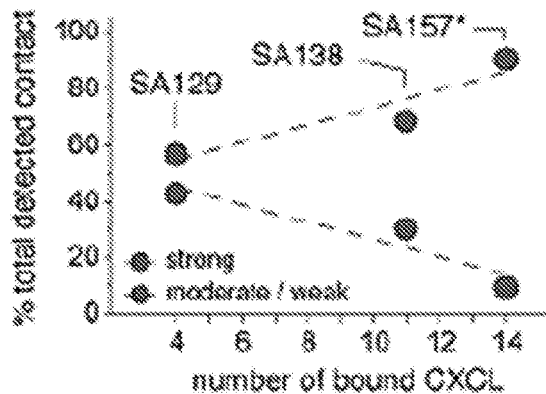


FIG. 4D

FIG. 5A

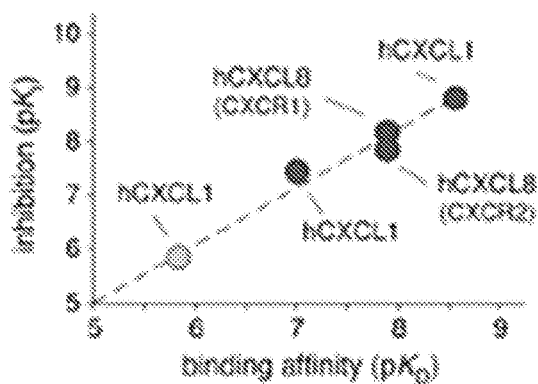
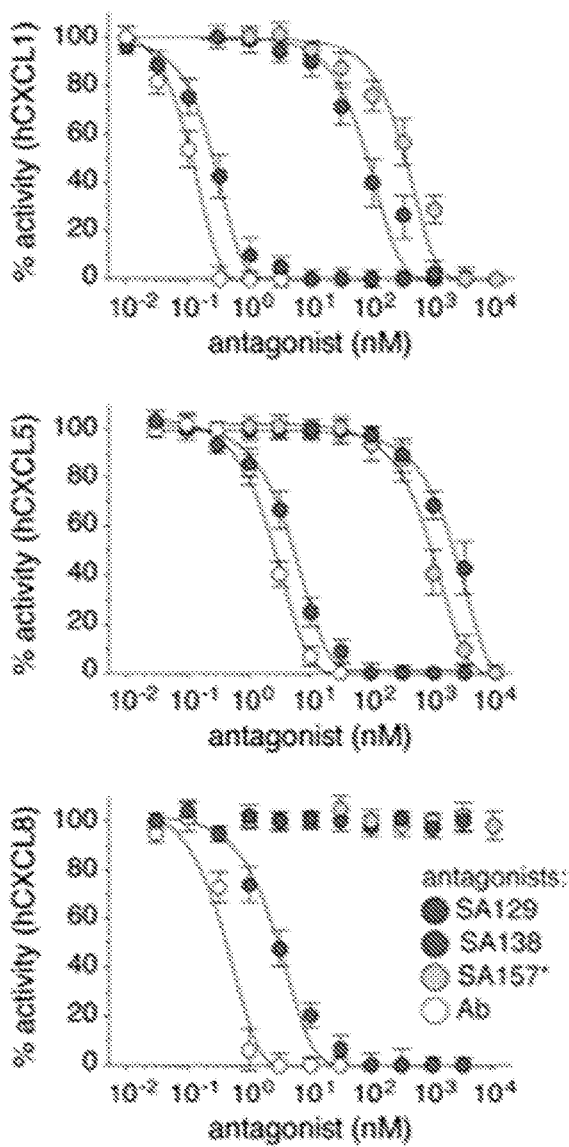


FIG. 5B



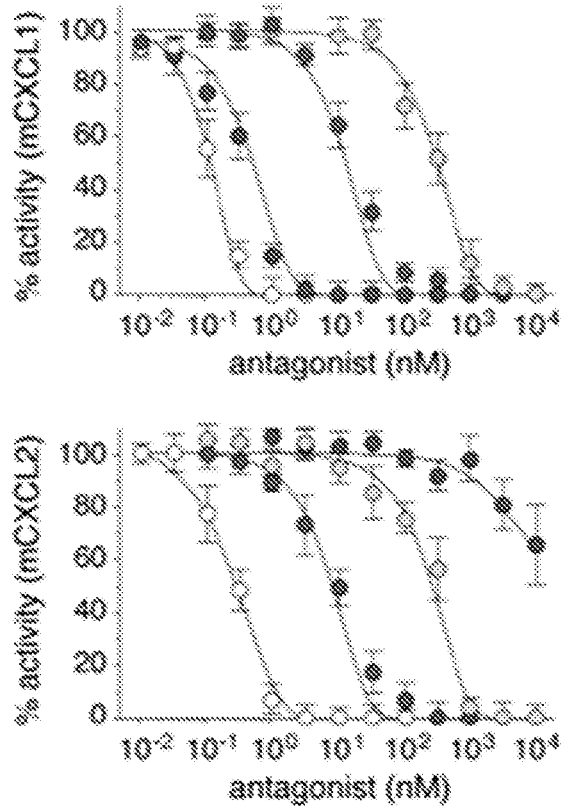


FIG. 5C

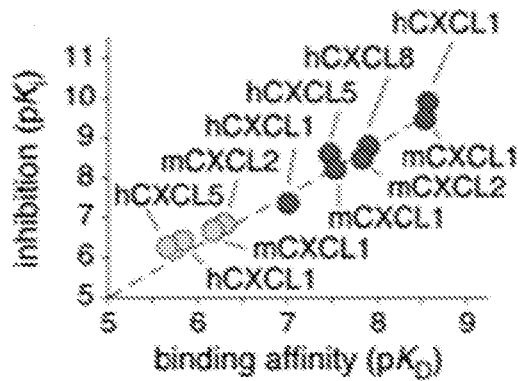


FIG. 5D

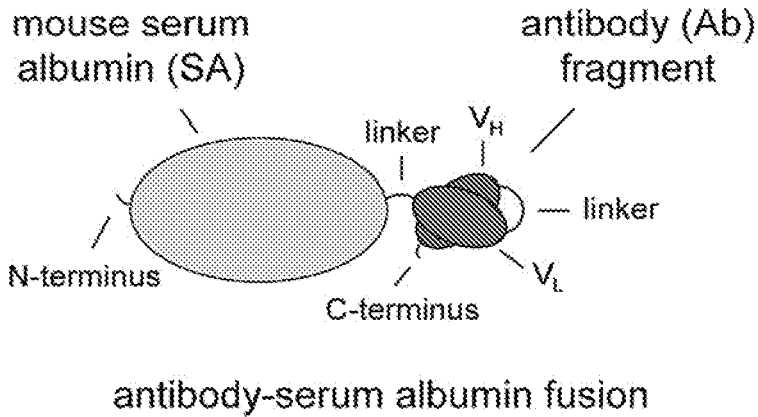


FIG. 6

FIG. 7A

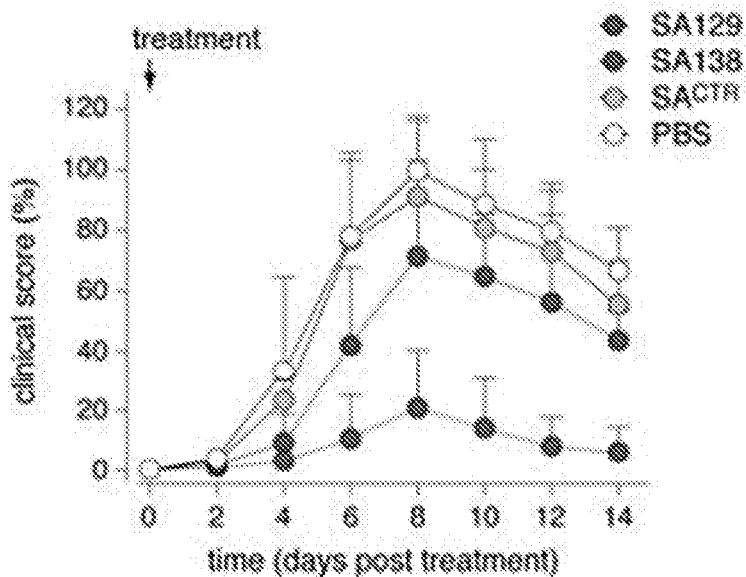


FIG. 7C

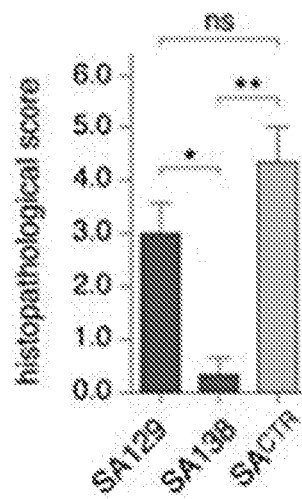
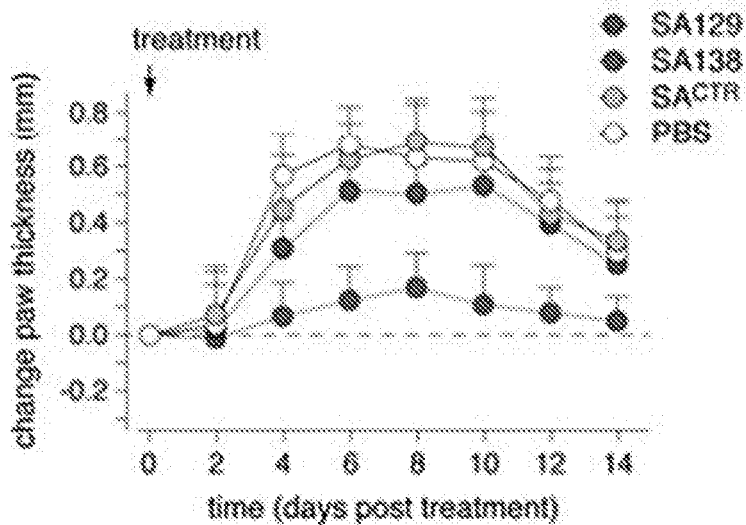
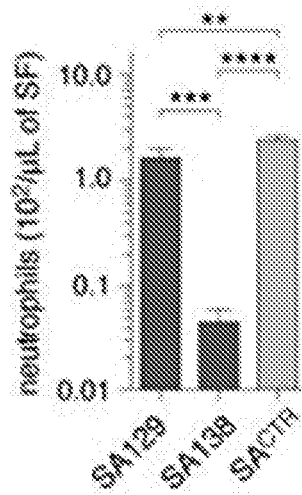


FIG. 7B

FIG. 7D



FIG. 7E

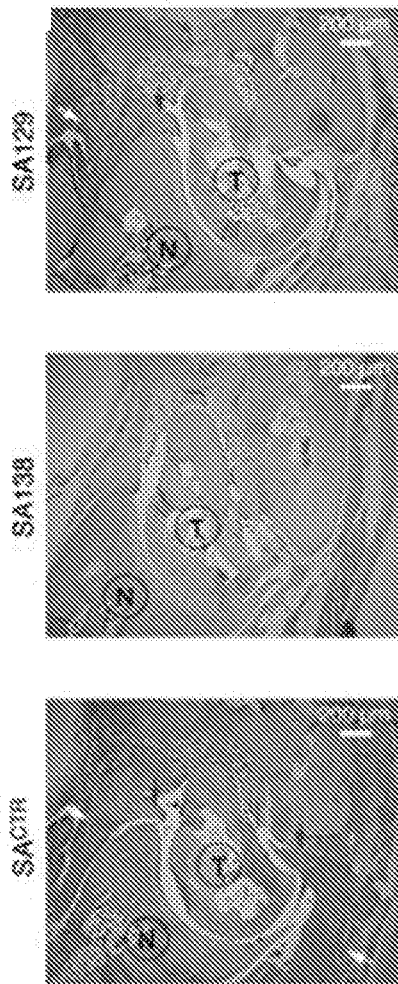


FIG. 7F

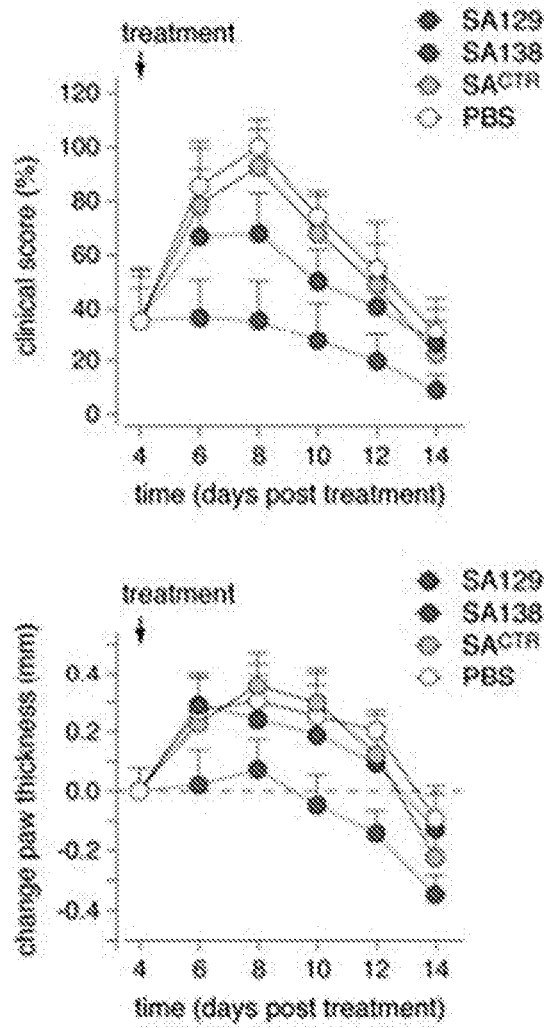


FIG. 7G

## MULTIPLE SPECIFICITY BINDERS OF CXC CHEMOKINES AND USES THEREOF

### RELATED INFORMATION PARAGRAPH

**[0001]** This application claims the benefit of the priority date of U.S. Provisional Application No. 62/546,814, filed on Aug. 17, 2017, the content of which is hereby incorporated by reference in its entirety.

### BACKGROUND

**[0002]** Chronic inflammatory diseases usually involve multiple ligands that act synergistically through promiscuous and diverse receptors (Cho, J. H & Feldman, M., *Nat Med.* 21, 730-738 (2015)). This complexity is well exemplified by the ELR+ CXC chemokine system, a large family of secreted proteins that play a prominent role in the development and progression of numerous inflammatory diseases, including rheumatoid arthritis (RA) (Cho, J. H & Feldman, M., *Nat Med.* 21, 730-738 (2015); Charo, I. F. & Ransohoff, R. M. *N. Engl. J. Med.* 354, 610-621 (2006); Viola, A. & Luster, A. D. *Annu. Rev. Pharmacol. Toxicol.* 48, 171-197 (2008)).

**[0003]** Despite their clinical and commercial success, monoclonal antibodies often fail to reduce the level of small antigens in circulation. For example, while small chemokines (~8-10 kDa) are rapidly eliminated through renal filtration ( $t_{1/2} < 10$  min) (Van Zee, K. J. et al. *J Immunol* 148, 1746-1752 (1992)), strategies targeting single or multiple chemokines using large monoclonal antibodies (150 kDa) that are long-lived in circulation ( $t_{1/2} \sim 2$  weeks) extends the systemic lifetimes of chemokines, thus increasing circulating chemokine levels. This buffering effect has been experimentally observed with numerous antibodies targeting small antigens (Mihara, M., Koishihara, Y., Fukui, H., Yasukawa, K. & Ohsugi, Y. *Immunology* 74, 55-59 (1991); Finkelman, F. D. et al. *J Immunol* 151, 1235-1244 (1993); May, L. T. et al. *J Immunol* 151, 3225-3236 (1993); Jayson, G. C. et al. *Eur J Cancer* 41, 555-563 (2005); Mostböck, S. *Curr Pharm Des* 15, 809-825 (2009); Letourneau, S. et al. *Proceedings of the National Academy of Sciences of the United States of America* 107, 2171-2176 (2010); O'Hear, C. & Foote, J. *Eur J Haematol* 84, 252-258 (2010)), including chemokines (Haringman, J. J. et al. *Arthritis and rheumatism* 54, 2387-2392 (2006)), and is consistent with the affinity, binding kinetics and pharmacokinetic profiles of the circulating antibody-small antigen complexes in the absence of efficient clearance (O'Hear, C. E. & Foote, J. *Proceedings of the National Academy of Sciences of the United States of America* 102, 40-44 (2005)). Furthermore, functional full length antibodies that are able to recruit additional immune system cells via FcγR receptors are not ideal for the treatment of inflammatory diseases that exploit autoantibodies.

**[0004]** As chronic inflammatory diseases are complex and involve multiple ligands and receptors acting in concert, therapies targeting a single pathological molecule are often insufficient to achieve the desired clinical outcome. Accordingly, therapeutics that bind multiple targets are needed.

### SUMMARY OF THE DISCLOSURE

**[0005]** The present disclosure is based on the discovery of engineered crossreactive therapeutic proteins that bind mul-

tipule homologous and orthologous targets, and are capable of preventing and reversing inflammation in an autoimmune model.

**[0006]** Accordingly, in some aspects the disclosure provides fusion proteins comprising a multispecific variable region operably coupled to a polymer, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines. In some aspects, the fusion protein comprises a multispecific variable region that binds human or murine ELR+ CXC chemokines. In other aspects, the fusion protein comprises a multispecific variable region that binds human and murine ELR+ CXC chemokines. In some aspects, the disclosure provides a fusion protein comprising a multispecific variable region that binds at least four ELR+ CXC chemokines selected from the group consisting of: human CXCL1 (Groα), human CXCL2 (Groβ), human CXCL3 (Groγ), human CXCL5 (ENA-78), human CXCL6 (GCP-2), human CXCL7 (NAP-2), human CXCL8 (IL-8), murine CXCL1 (KC), murine CXCL2 (MIP-2), murine CXCL3 (DCIP-1), murine CXCL5 (LIX), and murine CXCL7 (NAP-2). In some aspects, the at least four ELR+ CXC chemokines are hCXCL1, hCXCL2, hCXCL3 and mCXCL1.

**[0007]** In some aspects, the disclosure provides a fusion protein comprising a multispecific variable region that binds at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, or at least twelve ELR+ CXC chemokines selected from the group consisting of: human CXCL1 (Groα), human CXCL2 (Groβ), human CXCL3 (Groγ), human CXCL5 (ENA-78), human CXCL6 (GCP-2), human CXCL7 (NAP-2), human CXCL8 (IL-8), murine CXCL1 (KC), murine CXCL2 (MIP-2), murine CXCL3 (DCIP-1), murine CXCL5 (LIX), and murine CXCL7 (NAP-2). In some aspects, the at least six chemokines are human CXCL1, human CXCL5, human CXCL8, murine CXCL1, murine CXCL2 and murine CXCL5. In other aspects, the at least eleven chemokines are human CXCL8, murine CXCL2, murine CXCL1, murine CXCL3, human CXCL7, human CXCL5, human CXCL1, murine CXCL5, human CXCL3, human CXCL2, and human CXCL6.

**[0008]** In any of the foregoing aspects, the multispecific variable region is operably coupled to a polymer via a linker. In some aspects, the linker is a Gly-Ser linker.

**[0009]** In some aspects, the disclosure provides a fusion protein comprising a multispecific variable region operably coupled to a polymer, wherein the multispecific variable region is a scFv. In some aspects, the scFv is operably coupled to the C-terminus of the polymer. In some aspects, the scFv is operably coupled to the N-terminus of the polymer. In some aspects, the scFv is operably coupled to the polymer via a linker. In some aspects, the linker is a Gly-Ser linker.

**[0010]** In some aspects, the disclosure provides a fusion protein comprising a multispecific variable region described herein operably coupled to a polymer, wherein the polymer is a serum albumin moiety. In some aspects, the serum albumin moiety is mouse serum albumin. In other aspects, the serum albumin moiety is human serum albumin. In other aspects, the disclosure provides a fusion protein comprising a multispecific variable region operably coupled to a polymer, wherein the polymer is an Fc domain.

**[0011]** In any of the foregoing aspects, the disclosure provides a fusion protein wherein the multispecific variable region comprises a heavy chain variable region and a light

chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21.

**[0012]** In any of the foregoing aspects, the disclosure provides a fusion protein wherein the multispecific variable region comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

**[0013]** In any of the foregoing aspects, the disclosure provides a fusion protein wherein the multispecific variable region comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21, and wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

**[0014]** In other aspects, the disclosure provides a fusion protein comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises a heavy chain variable region and a light chain variable region comprising the amino acid sequences set forth in:

**[0015]** (a) SEQ ID NOs: 1 and 2, respectively;

**[0016]** (b) SEQ ID NOs: 11 and 12, respectively; or

**[0017]** (c) SEQ ID NOs: 21 and 22, respectively.

**[0018]** In another aspect, the disclosure provides a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises a heavy chain variable region and light chain variable region comprising amino acid sequences having 90% identity to the amino acid sequences set forth in:

**[0019]** (a) SEQ ID NOs: 1 and 2, respectively;

**[0020]** (b) SEQ ID NOs: 11 and 12, respectively; or

**[0021]** (c) SEQ ID NOs: 21 and 22, respectively.

**[0022]** In some aspects, the disclosure provides a fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises heavy and light chain CDRs selected from the group consisting of:

**[0023]** (a) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively;

**[0024]** (b) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 15, 16 and 17, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 18, 19 and 20, respectively; and

**[0025]** (c) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively.

**[0026]** In another aspect, the disclosure provides a fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises heavy and light chain variable regions, wherein

the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 11 and 21; and wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 12 and 22.

**[0027]** In another aspect, the disclosure provides a fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively. In another aspect, the disclosure provides a fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least human CXCL8, murine CXCL2, murine CXCL1, murine CXCL3, human CXCL7, human CXCL5, human CXCL1, murine CXCL5, human CXCL3, human CXCL2, and human CXCL6, and wherein the multispecific variable region comprises heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively.

**[0028]** In yet another aspect, the disclosure provides a fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively. In yet another aspect, the disclosure provides a fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least murine CXCL1, human CXCL1, human CXCL3, and human CXCL2, and wherein the multispecific variable region comprises heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively.

**[0029]** In another aspect, the disclosure provides a fusion protein comprising an amino acid sequence selected from the group consisting of SEQ ID Nos: 95-105 and 160-170.

**[0030]** In another aspect, the disclosure provides a fusion protein comprising an amino acid sequence having at least 90% identity to an amino acid sequence selected from the group consisting of SEQ ID Nos: 95-105 and 160-170.

**[0031]** In any of the foregoing aspects, the fusion protein inhibits binding of ELR+ CXC chemokines to their cognate CXCR1 and CXCR2.

**[0032]** In another aspect, the disclosure provides an isolated monoclonal antibody, or binding fragment thereof, that binds to at least four ELR+ CXC chemokines. In some aspects, the isolated monoclonal antibody, or binding fragment thereof, binds human or murine ELR+ CXC chemokines. In some aspects, the isolated monoclonal antibody, or binding fragment thereof, binds human and murine ELR+ CXC chemokines. In some aspects, the disclosure provides an isolated monoclonal antibody, or binding fragment thereof, that binds to at least four ELR+ CXC chemokines

selected from the group consisting of: human CXCL1 (Gro $\alpha$ ), human CXCL2 (Gro $\beta$ ), human CXCL3 (Gro $\gamma$ ), human CXCL5 (ENA-78), human CXCL6 (GCP-2), human CXCL7 (NAP-2), human CXCL8 (IL-8), murine CXCL1 (KC), murine CXCL2 (MIP-2), murine CXCL3 (DCIP-1), murine CXCL5 (LIX), and murine CXCL7 (NAP-2). In some aspects, the at least four ELR+ CXC chemokines are hCXCL1, hCXCL2, hCXCL3 and mCXCL1

**[0033]** In some aspects, the disclosure provides an isolated monoclonal antibody, or binding fragment thereof that binds at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, or at least twelve ELR+ CXC chemokines selected from the group consisting of: human CXCL1 (Gro $\alpha$ ), human CXCL2 (Gro $\beta$ ), human CXCL3 (Gro $\gamma$ ), human CXCL5 (ENA-78), human CXCL6 (GCP-2), human CXCL7 (NAP-2), human CXCL8 (IL-8), murine CXCL1 (KC), murine CXCL2 (MIP-2), murine CXCL3 (DCIP-1), murine CXCL5 (LIX), and murine CXCL7 (NAP-2). In some aspects, the at least six chemokines are human CXCL1, human CXCL5, human CXCL8, murine CXCL1, murine CXCL2 and murine CXCL5. In other aspects, the at least eleven chemokines are human CXCL8, murine CXCL2, murine CXCL1, murine CXCL3, human CXCL7, human CXCL5, human CXCL1, murine CXCL5, human CXCL3, human CXCL2, and human CXCL6.

**[0034]** In any of the foregoing aspects, the binding fragment thereof is a single chain variable fragment (scFv).

**[0035]** In any of the foregoing aspects, the antibody or binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21.

**[0036]** In any of the foregoing aspects, the antibody or binding fragment thereof, comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

**[0037]** In any of the foregoing aspects, the antibody or binding fragment thereof, comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21, and wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

**[0038]** In another aspect, the disclosure provides an isolated monoclonal antibody, or binding fragment thereof, that binds to at least four ELR+ CXC chemokines, comprising a heavy chain variable region and light chain variable region comprising the amino acid sequences set forth in:

**[0039]** (a) SEQ ID NOs: 1 and 2, respectively;

**[0040]** (b) SEQ ID NOs: 11 and 12, respectively; or

**[0041]** (c) SEQ ID NOs: 21 and 22, respectively.

**[0042]** In other aspects, the disclosure provides an isolated monoclonal antibody, or binding fragment thereof, that binds at least four ELR+ CXC chemokines, comprising a heavy chain variable region and light chain variable region comprising amino acid sequences having 90% identity to the amino acid sequences set forth in:

**[0043]** (a) SEQ ID NOs: 1 and 2, respectively;

**[0044]** (b) SEQ ID NOs: 11 and 12, respectively; or

**[0045]** (c) SEQ ID NOs: 21 and 22, respectively.

**[0046]** In another aspect, the disclosure provides an isolated monoclonal antibody, or binding fragment thereof, that

binds at least four ELR+ CXC chemokines, comprising heavy and light chain CDRs selected from the group consisting of:

**[0047]** (a) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively;

**[0048]** (b) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 15, 16 and 17, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 18, 19 and 20, respectively; and

**[0049]** (c) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively.

**[0050]** In other aspects, the disclosure provides an isolated monoclonal antibody, or binding fragment thereof, that binds at least four ELR+ CXC chemokines, comprising heavy and light chain variable regions, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 11 or 21; and wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 12 or 22.

**[0051]** In any of the foregoing aspects, the isolated monoclonal antibody, or binding fragment thereof, inhibits binding of ELR+ CXC chemokines to their cognate CXCR1 and CXCR2.

**[0052]** In another aspect, the disclosure provides methods of treating an autoimmune disorder in a subject in need thereof, the method comprising administering an effective amount of a fusion protein or isolated monoclonal antibody, or binding fragment thereof, described herein. In some aspects, the autoimmune disorder is rheumatoid arthritis.

**[0053]** In another aspect, the disclosure provides methods of blocking neutrophil infiltration in a subject with an autoimmune disorder, the method comprising administering an effective amount of a fusion protein or isolated monoclonal antibody, or binding fragment thereof, described herein. In some aspects, neutrophil infiltration of the synovial fluid of arthritic joints is blocked.

**[0054]** In another aspect, the disclosure provides methods of preventing establishment of an autoimmune disorder in a subject, the method comprising administering an effective amount of a fusion protein or isolated monoclonal antibody, or binding fragment thereof, described herein. In some aspects, the autoimmune disorder is rheumatoid arthritis.

**[0055]** In another aspect, the disclosure provides methods of reversing inflammatory arthritis in a subject in need thereof, the method comprising administering an effective amount of a fusion protein or isolated monoclonal antibody, or binding fragment thereof, described herein.

**[0056]** In another aspect, the disclosure provides a fusion protein or isolated monoclonal antibody, or binding fragment thereof, described herein, for use in treating an autoimmune disorder in a subject in need thereof, the method comprising administering an effective amount of. In some aspects, the autoimmune disorder is rheumatoid arthritis.

**[0057]** In another aspect, the disclosure provides a fusion protein or isolated monoclonal antibody, or binding fragment thereof, described herein, for use in blocking neutrophil infiltration in a subject with an autoimmune disorder. In some aspects, neutrophil infiltration of the synovial fluid of arthritic joints is blocked.

**[0058]** In another aspect, the disclosure provides a fusion protein or isolated monoclonal antibody, or binding fragment thereof, described herein, for use in preventing establishment of an autoimmune disorder in a subject. In some aspects, the autoimmune disorder is rheumatoid arthritis.

**[0059]** In another aspect, the disclosure provides a fusion protein or isolated monoclonal antibody, or binding fragment thereof, described herein, for use in reversing inflammatory arthritis in a subject in need thereof.

#### BRIEF DESCRIPTION OF THE FIGURES

**[0060]** The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

**[0061]** FIG. 1 is a schematic representation of the (i) Fc-ELR+ CXC chemokine fusion protein constructs (Fc-CXCL) and (ii) purification scheme applied to obtain pure, active, and biotinylated ELR+ CXC chemokines (CXCL-bio).

**[0062]** FIG. 2A is a heat map displaying the sequence identity among multiple human and murine ELR+ CXC chemokines. h=human, m=murine.

**[0063]** FIG. 2B is a schematic representation of the iterative selection pathways applied to isolate promiscuous binders from a naïve library of synthetic antibodies displayed on the surface of yeast. Two cycles of magnetic bead screening followed by four cycles of flow cytometry sorting are shown.

**[0064]** FIG. 2C is a plot showing the binding affinities of eighteen unique yeast-displayed synthetic antibody protein binders (CK) selected from six diverse human and murine ELR+ CXC chemokines. Data are represented as inverted equilibrium binding constants ( $1/K_D$ ;  $M^{-1}$ ) and indicate the means of at least three independent experiments. h=human, m=murine.

**[0065]** FIGS. 2D-2F provide plots of binding affinities of engineered clones derived from CK1 (FIG. 2D), CK2 (FIG. 2E), and CK4 (FIG. 2F) lineage after two independent processes of selection (I and II), each including the generation of random yeast-display antibody libraries and cycles of flow cytometry sorting, followed by a third round of site-directed mutagenesis (III). Data are represented as inverted equilibrium binding constants ( $1/K_D$ ;  $M^{-1}$ ) and indicate the means of at least three independent experiments.

**[0066]** FIGS. 2G and 2H show homology models and frequencies of enriched mutations of engineered CK138 (FIG. 2G) and CK157 (FIG. 2H) antibodies. The  $V_L$  and  $V_H$  backbones are represented as ribbons (light gray). Mutations acquired during the selection process are depicted as spheres at the Ca positions. Mutated amino acids belonging to CDR loops of CK138 and CK157 are shown in dark circles. Diversified amino acids belonging to FWR regions of CK138 and CK157 are shown in light circles.

**[0067]** FIG. 3A is a heat map indicating the normalized binding/display intensities of the engineered antibodies against twenty diverse human and murine CXC chemokines. Binding between soluble CXC chemokines and yeast-displayed CK129, CK138 and CK157 is shown on the left, and binding between soluble serum-albumin antibody fusions SA129, SA138 and SA157\* are shown on the right. The intensity of color correlates with the strength of the inter-

action with weak and strong interactions shown in light and dark colors, respectively. h=human, m=murine.

**[0068]** FIG. 3B provides graphs showing the binding isotherms of yeast-displayed human and murine CXC chemokines to soluble SA129, SA138 and SA157\* protein fusions. Equilibrium binding affinity ( $K_D$ ) values were determined only for clones exhibiting signals at high concentration of soluble agents. h=human, m=murine.

**[0069]** FIG. 3C is a plot of the binding affinities of yeast-displayed human and murine CXC chemokines to soluble SA129, SA138 and SA157\* protein fusions. The indicated values are displayed as filled circles and represent the means of at least three independent experiments presented as inverted of equilibrium binding constants ( $1/K_D$ ;  $M^{-1}$ ). h=human, m=murine.

**[0070]** FIG. 4A shows the normalized binding/display intensities of crossreactive protein fusions SA129, SA138 and SA157\*, and commercially available antibodies Ab276 and Ab275, to a defined panel of hCXCL1 alanine-mutants, as assessed by flow cytometry. The intensity of color correlates with the strength of the interaction with weak and strong interactions shown in light and dark colors, respectively. h=human.

**[0071]** FIG. 4B provides schematics showing residues of hCXCL1 contacted by SA129 (top left), SA138 (top middle), SA157\* (top right), Ab276 (bottom left) and Ab275 (bottom right). The intensity of color correlates with the strength of the interaction with weak and strong interactions shown in light and dark colors, respectively.

**[0072]** FIG. 4C is a graph showing the number of interacting residues plotted against the number of bound CXC chemokine ligands (CXCL).

**[0073]** FIG. 4D is a graph showing the percent of strong and combined weak and moderate interactions of each selected protein binders (SA129, SA138 and SA157) plotted against the number of bound CXC chemokines. Weak/moderate and strong interactions are shown in blue and red, respectively.

**[0074]** FIG. 5A is a plot showing the ability of serum albumin-antibody fusion SA129 (red), SA138 (blue) and SA157\* (gray) to block binding of hCXCL1 and hCXCL8 chemokines to CXCR1 and CXCR2 receptors, assessed by a flow cytometry based assay. The  $K_i$  values were determined, transformed to  $\log K_i$  and plotted against  $pK_D$ . h=human.

**[0075]** FIGS. 5B and 5C provide plots showing the ability of serum albumin-antibody fusion SA129, SA138 and SA157\* to antagonize the ELR+ CXC chemokine-induced receptors activation on mouse and human neutrophils, assessed by flow cytometry intracellular  $Ca^{2+}$  mobilization assay. The residual activity of human chemokines (hCXCL1, hCXCL5 and hCXCL8) (FIG. 5B) and mouse chemokines (mCXCL1 and mCXCL2) (FIG. 5C) incubated with varying concentrations of SA129 (red), SA138 (blue), SA157\* (gray) and commercial neutralizing antibody (Ab, white). The indicated values are means of three independent experiments. h=human, m=murine.

**[0076]** FIG. 5D is a plot showing calculated  $pK_i$  correlated linearly with the calculated  $pK_D$  suggesting a strict correlation between binding affinity and inhibitory activity. h=human, m=murine.

**[0077]** FIG. 6 is a schematic representation of the antibody single-chain variable fragment fused to the C-terminus of mouse serum albumin to generate SA129, SA138 and control SA<sup>CTR</sup> fusion proteins.

**[0078]** FIG. 7A is a plot showing the percent clinical score of mice treated with serum albumin-antibody fusion proteins on day 0 (preventative regimen). Arrows indicate day begin of treatment. All data are presented as mean (dots)  $\pm$ SE (bars).

**[0079]** FIG. 7B is a plot showing the change in ankle thickness (mm) of mice treated with serum albumin-antibody fusion proteins on day 0 (preventative regimen). Arrows indicate day begin of treatment. All data are presented as mean (dots)  $\pm$ SE (bars).

**[0080]** FIG. 7C is a graph showing quantification of purified infiltrating synovial fluid neutrophils (Ly6G+ cells) from the ankles of serum transfer arthritic mice measured at day 8 by flow cytometry (n=3 per condition). Statistical comparisons were made between each group using one-way analysis of variance (ANOVA). P values: \*P<0.05, \*\* P<0.01, \*\*\* P<0.001; \*\*\*\* P<0.0001. ns: non-significant.

**[0081]** FIG. 7D is a graph showing histopathological scoring of ankle tissue sections of mice treated with SA129, SA138 and control SA<sup>CTR</sup> on day 8.

**[0082]** FIG. 7E provides representative H&E staining of ankle tissue sections of mice treated with SA129 (top), SA138 (middle) and control SA<sup>CTR</sup> (bottom) on day 8. Scale bar represents 200 White arrow indicates the infiltrated inflammatory cell in the joints and red arrow indicates pannus formation. T, taurus; N, navicular.

**[0083]** FIGS. 7F and 7G are plots providing the percent clinical score (FIG. 7F) and change in ankle thickness (mm) (FIG. 7G) of K/BxN serum-induced arthritic mice treated beginning on day 4 with serum albumin-antibody fusion proteins (therapeutic regimen). Arrows indicate day treatment began. All data are presented as mean (dots)  $\pm$ SE (bars).

## DETAILED DESCRIPTION

### Overview

**[0084]** Various diseases are characterized by the development of immunological dysregulation in a patient. The presence of an impaired immune response in patients with autoimmune and related disorders has been particularly well-documented. Augmenting immune functions in patients may have beneficial effects for the alleviation of autoimmune and related diseases.

**[0085]** Described herein are fusion proteins, and isolated monoclonal antibodies, or antigen binding fragments thereof, that were designed to target soluble pro-inflammatory factors (e.g., ELR+ CXC chemokines).

**[0086]** ELR+ CXC chemokines (so-called because members of the chemokine family all possess an E-L-R amino acid motif immediately adjacent to their CXC motif) play an important role in a variety of pathogenic mechanisms, including the migration of neutrophils to sites of inflammation and angiogenesis. Neutrophils contribute to the pathogenesis of several acute and chronic inflammatory/autoimmune diseases.

**[0087]** In general, chemokines are grouped into four sub-families: CXC, CC, (X)C, and CX3C. In the CXC chemokines, one amino acid separates the first two cysteines ("the CXC motif"). ELR+ CXC chemokines are ligands for

CXCR1 and/or CXCR2 chemokine receptors, which are G-protein coupled seven transmembrane domain-type receptors that specifically bind ELR+ CXC chemokines. The seven human ELR+ CXC chemokines are human Gro-alpha (also known as CXCL1), human Gro-beta (also known as CXCL2), human Gro-gamma (also known as CXCL3), human ENA-78 (also known as CXCL5), human GCP-2 (also known as CXCL6), human NAP-2 (also known as CXCL7), and human IL-8 (also known as CXCL8). All ELR+ CXC chemokines bind the CXCR2 receptor; moreover, some ELR+ CXC chemokines bind both CXCR1 and CXCR2 receptors (i.e., CXCL6 and CXCL8), all of which contributes to redundancy in the activation pathways. The five murine ELR+ CXC chemokines are keratinocyte chemoattractant (KC) (also known as CXCL1), Macrophage Inflammatory Protein-2 (MIP-2) (also known as CXCL2), dendritic cell inflammatory protein-1 (DCIP-1) (also known as CXCL3), lipopolysaccharide-induced CXC chemokine (LIX) (also known as CXCL5), and neutrophil activating peptide-2 (NAP-2) (also known as CXCL7).

**[0088]** Crossreactive protein binders are challenging to obtain using traditional methodologies involving animal immunization and hybridoma development. Immune systems tend to remove self-reactive antibodies, making it difficult to generate in vivo antibodies against sequence- and structurally-related antigens derived from different species. In contrast, in vitro protein libraries associated with display technologies are unaffected by immune tolerance (Bradbury, A. R., et al. *Nature biotechnology* 29, 245-254 (2011)). Described herein are selection strategies for the isolation of protein binders with unprecedented crossreactivity towards a panel of structurally related, yet diverse in sequence, protein targets. Moreover, a serum albumin antibody fusion-based strategy was used to enable high drug dosing and optimal pharmacokinetic profiles, thus overcoming continuous receptor occupancy and buffering effect phenomena that have limited previous interventions.

**[0089]** Accordingly, in some aspects, the present disclosure provides fusion proteins comprising a multispecific variable region operably coupled to a polymer, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines. In other aspects, the present disclosure provides methods for treating or preventing a disorder associated with an abnormal immune response (e.g., autoimmune disorder, e.g., rheumatoid arthritis), comprising administering a fusion protein described herein.

### Definitions

**[0090]** Terms used in the claims and specification are defined as set forth below unless otherwise specified.

**[0091]** As used herein, "about" will be understood by persons of ordinary skill and will vary to some extent depending on the context in which it is used. If there are uses of the term which are not clear to persons of ordinary skill given the context in which it is used, "about" will mean up to plus or minus 10% of the particular value.

**[0092]** The term "ameliorating" refers to any therapeutically beneficial result in the treatment of a disease state, e.g., autoimmune disorder, including prophylaxis, lessening in the severity or progression, remission, or cure thereof.

**[0093]** "Amino acid" refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function in a manner similar to the naturally occurring amino acids. Naturally occurring amino

acids are those encoded by the genetic code, as well as those amino acids that are later modified, e.g., hydroxyproline,  $\gamma$ -carboxyglutamate, and O-phosphoserine. Amino acid analogs refers to compounds that have the same basic chemical structure as a naturally occurring amino acid, i.e., an  $\alpha$  carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, e.g., homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs have modified R groups {e.g., norleucine} or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refers to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that function in a manner similar to a naturally occurring amino acid.

**[0094]** Amino acids can be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, can be referred to by their commonly accepted single-letter codes.

**[0095]** An "amino acid substitution" refers to the replacement of at least one existing amino acid residue in a predetermined amino acid sequence (an amino acid sequence of a starting polypeptide) with a second, different "replacement" amino acid residue. An "amino acid insertion" refers to the incorporation of at least one additional amino acid into a predetermined amino acid sequence. While the insertion will usually consist of the insertion of one or two amino acid residues, larger "peptide insertions," can also be made, e.g. insertion of about three to about five or even up to about ten, fifteen, or twenty amino acid residues. The inserted residue(s) may be naturally occurring or non-naturally occurring as disclosed above. An "amino acid deletion" refers to the removal of at least one amino acid residue from a predetermined amino acid sequence.

**[0096]** A polypeptide or amino acid sequence "derived from" a designated polypeptide or protein refers to the origin of the polypeptide. Preferably, the polypeptide or amino acid sequence which is derived from a particular sequence has an amino acid sequence that is essentially identical to that sequence or a portion thereof, wherein the portion consists of at least 10-20 amino acids, preferably at least 20-30 amino acids, more preferably at least 30-50 amino acids, or which is otherwise identifiable to one of ordinary skill in the art as having its origin in the sequence. Polypeptides derived from another peptide may have one or more mutations relative to the starting polypeptide, e.g., one or more amino acid residues which have been substituted with another amino acid residue or which has one or more amino acid residue insertions or deletions. A polypeptide can comprise an amino acid sequence which is not naturally occurring. Such variants necessarily have less than 100% sequence identity or similarity with the starting molecule. In some embodiments, the variant will have an amino acid sequence from about 75% to less than 100% amino acid sequence identity or similarity with the amino acid sequence of the starting polypeptide. In some embodiments, the variant has an amino acid sequence from about 80% to less than 100% amino acid sequence identity or similarity with the amino acid sequence of the starting polypeptide. In some embodiments, the variant has an amino acid sequence from about 85% to less than 100%, amino acid sequence identity or similarity with the amino acid sequence of the starting

polypeptide. In some embodiments, the variant has an amino acid sequence from about 90% to less than 100% (e.g., 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%) amino acid sequence identity or similarity with the amino acid sequence of the starting polypeptide. In some embodiments, the variant has an amino acid sequence from about 95% to less than 100%, e.g., over the length of the variant molecule, amino acid sequence identity or similarity with the amino acid sequence of the starting polypeptide.

**[0097]** In some embodiments, there is one amino acid difference between a starting polypeptide sequence and the sequence derived therefrom. Identity or similarity with respect to this sequence is defined herein as the percentage of amino acid residues in the candidate sequence that are identical (i.e., same residue) with the starting amino acid residues, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. In some embodiments, a polypeptide consists of, consists essentially of, or comprises an amino acid sequence selected from SEQ ID NOs: 1, 2, 5-12, 15-22, 25-30, 37-42, 63-82, 95-106, 127-146, 148, and 160-182. In some embodiments, a polypeptide includes an amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to an amino acid sequence selected from SEQ ID NOs: 1, 2, 5-12, 15-22, 25-30, 37-42, 63-82, 95-106, 127-146, 148, and 160-182. In some embodiments, a polypeptide includes a contiguous amino acid sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a contiguous amino acid sequence selected from SEQ ID NOs: 1, 2, 5-12, 15-22, 25-30, 37-42, 63-82, 95-106, 127-146, 148, and 160-182. In some embodiments, a polypeptide includes an amino acid sequence having at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 200, 300, 400, or 500 (or any integer within these numbers) contiguous amino acids of an amino acid sequence selected from SEQ ID NOs: 1, 2, 5-12, 15-22, 25-30, 37-42, 63-82, 95-106, 127-146, 148, and 160-182.

**[0098]** In some embodiments, the polypeptides are encoded by a nucleotide sequence. Nucleotide sequences of the invention can be useful for a number of applications, including: cloning, gene therapy, protein expression and purification, mutation introduction, DNA vaccination of a host in need thereof, antibody generation for, e.g., passive immunization, PCR, primer and probe generation, and the like. In some embodiments, the nucleotide sequence described herein comprises, consists of, or consists essentially of, a nucleotide sequence selected from SEQ ID NOs: 3, 4, 13, 14, 23, 24, 31-36, 43-62, 83-94, 107-126, 147, 149, and 150-159. In some embodiments, a nucleotide sequence includes a nucleotide sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleotide sequence set forth in SEQ ID NOs: 3, 4, 13, 14, 23, 24, 31-36, 43-62, 83-94, 107-126, 147, 149, and 150-159. In some embodiments, a nucleotide sequence includes a contiguous nucleotide sequence at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a contiguous nucleotide sequence set forth in SEQ ID NOs: 3, 4, 13, 14, 23, 24, 31-36, 43-62, 83-94, 107-126, 147, 149, and 150-159. In some embodiments, a nucleotide sequence includes a nucleotide sequence having at least 10, 15, 20, 25,

30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 200, 300, 400, or 500 (or any integer within these numbers) contiguous nucleotides of a nucleotide sequence set forth in SEQ ID NOs: 3, 4, 13, 14, 23, 24, 31-36, 43-62, 83-94, 107-126, 147, 149, and 150-159.

**[0099]** It will also be understood by one of ordinary skill in the art that the polypeptides (e.g., fusion proteins) disclosed herein may be altered such that they vary in sequence from the naturally occurring or native sequences from which they were derived, while retaining the desirable activity of the native sequences. For example, nucleotide or amino acid substitutions leading to conservative substitutions or changes at “non-essential” amino acid residues may be made. Mutations may be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis.

**[0100]** The polypeptides disclosed herein may comprise conservative amino acid substitutions at one or more amino acid residues, e.g., at essential or non-essential amino acid residues. A “conservative amino acid substitution” is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art, including basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a nonessential amino acid residue in a binding polypeptide is preferably replaced with another amino acid residue from the same side chain family. In some embodiments, a string of amino acids can be replaced with a structurally similar string that differs in order and/or composition of side chain family members. Alternatively, in some embodiments, mutations may be introduced randomly along all or part of a coding sequence, such as by saturation mutagenesis, and the resultant mutants can be incorporated into binding polypeptides of the invention and screened for their ability to bind to the desired target.

**[0101]** As used herein, the term “antibody” refers to a whole antibody comprising two light chain polypeptides and two heavy chain polypeptides. Whole antibodies include different antibody isotypes including IgM, IgG, IgA, IgD, and IgE antibodies. The term “antibody” includes a polyclonal antibody, a monoclonal antibody, a chimerized or chimeric antibody, a humanized antibody, a primatized antibody, a deimmunized antibody, and a fully human antibody. The antibody can be made in or derived from any of a variety of species, e.g., mammals such as humans, non-human primates (e.g., orangutan, baboons, or chimpanzees), horses, cattle, pigs, sheep, goats, dogs, cats, rabbits, guinea pigs, gerbils, hamsters, rats, and mice. The antibody can be a purified or a recombinant antibody.

**[0102]** As used herein, the term “antibody fragment,” “antigen-binding fragment,” or similar terms refer to a fragment of an antibody that retains the ability to bind to a target antigen(s) (e.g., ELR+ CXC chemokine(s)) and promote, induce, and/or increase the activity of the target antigen. Such fragments include, e.g., a single chain antibody, a single chain Fv fragment (scFv), an Fd fragment, an Fab fragment, an Fab' fragment, or an F(ab')<sub>2</sub> fragment. An

scFv fragment is a single polypeptide chain that includes both the heavy and light chain variable regions of the antibody from which the scFv is derived. In addition, intrabodies, minibodies, triabodies, and diabodies are also included in the definition of antibody and are compatible for use in the methods described herein. See, e.g., Todorovska et al. (2001) *J Immunol Methods* 248(1):47-66; Hudson and Kortt (1999) *J Immunol Methods* 231(1):177-189; Poljak (1994) *Structure* 2(12):1121-1123; Rondon and Marasco (1997) *Annual Review of Microbiology* 51:257-283, the disclosures of each of which are incorporated herein by reference in their entirety.

**[0103]** As used herein, the term “antibody fragment” also includes, e.g., single domain antibodies such as camelized single domain antibodies. See, e.g., Muyldermans et al. (2001) *Trends Biochem Sci* 26:230-235; Nuttall et al. (2000) *Curr Pharm Biotech* 1:253-263; Reichmann et al. (1999) *J Immunol Meth* 231:25-38; PCT application publication nos. WO 94/04678 and WO 94/25591; and U.S. Pat. No. 6,005, 079, all of which are incorporated herein by reference in their entireties. In some embodiments, the disclosure provides single domain antibodies comprising two VH domains with modifications such that single domain antibodies are formed.

**[0104]** In some embodiment, an antigen-binding fragment includes the variable region of a heavy chain polypeptide and the variable region of a light chain polypeptide. In some embodiments, an antigen-binding fragment described herein comprises the CDRs of the light chain and heavy chain polypeptide of an antibody.

**[0105]** As used herein, the term “autoimmune and/or related diseases” refers to diseases, disorders, conditions, and/or syndromes arising from and/or directed against a patient’s own cells, tissues, and/or organs, or a co-segregate or manifestation thereof, or resulting condition therefrom. Examples of autoimmune and related diseases include graft rejection (e.g. graft vs. host disease), allergy, inflammatory diseases, and also include, but are not limited to, Acute Disseminated Encephalomyelitis (ADEM), Acute necrotizing hemorrhagic leukoencephalitis, Addison’s disease, Agammaglobulinemia, Allergic conjunctivitis, Allergic rhinitis, Allergic disorders of the gastrointestinal tract, Alopecia areata, Alzheimer’s disease, Amyloidosis, Ankylosing spondylitis, Anti-GBM/Anti-TBM nephritis, Antiphospholipid syndrome (APS), Arteriosclerosis, Asthma, Autoimmune angioedema, Autoimmune aplastic anemia, Autoimmune-associated infertility, Autoimmune dysautonomia, Autoimmune encephalomyelitis, Autoimmune hemophilia, Autoimmune hepatitis, Autoimmune hyperlipidemia, Autoimmune immunodeficiency, Autoimmune inner ear disease (AIED), Autoimmune lymphoproliferative syndrome, Autoimmune myocarditis, Autoimmune oophoritis, Autoimmune pancreatitis, Autoimmune retinopathy, Autoimmune thrombocytopenic purpura (ATP), Autoimmune thyroid disease, Autoimmune urticaria, Autoimmune uveoretinitis, Axonal & neuronal neuropathies, Balo disease, Behcet’s disease, Bullous pemphigoid, Cardiomyopathy, Castleman disease, Celiac disease, Chagas disease, Chronic fatigue syndrome, Chronic inflammatory demyelinating polyneuropathy (CIDP), Chronic recurrent multifocal osteomyelitis (CRMO), Churg-Strauss syndrome, Cicatricial pemphigoid/benign mucosal pemphigoid, Crohn’s disease, Cogans syndrome, Cold agglutinin disease, Congenital heart block, Cocksackie myocarditis, CREST disease, Essential mixed cryoglobul-



linemia, Demyelinating neuropathies, Dermatitis herpetiformis, Dermatomyositis, Devic's disease (neuromyelitis optica), Discoid lupus, Dressler's syndrome, Eczema, Endometriosis, Eosinophilic esophagitis, Eosinophilic fasciitis, Erythema nodosum, Eustachian tube itching, Experimental allergic encephalomyelitis, Evans syndrome, Fibromyalgia, Fibrosing alveolitis, Giant cell arteritis (temporal arteritis), Giant cell myocarditis, Giant papillary conjunctivitis, Glomerulonephritis, Goodpasture's syndrome, Granulomatosis with Polyangiitis (GPA) (formerly called Wegener's Granulomatosis), Graves' disease, Guillain-Barre syndrome, Hashimoto's encephalitis, Hashimoto's thyroiditis, Hemolytic anemia, Henoch-Schonlein purpura, Herpes gestationis, Hypogammaglobulinemia, Idiopathic thrombocytopenic purpura (ITP), IgA nephropathy, IgG4-related sclerosing disease, Immunoregulatory lipoproteins, Inclusion body myositis, Inflammatory Bowel Disease, Insulin resistance, Interstitial cystitis, Juvenile rheumatoid arthritis, Juvenile diabetes (Type 1 diabetes), Juvenile myositis, Kawasaki disease/syndrome, Lambert-Eaton syndrome, Leukocytoclastic vasculitis, Lichen planus, Lichen sclerosus, Ligneous conjunctivitis, Linear IgA disease (LAD), Lyme disease, chronic, Meniere's disease, Microscopic polyangiitis, Mixed connective tissue disease (MCTD), Mooren's ulcer, Mucha-Habermann disease, Multiple sclerosis, Myasthenia gravis, Myositis, Narcolepsy, Neuromyelitis optica (Devic's), Neutropenia, Osteoarthritis, Ocular cicatricial pemphigoid, Optic neuritis, Palindromic rheumatism, PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with *Streptococcus*), Paraneoplastic cerebellar degeneration, Paroxysmal nocturnal hemoglobinuria (PNH), Parry Romberg syndrome, Parsonnage-Turner syndrome, Pars planitis (peripheral uveitis), Pemphigus, Peripheral neuropathy, Perivascular encephalomyelitis, Pernicious anemia, POEMS syndrome, Polyarteritis nodosa, Type I, II, & III autoimmune polyglandular syndromes, Polymyalgia rheumatic, Polymyositis, Postmyocardial infarction syndrome, Postpericardiotomy syndrome, Progesterone dermatitis, Primary biliary cirrhosis, Primary sclerosing cholangitis, Psoriasis, Psoriatic arthritis, Idiopathic pulmonary fibrosis, Pyoderma gangrenosum, Pure red cell aplasia, Raynauds phenomenon, Reactive Arthritis, Reflex sympathetic dystrophy, Reiter's syndrome, Relapsing polychondritis, Restless legs syndrome, Retroperitoneal fibrosis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Schmidt syndrome, Scleritis, Scleroderma, Sinusitis, Sjogren's syndrome, Sperm & testicular autoimmunity, Stiff person syndrome, Subacute bacterial endocarditis (SBE), Susac's syndrome, Sympathetic ophthalmia, Systemic lupus erythematosus (SLE), Takayasu's arteritis, Temporal arteritis/Giant cell arteritis, Thrombocytopenic purpura (TTP), Tolosa-Hunt syndrome, Transverse myelitis, Type 1 diabetes, Ulcerative colitis, Undifferentiated connective tissue disease (UCTD), Uveitis, Vernal conjunctivitis, Vernal keratoconjunctivitis, Vasculitis, Vesiculobullous dermatosis, Vitiligo, Wegener's granulomatosis (now termed Granulomatosis with Polyangiitis (GPA)). Any one or more of the aforementioned or unmentioned autoimmune and/or related diseases may be the target disease for a method of treatment as disclosed herein.

**[0106]** As used herein, the term "bispecific" or "bifunctional antibody" refers to an artificial hybrid antibody having two different heavy/light chain pairs and two different binding sites. Bispecific antibodies can be produced by a variety

of methods including fusion of hybridomas or linking of Fab' fragments. See, e.g., Songsivilai & Lachmann, *Clin. Exp. Immunol.* 79:315-321 (1990); Kostelny et al., *J. Immunol.* 148, 1547-1553 (1992).

**[0107]** Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chain/light-chain pairs have different specificities (Milstein and Cuello (1983) *Nature* 305:537-539). Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion of the heavy chain variable region is preferably with an immunoglobulin heavy-chain constant domain, including at least part of the hinge, CH2, and CH3 regions. For further details of illustrative currently known methods for generating bispecific antibodies see, e.g., Suresh et al. (1986) *Methods in Enzymology* 121:210; PCT Publication No. WO 96/27011; Brennan et al. (1985) *Science* 229:81; Shalaby et al., *J Exp Med* (1992) 175:217-225; Kostelny et al. (1992) *J Immunol* 148(5):1547-1553; Hollinger et al. (1993) *Proc Natl Acad Sci USA* 90:6444-6448; Gruber et al. (1994) *J Immunol* 152:5368; and Tutt et al. (1991) *J Immunol* 147:60. Bispecific antibodies also include cross-linked or heteroconjugate antibodies. Heteroconjugate antibodies may be made using any convenient cross-linking methods. Suitable cross-linking agents are well known in the art, and are disclosed in U.S. Pat. No. 4,676,980, along with a number of cross-linking techniques.

**[0108]** Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. See, e.g., Kostelny et al. (1992) *J Immunol* 148(5):1547-1553. The leucine zipper peptides from the Fos and Jun proteins may be linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers may be reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al. (1993) *Proc Natl Acad Sci USA* 90:6444-6448 has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (VH) connected to a light-chain variable domain (VL) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the VH and VL domains of one fragment are forced to pair with the complementary VL and VH domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (scFv) dimers has also been reported. See, e.g., Gruber et al. (1994) *J Immunol* 152:5368. Alternatively, the antibodies can be "linear antibodies" as described in, e.g., Zapata et al. (1995) *Protein Eng.* 8(10):1057-1062. Briefly, these antibodies comprise a pair of tandem Fd segments (VH-CH1-VH-CH1) which form a pair of antigen binding regions. Linear antibodies can be bispecific or monospecific. Antibodies with more than two valencies (e.g., trispecific antibodies) are contemplated and described in, e.g., Tutt et al. (1991) *J Immunol* 147:60.

**[0109]** As used herein, the term "chemokine" refers to a member of the family of small cytokines, or signaling proteins, that induce directed chemotaxis. Chemokines are

grouped into four subfamilies: CXC, CC, (X)C, and CX3C. In some embodiments, the chemokine or chemokines of interest are CXC chemokines. In the CXC chemokines, one amino acid separates the first two cysteines (“the CXC motif”).

**[0110]** As used herein, the term “cross-reacts” refers to the ability of an antibody or fusion protein of the disclosure to bind to chemokines from a different species. For example, an antibody or fusion protein of the present disclosure which binds human ELR+ CXC chemokines may also bind another species of ELR+ CXC chemokines. As used herein, cross-reactivity is measured by detecting a specific reactivity with purified antigen in binding assays (e.g., SPR, ELISA). Methods for determining cross-reactivity include standard binding assays as described herein, for example, by Biacore™ surface plasmon resonance (SPR) analysis using a Biacore™ 2000 SPR instrument (Biacore AB, Uppsala, Sweden), or flow cytometric techniques. In some embodiments, a fusion protein described herein comprises a multispecific variable region that binds human and murine ELR+ CXC chemokines.

**[0111]** As used herein, the term “ELR+ CXC chemokine” refers to a chemokine possessing an E-L-R amino acid motif immediately adjacent to a CXC motif. ELR+ CXC chemokines are ligands for CXCR1 and/or CXCR2 chemokine receptors, which are G-protein coupled seven transmembrane domain-type receptors that specifically binds ELR+ CXC chemokines. All ELR+ CXC chemokines bind the CXCR2 receptor, whereas some bind both CXCR1 and CXCR2 receptors. The ELR+ CXC chemokines are human Gro-alpha (also known as CXCL1), human Gro-beta (also known as CXCL2), human Gro-gamma (also known as CXCL3), human ENA-78 (also known as CXCL5), human GCP-2 (also known as CXCL6), human NAP-2 (also known as CXCL7), human IL-8 (also known as CXCL58). The five murine ELR+ CXC chemokines are keratinocyte chemoattractant (KC), Macrophage Inflammatory Protein-2 (MIP-2), dendritic cell inflammatory protein-1 (DCIP-1), neutrophil activating peptide-2 (NAP-2) and lipopolysaccharide-induced CXC chemokine (LIX). The table below provides the list of ELR+ CXC chemokines, their alternative names, including the murine equivalent, and what receptors they bind to.

Chemokine	Alternative Names	Receptor(s) Binding
CXCL1	GRO $\alpha$ , MGSA, murine KC	CXCR2
CXCL2	GRO $\beta$ , MIP-2a, murine MIP-2	CXCR2
CXCL3	GRO $\gamma$ , MIP-2b, murine DCIP-1	CXCR2
CXCL5	ENA-78, murine LIX	CXCR2
CXCL6	GCP-2 (no murine equivalent)	CXCR1, CXCR2
CXCL7	NAP-2	CXCR2
CXCL8	IL-8 (no murine equivalent)	CXCR1, CXCR2

**[0112]** As used herein, the term “epitope” or “antigenic determinant” refers to a site on an antigen (e.g., ELR+ CXC chemokine) to which an immunoglobulin or antibody specifically binds. Epitopes can be formed both from contiguous amino acids or noncontiguous amino acids juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained on exposure to denaturing solvents, whereas epitopes formed by tertiary folding are typically lost on treatment with denaturing solvents. An epitope typically includes at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 amino acids in a unique spatial

conformation. Methods for determining what epitopes are bound by a given antibody (i.e., epitope mapping) are well known in the art and include, for example, immunoblotting and immunoprecipitation assays, wherein overlapping or contiguous peptides from a chemokine are tested for reactivity with the given antibody. Methods of determining spatial conformation of epitopes include techniques in the art and those described herein, for example, x-ray crystallography and 2-dimensional nuclear magnetic resonance (see, e.g., *Epitope Mapping Protocols in Methods in Molecular Biology*, Vol. 66, G. E. Morris, Ed. (1996)).

**[0113]** Also, encompassed by the present disclosure are antibodies that bind to epitopes on chemokines (e.g., ELR+ CXC chemokines) which comprises all or a portion of an epitope recognized by the particular antibodies described herein (e.g., the same or an overlapping region or a region between or spanning the region).

**[0114]** Also encompassed by the present disclosure are antibodies that bind the same epitope and/or antibodies that compete for binding to chemokines (e.g., ELR+ CXC chemokines) with the antibodies described herein. Antibodies that recognize the same epitope or compete for binding can be identified using routine techniques. Such techniques include, for example, an immunoassay, which shows the ability of one antibody to block the binding of another antibody to a target antigen, i.e., a competitive binding assay. Competitive binding is determined in an assay in which the immunoglobulin under test inhibits specific binding of a reference antibody to a common antigen. Numerous types of competitive binding assays are known, for example: solid phase direct or indirect radioimmunoassay (RIA), solid phase direct or indirect enzyme immunoassay (EIA), sandwich competition assay (see Stahli et al., *Methods in Enzymology* 9:242 (1983)); solid phase direct biotin-avidin EIA (see Kirkland et al., *J. Immunol.* 137:3614 (1986)); solid phase direct labeled assay, solid phase direct labeled sandwich assay (see Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Press (1988)); solid phase direct label RIA using I-125 label (see Morel et al., *Mol. Immunol.* 25(1):7 (1988)); solid phase direct biotin-avidin EIA (Cheung et al., *Virology* 176:546 (1990)); and direct labeled RIA. (Moldenhauer et al., *Scand. J. Immunol.* 32:77 (1990)). Typically, such an assay involves the use of purified antigen bound to a solid surface or cells bearing either of these, an unlabeled test immunoglobulin and a labeled reference immunoglobulin. Competitive inhibition is measured by determining the amount of label bound to the solid surface or cells in the presence of the test immunoglobulin. Usually the test immunoglobulin is present in excess. Usually, when a competing antibody is present in excess, it will inhibit specific binding of a reference antibody to a common antigen by at least 50-55%, 55-60%, 60-65%, 65-70% 70-75% or more.

**[0115]** Other techniques include, for example, epitope mapping methods, such as, x-ray analyses of crystals of antigen:antibody complexes which provides atomic resolution of the epitope. Other methods monitor the binding of the antibody to antigen fragments or mutated variations of the antigen where loss of binding due to a modification of an amino acid residue within the antigen sequence is often considered an indication of an epitope component. In addition, computational combinatorial methods for epitope mapping can also be used. These methods rely on the ability of the antibody of interest to affinity isolate specific short

peptides from combinatorial phage display peptide libraries. The peptides are then regarded as leads for the definition of the epitope corresponding to the antibody used to screen the peptide library. For epitope mapping, computational algorithms have also been developed which have been shown to map conformational discontinuous epitopes.

**[0116]** As used herein, the term “Fc region” refers to the portion of a native immunoglobulin formed by the respective Fc domains (or Fc moieties) of its two heavy chains. As used herein, the term “Fc domain” refers to a portion of a single immunoglobulin (Ig) heavy chain wherein the Fc domain does not comprise an Fv domain. As such, an Fc domain can also be referred to as “Ig” or “IgG.” In some embodiments, an Fc domain begins in the hinge region just upstream of the papain cleavage site and ends at the C-terminus of the antibody. Accordingly, a complete Fc domain comprises at least a hinge domain, a CH2 domain, and a CH3 domain. In some embodiments, an Fc domain comprises at least one of: a hinge (e.g., upper, middle, and/or lower hinge region) domain, a CH2 domain, a CH3 domain, a CH4 domain, or a variant, portion, or fragment thereof. In some embodiments, an Fc domain comprises a complete Fc domain (i.e., a hinge domain, a CH2 domain, and a CH3 domain). In some embodiments, an Fc domain comprises a hinge domain (or portion thereof) fused to a CH3 domain (or portion thereof). In some embodiments, an Fc domain comprises a CH2 domain (or portion thereof) fused to a CH3 domain (or portion thereof). In some embodiments, an Fc domain consists of a CH3 domain or portion thereof. In some embodiments, an Fc domain consists of a hinge domain (or portion thereof) and a CH3 domain (or portion thereof). In some embodiments, an Fc domain consists of a CH2 domain (or portion thereof) and a CH3 domain. In some embodiments, an Fc domain consists of a hinge domain (or portion thereof) and a CH2 domain (or portion thereof). In some embodiments, an Fc domain lacks at least a portion of a CH2 domain (e.g., all or part of a CH2 domain). An Fc domain herein generally refers to a polypeptide comprising all or part of the Fc domain of an immunoglobulin heavy-chain. This includes, but is not limited to, polypeptides comprising the entire CH1, hinge, CH2, and/or CH3 domains as well as fragments of such peptides comprising only, e.g., the hinge, CH2, and CH3 domain. In some embodiments, the Fc domain is derived from an immunoglobulin of any species and/or any subtype, including, but not limited to, a human IgG1, IgG2, IgG3, IgG4, IgD, IgA, IgE, or IgM antibody. A human IgG1 constant region can be found at Uniprot P01857 and in Table 12 (i.e., SEQ ID NO: 172). The Fc domain of human IgG1 can be found in Table 12 (i.e., SEQ ID NO: 173). The Fc domain encompasses native Fc and Fc variant molecules. As with Fc variants and native Fc’s, the term Fc domain includes molecules in monomeric or multimeric form, whether digested from whole antibody or produced by other means. The assignment of amino acid residue numbers to an Fc domain is in accordance with the definitions of Kabat. See, e.g., Sequences of Proteins of Immunological Interest (Table of Contents, Introduction and Constant Region Sequences sections), 5th edition, Bethesda, Md.:NIH vol. 1:647-723 (1991); Kabat et al., “Introduction” Sequences of Proteins of Immunological Interest, US Dept of Health and Human Services, NIH, 5th edition, Bethesda, Md. vol. 1:xiii-xcvi (1991); Chothia & Lesk, J. Mol. Biol. 196:901-917 (1987);

Chothia et al., Nature 342:878-883 (1989), each of which is herein incorporated by reference for all purposes.

**[0117]** As set forth herein, it will be understood by one of ordinary skill in the art that any Fc domain may be modified such that it varies in amino acid sequence from the native Fc domain of a naturally occurring immunoglobulin molecule. In some embodiments, the Fc domain has reduced effector function (e.g., FcγR binding).

**[0118]** In some embodiments, the Fc domains are derived from different immunoglobulin molecules. For example, an Fc domain may comprise a CH2 and/or CH3 domain derived from an IgG1 molecule and a hinge region derived from an IgG3 molecule. In another example, an Fc domain can comprise a chimeric hinge region derived, in part, from an IgG1 molecule and, in part, from an IgG3 molecule. In another example, an Fc domain can comprise a chimeric hinge derived, in part, from an IgG1 molecule and, in part, from an IgG4 molecule.

**[0119]** As used herein, the term “fusion protein” refers to a recombinant protein prepared by fusion of a multispecific variable region described herein, and a polymer (e.g., serum albumin).

**[0120]** As used herein, the term “gly-ser polypeptide linker” refers to a peptide that consists of glycine and serine residues. An exemplary gly-ser polypeptide linker comprises the amino acid sequence Ser(Gly<sub>4</sub>Ser)<sub>n</sub>. In some embodiments, n=1. In some embodiments, n=2. In some embodiments, n=3, i.e., Ser(Gly<sub>4</sub>Ser)<sub>3</sub>. In some embodiments, n=4, i.e., Ser(Gly<sub>4</sub>Ser)<sub>4</sub>. In some embodiments, n=5. In some embodiments, n=6. In some embodiments, n=7. In some embodiments, n=8. In some embodiments, n=9. In some embodiments, n=10. Another exemplary gly-ser polypeptide linker comprises the amino acid sequence (Gly<sub>4</sub>Ser)<sub>n</sub>. In some embodiments, n=1. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises the amino acid sequence (Gly<sub>3</sub>Ser)<sub>n</sub>. In some embodiments, n=1. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In some embodiments, n=5. In some embodiments, n=6.

**[0121]** As used herein, “half-life” refers to the time taken for the serum or plasma concentration of a polypeptide to reduce by 50%, in vivo, for example due to degradation and/or clearance or sequestration by natural mechanisms. The fusion protein disclosed herein is stabilized in vivo and its half-life increased by, e.g., fusion to an Fc region, fusion to serum albumin (e.g., HSA or MSA), through PEGylation, or by binding to serum albumin molecules (e.g., human serum albumin) which resist degradation and/or clearance or sequestration. The half-life can be determined in any manner known per se, such as by pharmacokinetic analysis. Suitable techniques will be clear to the person skilled in the art, and may for example generally involve the steps of suitably administering a suitable dose of the amino acid sequence or compound to a subject; collecting blood samples or other samples from said subject at regular intervals; determining the level or concentration of the amino acid sequence or compound in said blood sample; and calculating, from (a plot of) the data thus obtained, the time until the level or concentration of the amino acid sequence or compound has been reduced by 50% compared to the initial level upon dosing. Further details are provided in, e.g., standard handbooks, such as Kenneth, A. et al., Chemical Stability of

Pharmaceuticals: A Handbook for Pharmacists and in Peters et al., *Pharmacokinetic Analysis: A Practical Approach* (1996). Reference is also made to Gibaldi, M. et al., *Pharmacokinetics*, 2nd Rev. Edition, Marcel Dekker (1982).

**[0122]** As used herein, the term “human antibody” includes antibodies having variable and constant regions (if present) of human germline immunoglobulin sequences. Human antibodies of the disclosure can include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations introduced by random or site-specific mutagenesis in vitro or by somatic mutation in vivo) (see, Lonberg, N. et al. (1994) *Nature* 368(6474): 856-859); Lonberg, N. (1994) *Handbook of Experimental Pharmacology* 113:49-101; Lonberg, N. and Huszar, D. (1995) *Intern. Rev. Immunol. Vol. 13*: 65-93, and Harding, F. and Lonberg, N. (1995) *Ann. N.Y. Acad. Sci* 764:536-546). However, the term “human antibody” does not include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences (i.e., humanized antibodies).

**[0123]** As used herein, the term a “heterologous antibody” is defined in relation to the transgenic non-human organism producing such an antibody. This term refers to an antibody having an amino acid sequence or an encoding nucleic acid sequence corresponding to that found in an organism not consisting of the transgenic non-human animal, and generally from a species other than that of the transgenic non-human animal.

**[0124]** As used herein, “immune cell” is a cell of hematopoietic origin and that plays a role in the immune response. Immune cells include lymphocytes (e.g., B cells and T cells), natural killer cells, and myeloid cells (e.g., monocytes, macrophages, eosinophils, mast cells, basophils, and granulocytes).

**[0125]** As used herein, a subject “in need of prevention,” “in need of treatment,” or “in need thereof,” refers to one, who by the judgment of an appropriate medical practitioner (e.g., a doctor, a nurse, or a nurse practitioner in the case of humans; a veterinarian in the case of non-human mammals), would reasonably benefit from a given treatment (such as treatment with a composition comprising a fusion protein described herein).

**[0126]** The term “in vivo” refers to processes that occur in a living organism.

**[0127]** As used herein, the term “isolated antibody” is intended to refer to an antibody which is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that binds to chemokines (e.g., ELR+ CXC chemokines) is substantially free of antibodies that specifically bind antigens other than chemokines (e.g., ELR+ CXC chemokines)). An isolated antibody that specifically binds to an epitope may, however, have cross-reactivity to other chemokines (e.g., ELR+ CXC chemokines) from different species. In addition, an isolated antibody is typically substantially free of other cellular material and/or chemicals.

**[0128]** As used herein, the term “isolated nucleic acid molecule” refers to nucleic acids encoding fusion proteins, antibodies or antibody portions (e.g.,  $V_H$ ,  $V_L$ , CDR3) that bind to chemokines (e.g., ELR+ CXC chemokines), is intended to refer to a nucleic acid molecule in which the nucleotide sequences encoding the fusion protein, antibody or antibody portion are free of other nucleotide sequences encoding fusion proteins, antibodies or antibody portions

that bind antigens other than chemokines (e.g., ELR+ CXC chemokines), which other sequences may naturally flank the nucleic acid in human genomic DNA. For example, Table 12 shows nucleotide sequences comprising the heavy chain ( $V_H$ ) and light chain ( $V_L$ ) variable regions of multispecific monoclonal antibodies described herein.

**[0129]** As used herein, “isotype” refers to the antibody class (e.g., IgM or IgG1) that is encoded by heavy chain constant region genes. In some embodiments, an antibody of the disclosure is of the IgG1 isotype. In some embodiments, an antibody of the disclosure is of the IgG2 isotype. In some embodiments, an antibody of the disclosure is of the IgG3 isotype. In some embodiments, an antibody of the disclosure is of the IgG4 isotype.

**[0130]** As used herein, the term “isotype switching” refers to the phenomenon by which the class, or isotype, of an antibody changes from one Ig class to one of the other Ig classes.

**[0131]** As used herein, the term “kd” is intended to refer to the off rate constant for the dissociation of an antibody from the antibody/antigen complex.

**[0132]** As used herein, the term “ka” is intended to refer to the on rate constant for the association of an antibody with the antigen.

**[0133]** As used herein, the terms “linked,” “fused”, or “fusion”, are used interchangeably. These terms refer to the joining together of two more elements or components or domains, by whatever means including chemical conjugation or recombinant means. Methods of chemical conjugation (e.g., using heterobifunctional crosslinking agents) are known in the art.

**[0134]** As used herein, “local administration” or “local delivery,” refers to delivery that does not rely upon transport of the composition or agent to its intended target tissue or site via the vascular system. For example, the composition may be delivered by injection or implantation of the composition or agent or by injection or implantation of a device containing the composition or agent. Following local administration in the vicinity of a target tissue or site, the composition or agent, or one or more components thereof, may diffuse to the intended target tissue or site.

**[0135]** The term “mammal” or “subject” or “patient” as used herein includes both humans and non-humans and includes, but is not limited to, humans, non-human primates, canines, felines, murines, bovines, equines, and porcines.

**[0136]** The term “multispecific” as used herein refers to a polypeptide (e.g., fusion protein and/or variable region) capable of binding more than one target of interest (e.g., ELR+ CXC chemokine). In some embodiments, the terms “multispecific” and “crossreactive” are interchangeable. In some embodiments, the polypeptide binds at least two targets of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least four targets of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least five targets of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least six targets of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least seven targets of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least eight targets of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least nine targets of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least ten targets

of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least eleven targets of interest (e.g., ELR+ CXC chemokines). In some embodiments, the polypeptide binds at least twelve targets of interest (e.g., ELR+ CXC chemokines).

**[0137]** “Nucleic acid” refers to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. Unless specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions) and complementary sequences and as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions can be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al., *Nucleic Acid Res.* 19:5081, 1991; Ohtsuka et al., *Biol. Chem.* 260:2605-2608, 1985; and Cassol et al, 1992; Rossolini et al, *Mol. Cell. Probes* 8:91-98, 1994). For arginine and leucine, modifications at the second base can also be conservative. The term nucleic acid is used interchangeably with gene, cDNA, and mRNA encoded by a gene.

**[0138]** Polynucleotides used herein can be composed of any polyribonucleotide or polydeoxyribonucleotide, which can be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that can be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide can also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. “Modified” bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, “polynucleotide” embraces chemically, enzymatically, or metabolically modified forms.

**[0139]** As used herein, the term “operably linked” or “operably coupled” refers to a juxtaposition wherein the components described are in a relationship permitting them to function in their intended manner.

**[0140]** As used herein, “parenteral administration,” “administered parenterally,” and other grammatically equivalent phrases, refer to modes of administration other than enteral and topical administration, usually by injection, and include, without limitation, intravenous, intranasal, intraocular, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural, intracerebral, intracranial, intracarotid and intrasternal injection and infusion.

**[0141]** As used herein, the term “patient” includes human and other mammalian subjects that receive either prophylactic or therapeutic treatment.

**[0142]** The term “percent identity,” in the context of two or more nucleic acid or polypeptide sequences, refer to two or more sequences or subsequences that have a specified percentage of nucleotides or amino acid residues that are the same, when compared and aligned for maximum correspondence, as measured using one of the sequence comparison algorithms described below (e.g., BLASTP and BLASTN or other algorithms available to persons of skill) or by visual inspection. Depending on the application, the “percent identity” can exist over a region of the sequence being compared, e.g., over a functional domain, or, alternatively, exist over the full length of the two sequences to be compared. For sequence comparison, typically one sequence acts as a reference sequence to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are input into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. The sequence comparison algorithm then calculates the percent sequence identity for the test sequence(s) relative to the reference sequence, based on the designated program parameters.

**[0143]** The percent identity between two sequences is a function of the number of identical positions shared by the sequences (i.e., % homology=# of identical positions/total # of positions×100), taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm, as described in the non-limiting examples below.

**[0144]** Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Nat'l. Acad. Sci. USA* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by visual inspection (see generally Ausubel et al., *infra*).

**[0145]** One example of an algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul et al., *J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information website.

**[0146]** As generally used herein, “pharmaceutically acceptable” refers to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues, organs, and/or bodily fluids of human beings and animals without excessive toxicity, irritation, allergic response, or other problems or complications commensurate with a reasonable benefit/risk ratio.

**[0147]** As used herein, a “pharmaceutically acceptable carrier” refers to, and includes, any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible. The compositions can include a pharmaceutically acceptable salt, e.g., an acid addition salt or a base addition salt (see, e.g., Berge et al. (1977) *J Pharm Sci* 66:1-19).

**[0148]** As used herein, the term “PK” is an acronym for “pharmacokinetic” and encompasses properties of a compound including, by way of example, absorption, distribution, metabolism, and elimination by a subject. As used herein, an “extended-PK group” refers to a polymer, protein, peptide, or moiety that increases the circulation half-life of a biologically active molecule when fused to or administered together with the multispecific variable region. Examples of an extended-PK group include PEG, human serum albumin (HSA) binders (as disclosed in U.S. Publication Nos. 2005/0287153 and 2007/0003549, PCT Publication Nos. WO 2009/083804 and WO 2009/133208, and SABA molecules as described in US2012/094909), serum albumin (e.g., HSA), Fc or Fc fragments and variants thereof, transferrin and variants thereof, and sugars (e.g., sialic acid). Other exemplary extended-PK groups are disclosed in Kontermann et al., *Current Opinion in Biotechnology* 2011; 22:868-876, which is herein incorporated by reference in its entirety.

**[0149]** “Polypeptide,” “peptide,” and “protein” are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers and non-naturally occurring amino acid polymer.

**[0150]** As used herein, the term “preventing” when used in relation to a condition, refers to administration of a composition which reduces the frequency of, or delays the onset of, symptoms of a medical condition in a subject relative to a subject which does not receive the composition.

**[0151]** As used herein, the term “purified” or “isolated” as applied to any of the proteins (fusion proteins, antibodies or fragments) described herein refers to a polypeptide that has been separated or purified from components (e.g., proteins or other naturally-occurring biological or organic molecules) which naturally accompany it, e.g., other proteins, lipids, and nucleic acid in a prokaryote expressing the proteins. Typically, a polypeptide is purified when it constitutes at least 60 (e.g., at least 65, 70, 75, 80, 85, 90, 92, 95, 97, or 99) %, by weight, of the total protein in a sample.

**[0152]** As used herein, the term “recombinant host cell” (or simply “host cell”) is intended to refer to a cell into which a recombinant expression vector has been introduced. It should be understood that such terms are intended to refer not only to the particular subject cell but to the progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term “host cell” as used herein.

**[0153]** As used herein, the term “recombinant human antibody” includes all human antibodies that are prepared, expressed, created or isolated by recombinant means, such as (a) antibodies isolated from an animal (e.g., a mouse) that is transgenic or transchromosomal for human immunoglobulin genes or a hybridoma prepared therefrom, (b) antibodies isolated from a host cell transformed to express the antibody, e.g., from a transfectoma, (c) antibodies isolated from a recombinant, combinatorial human antibody library, and (d) antibodies prepared, expressed, created or isolated by any other means that involve splicing of human immunoglobulin gene sequences to other DNA sequences. Such recombinant human antibodies comprise variable and

constant regions that utilize particular human germline immunoglobulin sequences are encoded by the germline genes, but include subsequent rearrangements and mutations which occur, for example, during antibody maturation. As known in the art (see, e.g., Lonberg (2005) *Nature Biotech.* 23(9):1117-1125), the variable region contains the antigen binding domain, which is encoded by various genes that rearrange to form an antibody specific for a foreign antigen. In addition to rearrangement, the variable region can be further modified by multiple single amino acid changes (referred to as somatic mutation or hypermutation) to increase the affinity of the antibody to the foreign antigen. The constant region will change in further response to an antigen (i.e., isotype switch). Therefore, the rearranged and somatically mutated nucleic acid molecules that encode the light chain and heavy chain immunoglobulin polypeptides in response to an antigen may not have sequence identity with the original nucleic acid molecules, but instead will be substantially identical or similar (i.e., have at least 80% identity).

**[0154]** As used herein, the terms “specific binding,” “selective binding,” “selectively binds,” and “specifically binds,” refer to fusion protein or antibody binding to an epitope on a predetermined antigen. Typically, the fusion protein or antibody binds with an equilibrium dissociation constant ( $K_d$ ) of approximately less than  $10^{-6}$  M, such as approximately less than  $10^{-7}$  M,  $10^{-8}$  M,  $10^{-9}$  M or  $10^{-10}$  M or even lower when determined by surface plasmon resonance (SPR) technology in a BIACORE 2000 instrument using an ELR+ CXC chemokine of interest as the analyte and the fusion protein or antibody as the ligand and binds to the predetermined antigen with an affinity that is at least two-fold greater than its affinity for binding to a non-specific antigen (e.g., BSA, casein) other than the predetermined antigen or a closely-related antigen. The phrases “recognizing an antigen” and “specific for an antigen” are used interchangeably herein with the term “binds specifically to an antigen.”

**[0155]** As used herein, the term “subject” includes any human or non-human animal. For example, the methods and compositions of the present disclosure can be used to treat a subject with an immune disorder. The term “non-human animal” includes all vertebrates, e.g., mammals and non-mammals, such as non-human primates, sheep, dog, cow, chickens, amphibians, reptiles, etc.

**[0156]** The term “sufficient amount” or “amount sufficient to” means an amount sufficient to produce a desired effect, e.g., an amount sufficient to reduce the size of a tumor.

**[0157]** The term “substantial homology” indicates that two nucleotide sequences or two amino acid sequences, when optimally aligned and compared, are identical, with appropriate insertions or deletions, in at least about 80% of the nucleotides or amino acids, usually at least about 90% to 95%, and more preferably at least about 98% to 99.5% of the nucleotides or amino acids. Alternatively, substantial homology exists when the segments will hybridize under selective hybridization conditions, to the complement of the strand.

**[0158]** The nucleic acids may be present in whole cells, in a cell lysate, or in a partially purified or substantially pure form. A nucleic acid is “isolated” or “rendered substantially pure” when purified away from other cellular components or other contaminants, e.g., other cellular nucleic acids or proteins, by standard techniques, including alkaline/SDS treatment, CsCl banding, column chromatography, agarose

gel electrophoresis and others well known in the art. See, F. Ausubel, et al., ed. *Current Protocols in Molecular Biology*, Greene Publishing and Wiley Interscience, New York (1987).

**[0159]** The nucleic acid compositions of the present disclosure, while often in a native sequence (except for modified restriction sites and the like), from either cDNA, genomic or mixtures thereof may be mutated, in accordance with standard techniques to provide gene sequences. For coding sequences, these mutations, may affect amino acid sequence as desired. In particular, DNA sequences substantially homologous to or derived from native V, D, J, constant, switches and other such sequences described herein are contemplated (where “derived” indicates that a sequence is identical or modified from another sequence).

**[0160]** The term “T cell” refers to a type of white blood cell that can be distinguished from other white blood cells by the presence of a T cell receptor on the cell surface. There are several subsets of T cells, including, but not limited to, T helper cells (a.k.a.  $T_H$  cells or  $CD4^+$  T cells) and subtypes, including  $T_{H1}$ ,  $T_{H2}$ ,  $T_{H3}$ ,  $T_{H17}$ ,  $T_{H9}$ , and  $T_{FH}$  cells, cytotoxic T cells (a.k.a.  $T_C$  cells,  $CD8^+$  T cells, cytotoxic T lymphocytes, T-killer cells, killer T cells), memory T cells and subtypes, including central memory T cells ( $T_{CM}$  cells), effector memory T cells ( $T_{EM}$  and  $T_{EMRA}$  cells), and resident memory T cells ( $T_{RM}$  cells), regulatory T cells (a.k.a.  $T_{reg}$  cells or suppressor T cells) and subtypes, including  $CD4^+$   $FOXP3^+$   $T_{reg}$  cells,  $CD4^+$   $FOXP3^-$   $T_{reg}$  cells, Tr1 cells, Th3 cells, and  $T_{reg17}$  cells, natural killer T cells (a.k.a. NKT cells), mucosal associated invariant T cells (MAITs), and gamma delta T cells ( $\gamma\delta$  T cells), including  $V\gamma9/V\delta2$  T cells. Any one or more of the aforementioned or unmentioned T cells may be the target cell type for a method as disclosed herein.

**[0161]** The term “therapeutically effective amount” is an amount that is effective to ameliorate a symptom of a disease. A therapeutically effective amount can be a “prophylactically effective amount” as prophylaxis can be considered therapy.

**[0162]** The terms “treat,” “treating,” and “treatment,” as used herein, refer to therapeutic or preventative measures described herein. The methods of “treatment” employ administration to a subject, in need of such treatment, a fusion protein or antibody, or antigen binding fragment thereof, of the present disclosure, for example, a subject in need of a reduced immune response or a subject who ultimately may acquire such a disorder, in order to prevent, cure, delay, reduce the severity of, or ameliorate one or more symptoms of the disorder or recurring disorder, or in order to prolong the survival of a subject beyond that expected in the absence of such treatment.

**[0163]** As used herein, the term “vector” is intended to refer to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a “plasmid,” which refers to a circular double stranded DNA loop into which additional DNA segments may be ligated. Another type of vector is a viral vector, wherein additional DNA segments may be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) can be integrated into the genome of a host cell upon introduction into the host cell,

and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as “recombinant expression vectors” (or simply, “expression vectors”) In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, “plasmid” and “vector” may be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

**[0164]** It must be noted that, as used in the specification and the appended claims, the singular forms “a,” “an” and “the” include plural referents unless the context clearly dictates otherwise.

#### Multispecific Variable Regions and Antibodies

**[0165]** The present disclosure provides multispecific variable regions capable of binding more than one ELR+ CXC chemokine (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve). In some embodiments, the multispecific variable region is a single chain variable fragment (scFv). In some embodiments, the present disclosure also provides isolated monoclonal antibodies, or antigen binding fragments thereof, capable of binding more than one ELR+ CXC chemokine (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve).

**[0166]** The ELR+ CXC chemokine system consists of numerous small and structurally similar chemoattractant ligands capable of binding to and activating the related CXCR1 and CXCR2 G protein-coupled receptors (GPCRs) expressed abundantly on the surface of neutrophils (Griffith, J. W. et al. *Annu Rev Immunol* 32, 659-702(2014)). These ligands act either by autocrine or paracrine mechanisms to induce signaling networks that direct neutrophils to sites of inflammation. Studies in animals have demonstrated that genetic deletion of the most promiscuous ELR+ CXC chemokine receptor, CXCR2, can block the development of joint inflammation in anti-type II collagen antibody-induced arthritis (CAIA) (Min, S. H. et al *Biochem Biophys Res Commun* 391, 1080-1086 (2010)), adjuvant-induced arthritis (AIA) (Barsante, M. M. et al *Br J Pharmacol* 153, 992-2001 (2008); Coelho, F. M. et al *Arthritis Rheum* 58, 2329-2337 (2008); Grespan, R. et al *Arthritis Rheum* 58, 2030-2040 (2008)), and K/BxN serum transfer induced arthritis (Jacobs, J. P. et al *Arthritis Rheum* 62, 1921-1932 (2010); Chou, R. C. et al *Immunity* 33, 266-278 (2010)).

**[0167]** Inhibition of ELR+ CXC chemokine-driven signaling has been previously attempted by employing various antagonists against CXCR1 and CXCR2 receptors, including neutralizing antibodies, small molecules and peptide-derived inhibitors. However, these antagonists have shown limited therapeutic effects (Schall, T. J. & Proudfoot, A. E. *Nat Rev Immunol* 11, 355-363 (2011); Szekanecz, Z. & Koch, A. E. *Nat Rev Rheumatol* 12, 5-13 (2016)). Failures of such receptor-based therapies have been attributed to (i) difference between the orthologous rodent (pre-clinical) and human (clinical systems); and (ii) the extremely high doses

of antagonist required to guarantee continuous receptor occupancy, such that all receptors in the body are antagonized (Id.).

**[0168]** Accordingly, the present disclosure provides multispecific variable regions, and isolated monoclonal antibodies, or antigen binding fragments thereof, that bind to the ELR+ CXC chemokine ligands themselves. In some embodiments, the multispecific variable regions, and isolated monoclonal antibodies, or antigen binding fragments thereof, described herein, bind to and inhibit or reduce the activity of the ELR+ CXC chemokine ligands.

**[0169]** In some embodiments, the multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21. In some embodiments, the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 1. In some embodiments, the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11. In some embodiments, the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 21.

**[0170]** In some embodiments, the multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22. In some embodiments, the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 2. In some embodiments, the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 12. In some embodiments, the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 22.

**[0171]** In some embodiments, the multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21, and wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

**[0172]** In some embodiments, the multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, comprises a heavy chain variable region and a light chain variable region comprising the amino acid sequences set forth in:

**[0173]** (a) SEQ ID NOs: 1 and 2, respectively;

**[0174]** (b) SEQ ID NOs: 11 and 12, respectively; or

**[0175]** (c) SEQ ID NOs: 21 and 22, respectively.

**[0176]** In some embodiments, the multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, comprises a heavy chain variable region and light chain variable region comprising amino acid sequences having 90% identity to the amino acid sequences set forth in:

**[0177]** (a) SEQ ID NOs: 1 and 2, respectively;

**[0178]** (b) SEQ ID NOs: 11 and 12, respectively; or

**[0179]** (c) SEQ ID NOs: 21 and 22, respectively.

**[0180]** In some embodiments, the multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, comprises heavy and light chain CDRs selected from the group consisting of:

**[0181]** (a) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively;

**[0182]** (b) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 15, 16 and 17, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 18, 19 and 20, respectively; and

**[0183]** (c) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively.

**[0184]** In some embodiments, the multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, comprises heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively.

**[0185]** In some embodiments, the multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, comprises heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively.

**[0186]** In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to human CXCL1, human CXCL2, human CXCL3, human CXCL5, human CXCL6, human CXCL7, human CXCL8, murine CXCL1, murine CXCL2, murine CXCL3, murine CXCL5, murine CXCL7, or any combination thereof.

**[0187]** In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to at least two ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to at least four ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody provided herein, binds to at least four ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to at least five ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to at least six ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody provided herein, binds to at least seven ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody provided herein, binds to at least eight ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody provided herein, binds to at least nine ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody provided herein, binds to at least ten ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody provided herein, binds to at least eleven ELR+ CXC chemokines. In some embodiments,



a multispecific variable region, or isolated monoclonal antibody provided herein, binds to at least twelve ELR+ CXC chemokines.

**[0188]** In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to human CXCL1, human CXCL2, human CXCL3, and murine CXCL1. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to human CXCL5, human CXCL8, murine CXCL1, murine CXCL2 and murine CXCL5. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to human CXCL1, human CXCL2, human CXCL3, human CXCL5, human CXCL6, human CXCL7, human CXCL8, murine CXCL1, murine CXCL2, murine CXCL3 and murine CXCL5.

**[0189]** In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to human ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to murine ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to human and murine ELR+ CXC chemokines. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, binds to human and murine ELR- CXC chemokines (e.g., murine CXCL4, human CXCL4, human CXCL10 and human CXCL11).

**[0190]** In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, inhibits or reduces binding of an ELR+ CXC chemokine of interest to its cognate receptor. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, inhibits or reduces binding of an ELR+ CXC chemokine of interest to CXCR2. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, inhibits or reduces binding of an ELR+ CXC chemokine of interest to CXCR1. In some embodiments, a multispecific variable region, or isolated monoclonal antibody, or antigen binding fragment thereof, provided herein, inhibits or reduces binding of an ELR+ CXC chemokine of interest to CXCR1 and CXCR2.

**[0191]** Fusion Protein

**[0192]** In some embodiments, the present disclosure provides fusion proteins comprising a multispecific variable region (e.g., scFv) described herein, operably coupled to a polymer. Examples of polymers suitable for use in the fusion proteins described herein, are provided in Strohl, W. R. *BioDrugs*, Vol. 29: 215-239 (2015), herein incorporated by reference in its entirety. The coupling of a polymer to multispecific variable region, either covalently or non-covalently, enhances the solubility and stability of the multispecific variable region.

**[0193]** Moreover, in some embodiments, the conjugating of a polymer to a multispecific variable region extends the pharmacokinetic profile (e.g., serum half-life) of the multispecific variable region. In some embodiments, the serum

half-life of a fusion protein described herein is increased relative to the multispecific variable region alone. In some embodiments, the serum half-life of a fusion protein described herein is at least 20, 40, 60, 80, 100, 120, 150, 180, 200, 400, 600, 800, or 1000% longer relative to the multispecific variable region alone. In certain embodiments, the serum half-life of a fusion protein described herein is at least 1.5-fold, 2-fold, 2.5-fold, 3-fold, 3.5 fold, 4-fold, 4.5-fold, 5-fold, 6-fold, 7-fold, 8-fold, 10-fold, 12-fold, 13-fold, 15-fold, 17-fold, 20-fold, 22-fold, 25-fold, 27-fold, 30-fold, 35-fold, 40-fold, or 50-fold greater than the serum half-life of the multispecific variable region alone. In certain embodiments, the serum half-life of a fusion protein described herein is at least 10 hours, 15 hours, 20 hours, 25 hours, 30 hours, 35 hours, 40 hours, 50 hours, 60 hours, 70 hours, 80 hours, 90 hours, 100 hours, 110 hours, 120 hours, 130 hours, 135 hours, 140 hours, 150 hours, 160 hours, or 200 hours.

**[0194]** In some embodiments, the polymer is an albumin moiety (e.g., serum albumin). In some embodiments, the polymer is an Fc domain. In some embodiments, the polymer is polyethylene glycol (PEG). In some embodiments, the polymer is transferrin. In some embodiments, the polymer is a serum immunoglobulin binding protein. In some embodiments, the polymer is an albumin binding moiety.

#### Serum Albumin

**[0195]** In some embodiments, the fusion protein comprises a multispecific variable region (e.g., scFv) described herein, operably coupled to an albumin moiety, or fragment thereof. Suitable albumins for use in the fusion proteins can be from human, primate, rodent, bovine, equine, donkey, rabbit, goat, sheep, dog, chicken or pig. In some embodiments, the albumin is a serum albumin, for example, a human serum albumin, primate serum albumin (e.g., chimpanzee serum albumin, gorilla serum albumin), rodent serum albumin (e.g., hamster serum albumin, guinea pig serum albumin, mouse serum albumin and rat serum albumin), bovine serum albumin, equine serum albumin, donkey serum albumin, rabbit serum albumin, goat serum albumin, sheep serum albumin, dog serum albumin, chicken serum albumin, and pig serum albumin.

**[0196]** Serum albumin exploits the FcRn receptor to achieve long half-life in circulation but its plasma persistence is still shorter than full length monoclonal antibodies, thus avoiding "buffering" effects associated with the use of full-length antibody-based strategies (Sand, K. M. et al *Front Immunol* 5, 682 (2014); Mihara, M. et al *Immunology* 74, 55-59 (1991); O'Hear, C. E. & Foote, J. *Proc Natl Acad Sci USA* 102, 40-44 (2005); Haringman, J. J. et al *Arthritis and Rheumatism* 54, 2387-2393 (2006)). Unlike an antibody, serum albumin does not bind the FcγR receptors expressed on the surface of immune system cells, thus eluding extra immune system activation and inflammation mediated by antibody-dependent cell-mediated cytotoxicity (ADCC).

**[0197]** In some embodiments, the fusion protein comprises a human serum albumin (HSA), or variants or fragments thereof, such as those disclosed in U.S. Pat. No. 5,876,969, WO 2011/124718, WO 2013/075066, and WO 2011/0514789. In some embodiments, the serum albumin moiety used in the fusion protein described herein, has sequence identity to the sequence of wild-type HSA as set forth in SEQ ID NO: 171. of at least 50%, such as at least 60%, at least 70%, at least 80%, at least 85%, at least 86%,

at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%.

**[0198]** In some embodiments, the fusion protein comprises a mouse serum albumin (MSA), or variants or fragments thereof. In some embodiments, the serum albumin moiety used in the fusion protein described herein, has sequence identity to the sequence of wild-type MSA as set forth in SEQ ID NO: 173, of at least 50%, such as at least 60%, at least 70%, at least 80%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%.

**[0199]** In some embodiments, the number of alternations, e.g., substitutions, insertions, or deletions in the albumin variants of the present disclosure is 1-20, e.g., 1-10, 1-5, such as 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 alterations compared to the corresponding wild-type albumin (e.g., HSA or MSA).

**[0200]** In addition to wild-type albumin, albumin variants are considered applicable as fusion partners with the multispecific variable regions (e.g., scFv) of the disclosure. Non-limiting examples of such variants include one or more alterations (e.g., substitutions, deletions, or insertions) in one or more positions corresponding to positions 417, 440, 464, 490, 492, 493, 494, 495, 496, 499, 500, 501, 503, 504, 505, 506, 510, 535, 536, 537, 538, 540, 541, 542, 550, 573, 574, 575, 577, 578, 579, 580, 581, 582 and 584 of HSA (SEQ ID NO: 171). In some embodiments, a variant comprises an alteration of at least one of these positions, such as 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or all of these positions. The substitution(s) may be any substitution(s) where the amino acid in the natural albumin sequence is substituted with a different amino acid selected among the remaining 19 natural occurring amino acids, provided that the substitution(s) increases the half-life of the polypeptide it is fused or conjugated to relative to the polypeptide not fused to the variant or a polypeptide fused to the wild-type albumin. Exemplary variants with altered serum half-life and/or binding to FcRn are those that include one or more of the following amino acid substitutions in HSA (SEQ ID NO: 171), as disclosed in U.S. Published Application No. 2012-0220530: Q417A, Q417H, H440Q, H464Q, A490D, E492G, E492T, E492P, E492H, V493P, V493L, D494N, D494Q, D494A, D494E, D494P, E495Q, E495A, T496A, P499A, K500E, K500G, K500A, K500S, K500C, K500P, K500H, K500F, K500N, K500W, K500T, K500M, K500Y, K500V, K500Q, K500L, K500I, K500R, E501A, E501P, E501Q, N503K, N503D, E503H, A504E, E505K, E505D, T506F, T506S, H510Q, H535Q, K536A, P537A, K538A, K538H, T540S, K541A, K541D, K541G, K541N, K541E, E542P, E542D, D550N, K573Y, K573W, K573P, K573H, K573F, K573V, K573I, K573T, K573N, K573S, K573G, K573M, K573C, K573A, K573E, K573Q, K573R, K573L, K573D, K574N, Q580K, L575F, A577T, A577E, A578R, A578S, S579C, S579T, Q580K, A581D, A582T, G584A (the contents of which are incorporated herein by reference). In particular embodiments, the variant has position 573 of HSA (SEQ ID NO: 171) substituted with proline (P), tryptophan (W), or tyrosine (Y). In some embodiments, the variant comprises multiple alterations, such as substitutions, at positions corresponding to 494 and 496; 492 and 493; 494 and 417; 492 and 503; 492 and 573 (e.g., E492G+K573P, E492G+K573A); and 492, 503, and

573 (e.g., E492G+N503H+K573P). It should be understood that variants containing any alteration (e.g., substitution, insertion, deletion) at any one of the above positions of HSA (SEQ ID NO: 171), or at any other position(s), are suitable for use in the fusion proteins described herein.

**[0201]** In some embodiments, the albumin variant has an increased serum half-life compared to a wild-type albumin. Albumin variants with increased serum half-life, as disclosed in WO2011/051489, include E492G, K500R, N503H, N503K, D550E, K573Y, K573W, K573P, K573H, K573F, K573V, K573I, K573T, K573N, K573S, K573G, K573M, K573C, K573A, K573E, K573Q, K573R, K573L, K573D, K574N, Q580K, E492G+N503K, E492G+N503H, E492G+K573A, E492G+K573P, E492G+N503K+K573P, E492G+N503H+K573P, E492G+N503K+K573A, K573P+L575F+G584A, K573P+A578S+S579T+G584A, K573P+A577E+A578S+Q580K+A582T, K573P+K574N+A577T+A578R+S579C+Q580K+A581D+G584A, and E492H+E501P+N503H+E505D+T506S+T540S+K541E. It will be evident to the skilled artisan that variants with other amino acid substitutions or combinations of amino acid substitutions can be readily tested with routine methods to determine whether they exhibit increased serum half-life.

**[0202]** Some natural variants of albumin also exhibit increased serum half-life, and are suitable for use in the fusion proteins described herein. Such natural HSA variants with increased serum half-life are known in the art, such as E501K, E570K (Iwao et al. 2007, *B. B. A. Proteins and Proteomics* 1774, 1582-90), E505K (Gallino et al., supra), K536E, K574N (Minchiotti et al., *Biochim Biophys Acta* 1987:916:411-418), D550G (Takahashi et al., *PNAS* 1987: 84:4413-7), and D550A (Carlson et al., *PNAS* 1992:89: 8225-9).

**[0203]** In some embodiments, the variant albumin has an amino acid substitution that increases the affinity of the albumin to FcRn, which correlates with increased serum half-life. Such amino acid substitutions include, but are not limited to, HSA with K573P (i.e., lysine at position 573 substituted with a proline). Routine methods, such as surface plasmon resonance (SPR), as disclosed in WO2011/051489, can be used to determine whether a particular albumin variant exhibits increased affinity to FcRn relative to the corresponding wild-type albumin. It will be evident to the skilled artisan that increased affinity to FcRn can be determined by comparing the binding constants  $K_D$  of the albumin variant and wild-type albumin. In the context of the present disclosure, variant albumins having a  $K_D$  that is lower than the  $K_D$  for natural HSA is considered to have a higher plasma half-life than HSA.

**[0204]** In some embodiments, it may be desirable for the variant albumin, or fragment thereof, to decrease the serum half-life of a fusion protein. Such variant albumins, or fragments thereof, may decrease the binding of the fusion proteins to FcRn relative to non-albumin fused multispecific variable regions in which albumin is the corresponding wild-type albumin. Fusion proteins with decreased serum half-lives, e.g., those with decreased FcRn binding affinity, are useful, for example, for administration to a mammal where a shortened circulation time may be advantageous, e.g., for in vivo diagnostic imaging or in situations where the starting polypeptide has toxic side effects when present in the circulation for prolonged periods. Albumin variants with decreased FcRn binding affinity are also less likely to cross the placenta and, thus, are also useful in the treatment of

diseases or disorders in pregnant women. In addition, other applications in which reduced FcRn binding affinity may be desired include those applications in which localization in the brain, kidney, and/or liver is desired. In some embodiments, the fusion proteins described herein exhibit reduced transport across the epithelium of kidney glomeruli from the vasculature. In some embodiments, the fusion proteins described herein exhibit reduced transport across the blood brain barrier (BBB) from the brain, into the vascular space. In some embodiments, a fusion protein with altered FcRn binding comprises at least one albumin domain (e.g., domain III of HSA) having one or more amino acid substitutions within the "FcRn binding region" of an albumin domain. Exemplary albumin variants that exhibit decreased serum half-life are disclosed in, e.g., WO2011/124718, and include Q417A, H464Q, D494N, D494Q, D494A, E495Q, E495A, T496A, P499A, K500E, K500G, K500D, K500A, K500S, K500C, K500P, K500H, K500F, K500N, K500W, K500T, K500M, K500Y, K500V, K500Q, K500L, K500I, K500R, D500N, E501A, E501Q, N503K, N503D, H510Q, H535Q, K536A, P537A, K541G, K541D, K541A, K541N, E492T+N503D, E492G+V493P, D494E+Q417H, E495Q+T496A, D494N+E495Q+T496A, E492G+K538H+K541N+E542D, E492G+V493P+K538H+K541N+E542D, A490D+E492T+V493L+E501P+E503D+A504E+E505K+T506F+K541D. Exemplary natural albumin variants that exhibit decreased serum half-life include D494N (Peach et al., *Biochim Biophys Acta* 1991; 1097:49-54), and K541E and K560E (Iwao et al., *B. B. A. Proteins and Proteomics* 2007; 1774:1582-90).

**[0205]** One or more positions of albumin, or a variant or fragment thereof, can be altered to provide reactive surface residues for, e.g., conjugation with a multispecific variable region. Exemplary positions in HSA (SEQ ID NO: 171) that can be altered to provide conjugation competent cysteine residues include, but are not limited to, those disclosed in WO2010/092135, such as, D1C, A2C, T79C, E82C, E86C, D121C, D129C, S270C, A364C, A504C, E505C, D549C, D562C, A578C, A579C, A581C, L585C, and L595C. Alternatively a cysteine residue may be added to the N or C terminus of albumin. Methods suitable for producing conjugation competent albumin, or a variant or peptide thereof, as well as covalently linking albumin, or a variant or fragment thereof, with a conjugation partner or partners (e.g., a multispecific variable region) are routine in the art and disclosed in, e.g., WO2010/092135 and WO 2009/019314. In some embodiments, the conjugates may conveniently be linked via a free thiol group present on the surface of HSA (amino acid residue 34 of mature HSA) using art-recognized methods.

**[0206]** In addition to the albumin or variants thereof described supra, fragments of albumin, or fragments of variants thereof, are suitable for use as the albumin component of the fusion proteins described herein. Exemplary albumin fragments that are suitable for use in the fusion proteins are disclosed in WO 2011/124718. A fragment of albumin (e.g., a fragment of HSA) will typically be at least 20 amino acids in length, such as at least 40 amino acids, at least 60 amino acids, at least 80 amino acids, at least 100 amino acids, at least 150 amino acids, at least 200 amino acids, at least 300 amino acids, at least 400 amino acids, or at least 500 amino acids in length, and will alter (e.g.,

increase) the serum half-life of the polypeptide it is fused to (e.g., multispecific variable region) relative to the non-fused polypeptide.

**[0207]** In some embodiments, a fragment may comprise at least one whole sub-domain of albumin. Domains of HSA have been expressed as recombinant proteins (Dockal et al., *JBC* 1999; 274:29303-10), where domain I was defined as consisting of amino acids 1-197 (SEQ ID NO: 175), domain II was defined as consisting of amino acids 189-385 (SEQ ID NO: 176), and domain III was defined as consisting of amino acids 381-585 (SEQ ID NO: 177) of HSA (SEQ ID NO: 171). Partial overlap of the domains occurs given the extended  $\alpha$ -helix structure (h10-h1) which exists between domains I and II, and between domains II and III (Peters, 1996, op. cit, Table 2-4). HSA also comprises six sub-domains (sub-domains IA, IB, NA, NB, INA and NIB). Sub-domain IA comprises amino acids 6-105, sub-domain IB comprises amino acids 120-177, sub-domain NA comprises amino acids 200-291, sub-domain NB comprises amino acids 316-369, sub-domain INA comprises amino acids 392-491 and sub-domain NIB comprises amino acids 512-583 of SEQ ID NO: 171.

**[0208]** A fragment may comprise a whole or part of one or more domains or sub-domains as defined above, or any combination of those domains and/or sub-domains. A fragment may comprise or consist of at least 50, 60, 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99% of an albumin or of a domain of an albumin, or a variant or fragment thereof. Additionally, single or multiple heterologous fusions comprising any of the above; or single or multiple heterologous fusions to albumin, or a variant or fragment of any of these may be used. Such fusions include albumin N-terminal fusions, albumin C-terminal fusions and co-N-terminal and C-terminal albumin fusions as exemplified by WO 01/79271. In some embodiments, the fragment of albumin or variant thereof retains the ability to bind to FcRn. In some embodiments, the fusion proteins contain domain III of albumin, or a variant thereof. In some embodiments, the fusion proteins contain domain III of albumin and an additional domain selected from the group consisting of domain I, domain II, and domain III. In some embodiments, the fusion proteins contain domains I, II, and III of albumin.

**[0209]** In certain embodiments, the fusion protein comprises a serum albumin binding protein such as those described in US2005/0287153, US2007/0003549, US2007/0178082, US2007/0269422, US2010/0113339, WO2009/083804, and WO2009/133208, which are herein incorporated by reference in their entirety.

#### Fc Fragments

**[0210]** In some embodiments, the fusion protein comprises a multispecific variable region described herein, operably coupled to an Fc domain. In some embodiments, the Fc domain comprises the amino acid sequence set forth in SEQ ID NO: 174. It will be understood by those in the art that epitope tags corresponding to 6 $\times$  his tag on the fusion proteins are optional. The Fc domain does not contain a variable region that binds to antigen. Fc domains useful for producing the fusion proteins disclosed herein may be obtained from a number of different sources. In certain embodiments, an Fc domain of the fusion protein is derived from a human immunoglobulin. In certain embodiments, the Fc domain is from a human IgG1 constant region (SEQ ID NO: 172). The Fc domain of human IgG1 is set forth in SEQ

ID NO: 174. It is understood, however, that the Fc domain may be derived from an immunoglobulin of another mammalian species, including for example, a rodent (e.g. a mouse, rat, rabbit, guinea pig) or non-human primate (e.g. chimpanzee, macaque) species. Moreover, the Fc domain or portion thereof may be derived from any immunoglobulin class, including IgM, IgG, IgD, IgA, and IgE, and any immunoglobulin isotype, including IgG1, IgG2, IgG3, and IgG4.

**[0211]** In some embodiments, a fusion protein includes a mutant Fc domain. In some embodiments, a fusion protein includes a mutant, IgG1 Fc domain. In some embodiments, a mutant Fc domain comprises one or more mutations in the hinge, CH2, and/or CH3 domains. In some embodiments, a mutant Fc domain includes a D265A mutation.

**[0212]** A variety of Fc domain gene sequences (e.g., mouse and human constant region gene sequences) are available in the form of publicly accessible deposits. Constant region domains comprising an Fc domain sequence can be selected lacking a particular effector function and/or with a particular modification to reduce immunogenicity. Many sequences of antibodies and antibody-encoding genes have been published and suitable Fc domain sequences (e.g. hinge, CH2, and/or CH3 sequences, or portions thereof) can be derived from these sequences using art recognized techniques. The genetic material obtained using any of the foregoing methods may then be altered or synthesized to obtain polypeptides suitable for use in the methods disclosed herein. It will further be appreciated that the scope of this invention encompasses alleles, variants and mutations of constant region DNA sequences.

**[0213]** Fc domain sequences can be cloned, e.g., using the polymerase chain reaction and primers which are selected to amplify the domain of interest. To clone an Fc domain sequence from an antibody, mRNA can be isolated from hybridoma, spleen, or lymph cells, reverse transcribed into DNA, and antibody genes amplified by PCR. PCR amplification methods are described in detail in U.S. Pat. Nos. 4,683,195; 4,683,202; 4,800,159; 4,965,188; and in, e.g., "PCR Protocols: A Guide to Methods and Applications" Innis et al. eds., Academic Press, San Diego, Calif. (1990); Ho et al. 1989. *Gene* 77:51; Horton et al. 1993. *Methods Enzymol.* 217:270). PCR may be initiated by consensus constant region primers or by more specific primers based on the published heavy and light chain DNA and amino acid sequences. As discussed above, PCR also may be used to isolate DNA clones encoding the antibody light and heavy chains. In this case the libraries may be screened by consensus primers or larger homologous probes, such as mouse constant region probes. Numerous primer sets suitable for amplification of antibody genes are known in the art (e.g., 5' primers based on the N-terminal sequence of purified antibodies (Benhar and Pastan. 1994. *Protein Engineering* 7: 1509); rapid amplification of cDNA ends (Ruberti, F. et al. 1994. *J. Immunol. Methods* 173:33); antibody leader sequences (Larrick et al. *Biochem Biophys Res Commun* 1989; 160: 1250). The cloning of antibody sequences is further described in Newman et al., U.S. Pat. No. 5,658,570, filed Jan. 25, 1995, which is herein incorporated by reference.

**[0214]** Fusion proteins disclosed herein may comprise one or more Fc domains (e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10, or more Fc domains). In certain embodiments, the Fc domains may be of different types. In certain embodiments, at least one Fc

domain present in the fusion protein comprises a hinge domain or portion thereof. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain which comprises at least one CH2 domain or portion thereof. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain which comprises at least one CH3 domain or portion thereof. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain which comprises at least one CH4 domain or portion thereof. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain which comprises at least one hinge domain or portion thereof and at least one CH2 domain or portion thereof (e.g. in the hinge-CH2 orientation). In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain which comprises at least one CH2 domain or portion thereof and at least one CH3 domain or portion thereof (e.g. in the CH2-CH3 orientation). In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain comprising at least one hinge domain or portion thereof, at least one CH2 domain or portion thereof, and at least one CH3 domain or portion thereof, for example in the orientation hinge-CH2-CH3, hinge-CH3-CH2, or CH2-CH3-hinge.

**[0215]** In certain embodiments, the fusion protein comprises at least one complete Fc region derived from one or more immunoglobulin heavy chains (e.g., an Fc domain including hinge, CH2, and CH3 domains, although these need not be derived from the same antibody). In certain embodiments, the fusion protein comprises at least two complete Fc domains derived from one or more immunoglobulin heavy chains. In certain embodiments, the complete Fc domain is derived from a human IgG immunoglobulin heavy chain (e.g., human IgG1).

**[0216]** In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain comprising a complete CH3 domain. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain comprising a complete CH2 domain. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain comprising at least a CH3 domain, and at least one of a hinge region, and a CH2 domain. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain comprising a hinge and a CH3 domain. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain comprising a hinge, a CH2, and a CH3 domain. In certain embodiments, the Fc domain is derived from a human IgG immunoglobulin heavy chain (e.g., human IgG1).

**[0217]** The constant region domains or portions thereof making up an Fc domain of the fusion protein disclosed herein may be derived from different immunoglobulin molecules. For example, a fusion protein disclosed herein may comprise a CH2 domain or portion thereof derived from an IgG1 molecule and a CH3 region or portion thereof derived from an IgG3 molecule. In another example, the fusion protein comprises an Fc domain comprising a hinge domain derived, in part, from an IgG1 molecule and, in part, from an IgG3 molecule. As set forth herein, it will be understood by one of ordinary skill in the art that an Fc domain may be altered such that it varies in amino acid sequence from a naturally occurring antibody molecule.

**[0218]** In certain embodiments, the fusion protein disclosed herein lacks one or more constant region domains of a complete Fc region, i.e., they are partially or entirely

deleted. In certain embodiments, the fusion protein disclosed herein will lack an entire CH2 domain. In certain embodiments, the fusion protein disclosed herein comprise CH2 domain-deleted Fc regions derived from a vector (e.g., from IDEC Pharmaceuticals, San Diego) encoding an IgG1 human constant region domain (see, e.g., WO02/060955A2 and WO02/096948A2). This exemplary vector is engineered to delete the CH2 domain and provide a synthetic vector expressing a domain-deleted IgG1 constant region. It will be noted that these exemplary constructs are preferably engineered to fuse a binding CH3 domain directly to a hinge region of the respective Fc domain.

**[0219]** In other constructs it may be desirable to provide a peptide spacer between one or more constituent Fc domains. For example, a peptide spacer may be placed between a hinge region and a CH2 domain and/or between a CH2 and a CH3 domain. For example, compatible constructs could be expressed wherein the CH2 domain has been deleted and the remaining CH3 domain (synthetic or unsynthetic) is joined to the hinge region with a 1-20, 1-10, or 1-5 amino acid peptide spacer. Such a peptide spacer may be added, for instance, to ensure that the regulatory elements of the constant region domain remain free and accessible or that the hinge region remains flexible. Preferably, any linker peptide compatible used in the instant invention will be relatively non-immunogenic and not prevent proper folding of the Fc.

#### Modified Fc Domains

**[0220]** In certain embodiments, an Fc domain employed in the fusion protein disclosed herein is altered or modified, e.g., by amino acid mutation (e.g., addition, deletion, or substitution). As used herein, the term "Fc domain variant" refers to an Fc domain having at least one amino acid modification, such as an amino acid substitution, as compared to the wild-type Fc from which the Fc domain is derived. For example, wherein the Fc domain is derived from a human IgG1 antibody, a variant comprises at least one amino acid mutation (e.g., substitution) as compared to a wild type amino acid at the corresponding position of the human IgG1 Fc region.

**[0221]** In certain embodiments, the Fc variant comprises a substitution at an amino acid position located in a hinge domain or portion thereof. In certain embodiments, the Fc variant comprises a substitution at an amino acid position located in a CH2 domain or portion thereof. In certain embodiments, the Fc variant comprises a substitution at an amino acid position located in a CH3 domain or portion thereof. In certain embodiments, the Fc variant comprises a substitution at an amino acid position located in a CH4 domain or portion thereof.

**[0222]** In certain embodiments, the fusion protein disclosed herein comprises an Fc variant comprising more than one amino acid substitution. The fusion protein disclosed herein may comprise, for example, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more amino acid substitutions. Preferably, the amino acid substitutions are spatially positioned from each other by an interval of at least 1 amino acid position or more, for example, at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acid positions or more. More preferably, the engineered amino acids are spatially positioned apart from each other by an interval of at least 5, 10, 15, 20, or 25 amino acid positions or more.

**[0223]** In some embodiments, an Fc domain includes changes in the region between amino acids 234-238, including the sequence LLGGP at the beginning of the CH2 domain. In some embodiments, an Fc variant alters Fc mediated effector function, particularly ADCC, and/or decrease binding avidity for Fc receptors. In some aspects, sequence changes closer to the CH2-CH3 junction, at positions such as K322 or P331 can eliminate complement mediated cytotoxicity and/or alter avidity for FcR binding. In some embodiments, an Fc domain incorporates changes at residues P238 and P331, e.g., changing the wild type prolines at these positions to serine. In some embodiments, alterations in the hinge region at one or more of the three hinge cysteines, to encode CCC, SCC, SSC, SCS, or SSS at these residues can also affect FcR binding and molecular homogeneity, e.g., by elimination of unpaired cysteines that may destabilize the folded protein.

**[0224]** Other amino acid mutations in the Fc domain are contemplated to reduce binding to the Fc gamma receptor and Fc gamma receptor subtypes. For example, mutations at positions 238, 239, 248, 249, 252, 254, 255, 256, 258, 265, 267, 268, 269, 270, 272, 279, 280, 283, 285, 298, 289, 290, 292, 293, 294, 295, 296, 298, 301, 303, 305, 307, 312, 315, 322, 324, 327, 329, 330, 331, 333, 334, 335, 337, 338, 340, 356, 360, 373, 376, 378, 379, 382, 388, 389, 398, 414, 416, 419, 430, 434, 435, 437, 438 or 439 of the Fc region can alter binding as described in U.S. Pat. No. 6,737,056, issued May 18, 2004, incorporated herein by reference in its entirety. This patent reported that changing Pro331 in IgG3 to Ser resulted in six fold lower affinity as compared to unmutated IgG3, indicating the involvement of Pro331 in Fc gamma RI binding. In addition, amino acid modifications at positions 234, 235, 236, and 237, 297, 318, 320 and 322 are disclosed as potentially altering receptor binding affinity in U.S. Pat. No. 5,624,821, issued Apr. 29, 1997 and incorporated herein by reference in its entirety.

**[0225]** Further mutations contemplated for use include, e.g., those described in U.S. Pat. App. Pub. No. 2006/0235208, published Oct. 19, 2006 and incorporated herein by reference in its entirety. This publication describes Fc variants that exhibit reduced binding to Fc gamma receptors, reduced antibody dependent cell-mediated cytotoxicity, or reduced complement dependent cytotoxicity, that comprise at least one amino acid modification in the Fc region, including 232G, 234G, 234H, 235D, 235G, 235H, 236I, 236N, 236P, 236R, 237K, 237L, 237N, 237P, 238K, 239R, 265G, 267R, 269R, 270H, 297S, 299A, 299I, 299V, 325A, 325L, 327R, 328R, 329K, 330I, 330L, 330N, 330P, 330R, and 331L (numbering is according to the EU index), as well as double mutants 236R/237K, 236R/325L, 236R/328R, 237K/325L, 237K/328R, 325L/328R, 235G/236R, 267R/269R, 234G/235G, 236R/237K/325L, 236R/325L/328R, 235G/236R/237K, and 237K/325L/328R. Other mutations contemplated for use as described in this publication include 227G, 234D, 234E, 234G, 234I, 234Y, 235D, 235I, 235S, 236S, 239D, 246H, 255Y, 258H, 260H, 264I, 267D, 267E, 268D, 268E, 272H, 272I, 272R, 281D, 282G, 283H, 284E, 293R, 295E, 304T, 324G, 324I, 327D, 327A, 328A, 328D, 328E, 328F, 328I, 328M, 328N, 328Q, 328T, 328V, 328Y, 330I, 330L, 330Y, 332D, 332E, 335D, an insertion of G between positions 235 and 236, an insertion of A between positions 235 and 236, an insertion of S between positions 235 and 236, an insertion of T between positions 235 and 236, an insertion of N between positions 235 and 236, an

insertion of D between positions 235 and 236, an insertion of V between positions 235 and 236, an insertion of L between positions 235 and 236, an insertion of G between positions 235 and 236, an insertion of A between positions 235 and 236, an insertion of S between positions 235 and 236, an insertion of T between positions 235 and 236, an insertion of N between positions 235 and 236, an insertion of D between positions 235 and 236, an insertion of V between positions 235 and 236, an insertion of L between positions 235 and 236, an insertion of G between positions 297 and 298, an insertion of A between positions 297 and 298, an insertion of S between positions 297 and 298, an insertion of D between positions 297 and 298, an insertion of G between positions 326 and 327, an insertion of A between positions 326 and 327, an insertion of T between positions 326 and 327, an insertion of D between positions 326 and 327, and an insertion of E between positions 326 and 327 (numbering is according to the EU index). Additionally, mutations described in U.S. Pat. App. Pub. No. 2006/0235208 include 227G/332E, 234D/332E, 234E/332E, 234Y/332E, 234I 332E, 234G/332E, 235I/332E, 235S/332E, 235D/332E, 235E/332E, 236S/332E, 236A/332E, 236S/332D, 236A/332D, 239D/268E, 246H/332E, 255Y/332E, 258H/332E, 260H/332E, 264I 332E, 267E/332E, 267D/332E, 268D/332D, 268E/332D, 268E/332E, 268D/332E, 268E/330Y, 268D/330Y, 272R/332E, 272H/332E, 283H/332E, 284E/332E, 293R/332E, 295E/332E, 304T/332E, 324I 332E, 324G/332E, 324I/332D, 324G/332D, 327D/332E, 328A/332E, 328T/332E, 328V/332E, 328I 332E, 328F/332E, 328Y/332E, 328M/332E, 328D/332E, 328E/332E, 328N/332E, 328Q/332E, 328A/332D, 328T/332D, 328V/332D, 328I 332D, 328F/332D, 328Y/332D, 328M/332D, 328I/332D, 328E/332D, 328N/332D, 328Q/332D, 330L/332E, 330Y/332E, 330I 332E, 332D/330Y, 335D/332E, 239D/332E, 239D/332E/330Y, 239D/332E/330L, 239D/332E/330I, 239D/332E/268E, 239D/332E/268D, 239D/332E/327D, 239D/332E/284E, 239D/268E/330Y, 239D/332E/268E/330Y, 239D/332E/327A, 239D/332E/268E/327A, 239D/332E/268E/330Y/327A, 332E/330Y/268E/327A, 239D/332E/268E/330Y/327A, Insert G>297-298/332E, Insert A>297-298/332E, Insert S>297-298/332E, Insert D>297-298/332E, Insert G>326-327/332E, Insert A>326-327/332E, Insert T>326-327/332E, Insert D>326-327/332E, Insert E>326-327/332E, Insert G>235-236/332E, Insert A>235-236/332E, Insert S>235-236/332E, Insert T>235-236/332E, Insert N>235-236/332E, Insert D>235-236/332E, Insert V>235-236/332E, Insert L>235-236/332E, Insert G>235-236/332D, Insert A>235-236/332D, Insert S>235-236/332D, Insert T>235-236/332D, Insert N>235-236/332D, Insert D>235-236/332D, Insert V>235-236/332D, and Insert L>235-236/332D (numbering according to the EU index) are contemplated for use. The mutant L234A/L235A is described, e.g., in U.S. Pat. App. Pub. No. 2003/0108548, published Jun. 12, 2003 and incorporated herein by reference in its entirety. In embodiments, the described modifications are included either individually or in combination. In certain embodiments, the mutation is D265A in human IgG1.

**[0226]** In certain embodiments, the fusion protein disclosed herein comprises an amino acid substitution to an Fc domain which alters antigen-independent effector functions of the polypeptide, in particular the circulating half-life of the polypeptide.

**[0227]** In certain embodiments, the fusion protein disclosed herein comprises an Fc variant comprising an amino acid substitution which alters the antigen-dependent effector functions of the polypeptide, in particular ADCC or complement activation, e.g., as compared to a wild type Fc region. Such fusion proteins exhibit decreased binding to FcR gamma when compared to wild-type polypeptides and, therefore, mediate reduced effector function. Fc variants with decreased FcR gamma binding affinity are expected to reduce effector function, and such molecules are also useful, for example, for treatment of conditions in which target cell destruction is undesirable, e.g., where normal cells may express target molecules, or where chronic administration of the polypeptide might result in unwanted immune system activation.

**[0228]** In certain embodiments, the fusion protein exhibits altered binding to an activating FcγR (e.g. FcγI, FcγIIa, or FcγRIIIa). In certain embodiments, the fusion protein exhibits altered binding affinity to an inhibitory FcγR (e.g. FcγRIIb). Exemplary amino acid substitutions which altered FcR or complement binding activity are disclosed in International PCT Publication No. WO05/063815 which is incorporated by reference herein.

**[0229]** The fusion protein disclosed herein may also comprise an amino acid substitution which alters the glycosylation of the fusion protein. For example, the Fc domain of the fusion protein may comprise an Fc domain having a mutation leading to reduced glycosylation (e.g., N- or O-linked glycosylation) or may comprise an altered glycoform of the wild-type Fc domain (e.g., a low fucose or fucose-free glycan). In certain embodiments, the fusion protein has an amino acid substitution near or within a glycosylation motif, for example, an N-linked glycosylation motif that contains the amino acid sequence NXT or NXS. Exemplary amino acid substitutions which reduce or alter glycosylation are disclosed in WO05/018572 and US2007/0111281, the contents of which are incorporated by reference herein. In certain embodiments, the fusion protein disclosed herein comprises at least one Fc domain having engineered cysteine residue or analog thereof which is located at the solvent-exposed surface. In certain embodiments, the fusion protein disclosed herein comprise an Fc domain comprising at least one engineered free cysteine residue or analog thereof that is substantially free of disulfide bonding with a second cysteine residue. Any of the above engineered cysteine residues or analogs thereof may subsequently be conjugated to a functional domain using art-recognized techniques (e.g., conjugated with a thiol-reactive heterobifunctional linker).

**[0230]** In certain embodiments, the fusion protein disclosed herein may comprise a genetically fused Fc domain having two or more of its constituent Fc domains independently selected from the Fc domains described herein. In certain embodiments, the Fc domains are the same. In certain embodiments, at least two of the Fc domains are different. For example, the Fc domains of the fusion protein disclosed herein comprise the same number of amino acid residues or they may differ in length by one or more amino acid residues (e.g., by about 5 amino acid residues (e.g., 1, 2, 3, 4, or 5 amino acid residues), about 10 residues, about 15 residues, about 20 residues, about 30 residues, about 40 residues, or about 50 residues). In certain embodiments, the Fc domains of the fusion protein disclosed herein may differ in sequence at one or more amino acid positions. For

example, at least two of the Fc domains may differ at about 5 amino acid positions (e.g., 1, 2, 3, 4, or 5 amino acid positions), about 10 positions, about 15 positions, about 20 positions, about 30 positions, about 40 positions, or about 50 positions).

#### Polyethylene Glycol (PEG)

**[0231]** In certain embodiments, a fusion protein disclosed herein comprises a polyethylene glycol (PEG) domain. PEGylation is well known in the art to confer increased circulation half-life to proteins. Methods of PEGylation are well known and disclosed in, e.g., U.S. Pat. Nos. 7,610,156, 7,847,062, all of which are hereby incorporated by reference.

**[0232]** PEG is a well-known, water soluble polymer that is commercially available or can be prepared by ring-opening polymerization of ethylene glycol according to methods well known in the art (Sandler and Karo, *Polymer Synthesis*, Academic Press, New York, Vol. 3, pages 138-161). The term "PEG" is used broadly to encompass any polyethylene glycol molecule, without regard to size or to modification at an end of the PEG, and can be represented by the formula:  $X-(CH_2CH_2O)_n-CH_2CH_2OH$ , where  $n$  is 20 to 2300 and  $X$  is H or a terminal modification, e.g., a  $C_{1-4}$  alkyl. In certain embodiments, the PEG suitable for use in the methods disclosed herein terminates on one end with hydroxy or methoxy, i.e.,  $X$  is H or  $CH_3$  ("methoxy PEG"). PEG can contain further chemical groups which are necessary for binding reactions; which results from the chemical synthesis of the molecule; or which is a spacer for optimal distance of parts of the molecule. In addition, such a PEG can consist of one or more PEG side-chains which are linked together. PEGs with more than one PEG chain are called multiarmed or branched PEGs. Branched PEGs can be prepared, for example, by the addition of polyethylene oxide to various polyols, including glycerol, pentaerythriol, and sorbitol. For example, a four-armed branched PEG can be prepared from pentaerythriol and ethylene oxide. Branched PEG are described in, for example, EP-A 0 473 084 and U.S. Pat. No. 5,932,462, both of which are hereby incorporated by reference. One form of PEGs includes two PEG side-chains (PEG2) linked via the primary amino groups of a lysine (Monfardini et al., *Bioconjugate Chem* 1995; 6:62-9).

**[0233]** In certain embodiments, the fusion protein comprising PEG is produced by site-directed pegylation, particularly by conjugation of PEG to a cysteine moiety at the N- or C-terminus. A PEG moiety may also be attached by other chemistry, including by conjugation to amines. PEG conjugation to peptides or proteins generally involves the activation of PEG and coupling of the activated PEG-intermediates directly to target proteins/peptides or to a linker, which is subsequently activated and coupled to target proteins/peptides (see Abuchowski et al., *JBC* 1977; 252: 3571 and *JBC* 1977; 252:3582, and Harris et al., in: *Poly(ethylene glycol) Chemistry: Biotechnical and Biomedical Applications*; (J. M. Harris ed.) Plenum Press: New York, 1992; Chap. 21 and 22). A variety of molecular mass forms of PEG can be selected, e.g., from about 1,000 Daltons (Da) to 100,000 Da ( $n$  is 20 to 2300), for conjugating to the variable region. The number of repeating units " $n$ " in the PEG is approximated for the molecular mass described in Daltons. It is preferred that the combined molecular mass of PEG on an activated linker is suitable for pharmaceutical use. Thus, in one embodiment, the molecu-

lar mass of the PEG molecules does not exceed 100,000 Da. For example, if three PEG molecules are attached to a linker, where each PEG molecule has the same molecular mass of 12,000 Da (each  $n$  is about 270), then the total molecular mass of PEG on the linker is about 36,000 Da (total  $n$  is about 820). The molecular masses of the PEG attached to the linker can also be different, e.g., of three molecules on a linker two PEG molecules can be 5,000 Da each (each  $n$  is about 110) and one PEG molecule can be 12,000 Da ( $n$  is about 270).

**[0234]** One skilled in the art can select a suitable molecular mass for PEG, e.g., based on how the fusion protein comprising PEG will be used therapeutically, the desired dosage, circulation time, resistance to proteolysis, immunogenicity, and other considerations. For a discussion of PEG and its use to enhance the properties of proteins, see N. V. Katre, *Advanced Drug Delivery Reviews* 1993; 10:91-114.

**[0235]** In certain embodiments, PEG molecules may be activated to react with amino groups on the variable region, such as with lysines (Bencham C. O. et al., *Anal. Biochem.*, 131, 25 (1983); Veronese, F. M. et al., *Appl. Biochem.*, 11, 141 (1985); Zalipsky, S. et al., *Polymeric Drugs and Drug Delivery Systems*, adrs 9-110 ACS Symposium Series 469 (1999); Zalipsky, S. et al., *Europ. Polym. J.*, 19, 1177-1183 (1983); Delgado, C. et al., *Biotechnology and Applied Biochemistry*, 12, 119-128 (1990)).

**[0236]** In certain embodiments, carbonate esters of PEG are used to form the fusion protein.  $N,N'$ -disuccinimidylcarbonate (DSC) may be used in the reaction with PEG to form active mixed PEG-succinimidyl carbonate that may be subsequently reacted with a nucleophilic group of a linker or an amino group of the variable region (see U.S. Pat. Nos. 5,281,698 and 5,932,462). In a similar type of reaction, 1,1'-(dibenzotriazolyl)carbonate and di-(2-pyridyl)carbonate may be reacted with PEG to form PEG-benzotriazolyl and PEG-pyridyl mixed carbonate (U.S. Pat. No. 5,382,657), respectively. Generation of a fusion protein comprising PEG can be performed according to the methods of the state of the art, for example by reaction of the variable region with electrophilically active PEGs (Shearwater Corp., USA, [www.shearwatercorp.com](http://www.shearwatercorp.com)). Preferred PEG reagents suitable for use in the methods disclosed herein are, e.g., N-hydroxysuccinimidyl propionates (PEG-SPA), butanoates (PEG-SBA), PEG-succinimidyl propionate or branched N-hydroxysuccinimides such as mPEG2-NHS (Monfardini, C, et al., *Bioconjugate Chem.* 6 (1995) 62-69).

**[0237]** In certain embodiments, PEG molecules may be coupled to sulfhydryl groups on the variable region (Sartore, L., et al., *Appl. Biochem. Biotechnol.*, 27, 45 (1991); Morpurgo et al., *Biocon. Chem.*, 7, 363-368 (1996); Goodson et al., *Bio/Technology* (1990) 8, 343; U.S. Pat. No. 5,766,897). U.S. Pat. Nos. 6,610,281 and 5,766,897 describe exemplary reactive PEG species that may be coupled to sulfhydryl groups.

**[0238]** In certain embodiments where PEG molecules are conjugated to cysteine residues native to the variable region, whereas in certain embodiments, one or more cysteine residues are engineered into the variable region. Mutations may be introduced into the coding sequence of the variable region to generate cysteine residues. This might be achieved, for example, by mutating one or more amino acid residues to cysteine. Preferred amino acids for mutating to a cysteine residue include serine, threonine, alanine and other hydrophilic residues. Preferably, the residue to be mutated to

cysteine is a surface-exposed residue. Algorithms are well-known in the art for predicting surface accessibility of residues based on primary sequence or a protein.

**[0239]** In certain embodiments, the fusion protein comprising PEG comprises one or more PEG molecules covalently attached to a linker.

**[0240]** In certain embodiments, the variable region is pegylated at the C-terminus. In certain embodiments, a protein is pegylated at the C-terminus by the introduction of C-terminal azido-methionine and the subsequent conjugation of a methyl-PEG-triarylphosphine compound via the Staudinger reaction. This C-terminal conjugation method is described in Cazalis et al., C-Terminal Site-Specific PEGylation of a Truncated Thrombomodulin Mutant with Retention of Full Bioactivity, *Bioconjug Chem.* 2004; 15(5): 1005-1009. Monopegylation of the variable region can also be achieved according to the general methods described in WO 94/01451. WO 94/01451 describes a method for preparing a recombinant polypeptide with a modified terminal amino acid alpha-carbon reactive group. The steps of the method involve forming the recombinant polypeptide and protecting it with one or more biologically added protecting groups at the N-terminal alpha-amine and C-terminal alpha-carboxyl. The polypeptide can then be reacted with chemical protecting agents to selectively protect reactive side chain groups and thereby prevent side chain groups from being modified. The polypeptide is then cleaved with a cleavage reagent specific for the biological protecting group to form an unprotected terminal amino acid alpha-carbon reactive group. The unprotected terminal amino acid alpha-carbon reactive group is modified with a chemical modifying agent. The side chain protected terminally modified single copy polypeptide is then deprotected at the side chain groups to form a terminally modified recombinant single copy polypeptide. The number and sequence of steps in the method can be varied to achieve selective modification at the N- and/or C-terminal amino acid of the polypeptide.

**[0241]** The ratio of variable region to activated PEG in the conjugation reaction can be from about 1:0.5 to 1:50, between from about 1:1 to 1:30, or from about 1:5 to 1:15. Various aqueous buffers can be used to catalyze the covalent addition of PEG to the variable region, or variants thereof. In certain embodiments, the pH of a buffer used is from about 7.0 to 9.0. In certain embodiments, the pH is in a slightly basic range, e.g., from about 7.5 to 8.5. Buffers having a pKa close to neutral pH range may be used, e.g., phosphate buffer.

**[0242]** Conventional separation and purification techniques known in the art can be used to purify the fusion protein comprising PEG, such as size exclusion (e.g. gel filtration) and ion exchange chromatography. Products may also be separated using SDS-PAGE. Products that may be separated include mono-, di-, tri- poly- and un-pegylated variable regions as well as free PEG. The percentage of mono-PEG conjugates can be controlled by pooling broader fractions around the elution peak to increase the percentage of mono-PEG in the composition.

**[0243]** In certain embodiments, the fusion protein comprising PEG contains one, two or more PEG moieties. In certain embodiments, the PEG moiety(ies) are bound to an amino acid residue which is on the surface of the protein and/or away from the surface that contacts the chemokine of interest. In certain embodiments, the combined or total molecular mass of PEG in the fusion protein comprising

PEG is from about 3,000 Da to 60,000 Da, optionally from about 10,000 Da to 36,000 Da. In certain embodiments, PEG of the fusion protein is a substantially linear, straight-chain PEG.

**[0244]** In certain embodiments, the fusion protein comprising PEG will preferably retain at least 25%, 50%, 60%, 70%, 80%, 85%, 90%, 95% or 100% of the biological activity associated with the unmodified protein. In certain embodiments, biological activity refers to the ability to bind the chemokine(s) of interest. The serum clearance rate of the fusion protein comprising PEG may be decreased by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or even 90%, relative to the clearance rate of the variable region alone. The fusion protein comprising PEG may have a circulation half-life ( $t'$ ) which is enhanced relative to the half-life of the variable region alone. The half-life of the fusion protein comprising PEG, or variants thereof, may be enhanced by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 125%, 150%, 175%, 200%, 250%, 300%, 400% or 500%, or even by 1000% relative to the half-life of the variable region alone. In certain embodiments, the protein half-life is determined in vitro, such as in a buffered saline solution or in serum. In certain embodiments, the protein half-life is an in vivo circulation half-life, such as the half-life of the protein in the serum or other bodily fluid of an animal.

#### Other Polymers

**[0245]** In certain embodiments, the fusion protein comprises transferrin, as disclosed in U.S. Pat. Nos. 7,176,278 and 8,158,579, which are herein incorporated by reference in their entirety.

**[0246]** In certain embodiments, the fusion protein comprises a serum immunoglobulin binding protein such as those disclosed in US2007/0178082, which is herein incorporated by reference in its entirety.

**[0247]** In certain embodiments, the fusion protein comprises a fibronectin (Fn)-based scaffold domain protein that binds to serum albumin, such as those disclosed in US2012/0094909, which is herein incorporated by reference in its entirety. Methods of making fibronectin-based scaffold domain proteins are also disclosed in US2012/0094909. A non-limiting example of a Fn3-based extended-PK group is Fn3(HSA), i.e., a Fn3 protein that binds to human serum albumin.

**[0248]** In some embodiments, the fusion protein comprises an XTEN moiety. An XTEN moiety comprises amino acid residues A, E, G, P, S and T. In some embodiments, an XTEN moiety ranges from 36 to 288 amino acid residues in length. Exemplary XTEN moieties are described in WO 2011/123830; Schellenberger V. et al., *Nat Biotechnol.* Vol. 27: 1186-90 (2009); and Geething N C. Et al *PLoS One* Vol. 5: e10175 (2010), each of which is herein incorporated by reference in its entirety.

**[0249]** In some embodiments, the fusion protein comprises an ELP moiety. An ELP moiety is a repeating peptide unit containing sequences commonly found in elastin. The ELP sequence contains repeats of V-P-G-x-G, wherein x is any amino acid except proline. ELP moieties can be degraded over time by human elastases, thereby making them biologically degradable. Examples of ELP moieties are described in, Floss, D M. et al *Trends Biotechnol.* Vol. 26:



489-501 (2013); and Floss, D M. et al, Hoboken: Wiley, p. 372-98 (2013), each of which is herein incorporated by reference.

**[0250]** In some embodiments, the fusion protein comprises a polymer of repeating amino acids proline, alanine and serine (i.e., PAS moiety). In some embodiments, a PAS moiety comprise 100-20 repeats in length. Exemplary PAS moieties are described in Huang, C. *Curr Opin Biotechnol Vol. 20: 692-9* (2009), herein incorporated by reference.

#### Linkers

**[0251]** In some embodiments, the multispecific variable region is operably coupled to a polymer (e.g., serum albumin) via a linker. In some embodiments, the fusion protein includes a plurality of linker domains. In some embodiments, the linker domain is a polypeptide linker. In some embodiments, it is desirable to employ a polypeptide linker to fuse a polymer (e.g., serum albumin) with a multispecific variable region to form a fusion protein described herein.

**[0252]** In some embodiments, the fusion proteins employ a polypeptide linker to join any two or more domains in frame in a single polypeptide chain. In some embodiments, the two or more domains may be independently selected from any of the polymers (e.g., serum albumin), or variants or fragments thereof, or multispecific variable regions discussed herein.

**[0253]** Linkers suitable for fusing the multispecific variable region to the polymer (e.g., serum albumin) are well known in the art, and are disclosed in, e.g., US2010/0210511 US2010/0179094, and US2012/0094909, which are herein incorporated by reference in its entirety. Exemplary linkers include gly- ser polypeptide linkers, glycine-proline polypeptide linkers, and proline-alanine polypeptide linkers, the Fc interlinker from human IgG1 C<sub>H2</sub> residues 297-322: NSTYRVVSVLTVLHQDWLNGKEYKCK, and the HSA interlinker from the D3 domain of human serum albumin: FQNALLVRYTKKVPQVSTPTLVEVS. See Fang et al., *Chines. Sci. Bull.*, 2003, 48:1912-1918, incorporated by reference in its entirety. Other linkers are provided, for example, in U.S. Pat. Nos. 5,525,491; Alfthan et al., *Protein Eng.*, 1995, 8:725-731; Shan et al., *J. Immunol.*, 1999, 162:6589-6595; Newton et al., *Biochemistry*, 1996, 35:545-553; Megeed et al.; *Biomacromolecules*, 2006, 7:999-1004; and Perisic et al., *Structure*, 1994, 12:1217-1226; each of which is incorporated by reference in its entirety. In certain embodiments, the linker is a gly-ser polypeptide linker, i.e., a peptide that consists of glycine and serine residues.

**[0254]** Exemplary gly-ser polypeptide linkers comprise the amino acid sequence Ser(Gly<sub>n</sub>Ser)<sub>n</sub>. In certain embodiments, n=1. In certain embodiments, n=2. In certain embodiments, n=3, i.e., Ser(Gly<sub>3</sub>Ser)<sub>3</sub>. In certain embodiments, n=4, i.e., Ser(Gly<sub>4</sub>Ser)<sub>4</sub>. In certain embodiments, n=5. In certain embodiments, n=6. In certain embodiments, n=7. In certain embodiments, n=8. In certain embodiments, n=9. In certain embodiments, n=10. Another exemplary gly-ser polypeptide linker comprises the amino acid sequence Ser(Gly<sub>n</sub>Ser)<sub>n</sub>. In certain embodiments, n=1. In certain embodiments, n=2. In certain embodiments, n=3. In certain embodiments, n=4. In certain embodiments, n=5. In certain embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises (Gly<sub>3</sub>Ser)<sub>n</sub>. In certain embodiments, n=1. In certain embodiments, n=2. In certain embodiments, n=3. In certain embodiments, n=4. In certain embodiments, n=5. In certain embodiments, n=6.

**[0255]** In some embodiments, the polypeptide linker is synthetic. As used herein, the term “synthetic” with respect to a polypeptide linker includes peptides (or polypeptides) which comprise an amino acid sequence (which may or may not be naturally occurring) that is linked in a linear sequence of amino acids to a sequence (which may or may not be naturally occurring) to which it is not naturally linked in nature. For example, the polypeptide linker may comprise non-naturally occurring polypeptides which are modified forms of naturally occurring polypeptides (e.g., comprising a mutation such as an addition, substitution or deletion) or which comprise a first amino acid sequence (which may or may not be naturally occurring). Polypeptide linkers may be employed, for instance, to ensure that the variable region, or a variant or fragment thereof, is juxtaposed to ensure proper folding and formation of a functional variable region, or a variant or fragment thereof. Polypeptide linkers may be employed, for instance, to ensure that the polymer (e.g., serum albumin moiety), or a variant or fragment thereof, is juxtaposed to ensure proper folding and formation of a functional polymer (e.g., serum albumin moiety), or a variant or fragment thereof. Preferably, a polypeptide linker will be relatively non-immunogenic and not inhibit any non-covalent association among monomer subunits of a binding protein.

**[0256]** In certain embodiments, the fusion protein comprising a multispecific variable region and a polymer employs a polypeptide linker to join any two or more domains in frame in a single polypeptide chain.

**[0257]** Other linkers that are suitable for use in a fusion protein are known in the art, for example, the serine-rich linkers disclosed in U.S. Pat. No. 5,525,491, the helix forming peptide linkers (e.g., A(EAAAK)<sub>n</sub>A (n=2-5)) disclosed in Arai et al. (*Protein Eng* 2001; 14:529-32), and the stable linkers disclosed in Chen et al. (*Mol Pharm* 2011; 8:457-65), i.e., the dipeptide linker LE, a thrombin-sensitive disulfide cyclopeptide linker, and the alpha-helix forming linker LEA(EAAAK)<sub>4</sub>ALEA(EAAAK)<sub>4</sub>ALE.

**[0258]** In some embodiments, a polypeptide linker for use in the fusion protein described herein, comprises a biologically relevant peptide sequence or a sequence portion thereof. For example, a biologically relevant peptide sequence may include, but is not limited to, sequences derived from an anti-rejection or anti-inflammatory peptide. Said anti-rejection or anti-inflammatory peptides may be selected from the group consisting of a cytokine inhibitory peptide, a cell adhesion inhibitory peptide, a thrombin inhibitory peptide, and a platelet inhibitory peptide. In some embodiments, a polypeptide linker comprises a peptide sequence selected from the group consisting of an IL-1 inhibitory or antagonist peptide sequence, an erythropoietin (EPO)-mimetic peptide sequence, a thrombopoietin (TPO)-mimetic peptide sequence, G-CSF mimetic peptide sequence, a TNF-antagonist peptide sequence, an integrin-binding peptide sequence, a selectin antagonist peptide sequence, an anti-pathogenic peptide sequence, a vasoactive intestinal peptide (VIP) mimetic peptide sequence, a calmodulin antagonist peptide sequence, a mast cell antagonist, a SH3 antagonist peptide sequence, an urokinase receptor (UKR) antagonist peptide sequence, a somatostatin or cortistatin mimetic peptide sequence, and a macrophage and/or T-cell inhibiting peptide sequence. Exemplary peptide sequences, any one of which may be employed as a poly-

peptide linker, are disclosed in U.S. Pat. No. 6,660,843, which is incorporated by reference herein.

**[0259]** Other exemplary linkers include GS linkers (i.e., (GS)<sub>n</sub>), GGSG linkers (i.e., (GGSG)<sub>n</sub>), GSAT linkers, SEG linkers, and GGS linkers (i.e., (GGSGGS)<sub>n</sub>), wherein n is a positive integer (e.g., 1, 2, 3, 4, or 5). Other suitable linkers for use in fusion proteins can be found using publicly available databases, such as the Linker Database ([ibi.vu.nl/programs/linkerdbwww](http://ibi.vu.nl/programs/linkerdbwww)). The Linker Database is a database of inter-domain linkers in multi-functional enzymes which serve as potential linkers in novel fusion proteins (see, e.g., George et al., *Protein Engineering* 2002; 15:871-9).

**[0260]** It will be understood that variant forms of these exemplary polypeptide linkers can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence encoding a polypeptide linker such that one or more amino acid substitutions, additions or deletions are introduced into the polypeptide linker. Mutations may be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis.

**[0261]** Polypeptide linkers are at least one amino acid in length and can be of varying lengths. In one embodiment, a polypeptide linker is from about 1 to about 50 amino acids in length. As used in this context, the term “about” indicates +/- two amino acid residues. Since linker length must be a positive integer, the length of from about 1 to about 50 amino acids in length, means a length of from 1 to 48-52 amino acids in length. In another embodiment, a polypeptide linker is from about 10-20 amino acids in length. In another embodiment, a polypeptide linker is from about 15 to about 50 amino acids in length.

**[0262]** In another embodiment, a polypeptide linker is from about 20 to about 45 amino acids in length. In another embodiment, a polypeptide linker is from about 15 to about 25 amino acids in length. In another embodiment, a polypeptide linker is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, or 61 or more amino acids in length.

**[0263]** Polypeptide linkers can be introduced into polypeptide sequences using techniques known in the art. Modifications can be confirmed by DNA sequence analysis. Plasmid DNA can be used to transform host cells for stable production of the polypeptides produced.

#### Exemplary Fusion Proteins

**[0264]** The fusion proteins of the disclosure are modular and can be configured to incorporate various individual domains. For example, in some embodiments, the fusion protein includes a multispecific variable region comprising the heavy and light chain variable regions set forth in SEQ ID NOs: 1 and 2, respectively. In some embodiments, the fusion protein includes a multispecific variable region comprising the heavy and light chain variable regions set forth in SEQ ID NOs: 11 and 12, respectively. In some embodiments, the fusion protein includes a multispecific variable region comprising the heavy and light chain variable regions set forth in SEQ ID NOs: 21 and 22, respectively.

**[0265]** In some embodiments, the multispecific variable region comprises amino acid substitutions that result in the formation of a cysteine bridge, useful for stabilization of the fusion protein. In some embodiments, the multispecific variable region comprises a heavy chain variable region

comprising the amino acid substitutions G44C, E44C, or Q105C (Kabat numbering). In some embodiments, the multispecific variable region comprises a light chain variable region comprising the amino acid substitutions A43C or Q100C (Kabat numbering). In some embodiments, the multispecific variable region comprises a heavy chain variable region comprising amino acid substitution E44C, and a light chain variable region comprising amino acid substitution Q100C. In some embodiments, the multispecific variable region comprises a heavy chain variable region comprising amino acid substitution G44C, and a light chain variable region comprising amino acid substitution Q100C. In some embodiments, the multispecific variable region comprises a heavy chain variable region comprising amino acid substitution Q105C, and a light chain variable region comprising amino acid substitution A43C.

**[0266]** In some embodiments, the fusion protein includes the HSA set forth in SEQ ID NO: 171. In some embodiments, the fusion protein includes the MSA set forth in SEQ ID NO: 173. In some embodiments, the fusion protein includes the (Gly<sub>4</sub>Ser)<sub>3</sub> linker domain set forth in SEQ ID NO: 178. In some embodiments, the fusion protein includes the secretory leader sequence set forth in SEQ ID NO: 179. In some embodiments, the fusion protein includes the His tag set forth in SEQ ID NO: 181. It will be understood to the skilled artisan that these individual domains can be operably coupled to each other in any order form a fusion protein that is active (e.g., reduces or inhibits the binding of an ELR+CXC chemokine to its cognate receptor). For example, as detailed in the specific examples below, the multispecific variable region comprising the heavy and light chain variable regions set forth in SEQ ID NOs: 1 and 2, is operably coupled to MSA. In another example, the multispecific variable region is operably coupled to MSA via a (Gly<sub>4</sub>Ser)<sub>3</sub> linker domain. In yet another example, the fusion protein comprises the secretory leader sequence set forth in SEQ ID NO: 179.

**[0267]** In some embodiments, a fusion protein comprises a multispecific variable region coupled to a wild-type albumin. In some embodiments, the fusion protein comprises a secretory leader sequence, followed by a wild-type MSA, operably coupled via a (Gly<sub>4</sub>Ser)<sub>3</sub> linker domain to a multispecific variable region comprising heavy and light chain variable regions set forth in SEQ ID NOs: 1 and 2, respectively, operably coupled via a (Gly<sub>4</sub>Ser) linker domain to a His-tag (e.g., SEQ ID NO: 95). In some embodiments, the multispecific variable region comprises the amino acid substitution Q100C within the light chain variable region, and the amino acid substitution G44C within the heavy chain variable region (SEQ ID NO: 98; Kabat numbering). In some embodiments, the multispecific variable region comprises the amino acid substitution A43C within the light chain variable region, and the amino acid substitution Q105C within the heavy chain variable region (SEQ ID NO: 99; Kabat numbering). In one embodiment, the fusion protein lacks the leader sequence and the His-tag (SEQ ID NOs: 160, 163 and 164).

**[0268]** In some embodiments, the fusion protein comprises a secretory leader sequence, followed by a wild-type MSA, operably coupled via a (Gly<sub>4</sub>Ser)<sub>3</sub> linker domain to a multispecific variable region comprising heavy and light chain variable regions set forth in SEQ ID NOs: 11 and 12, respectively, operably coupled via a (Gly<sub>4</sub>Ser) linker domain to a His-tag (e.g., SEQ ID NO: 96). In some embodiments,

the multispecific variable region comprises the amino acid substitution Q100C within the light chain variable region, and the amino acid substitution E44C within the heavy chain variable region (SEQ ID NO: 100; Kabat numbering). In some embodiments, the multispecific variable region comprises the amino acid substitution A43C within the light chain variable region, and the amino acid substitution Q105C within the heavy chain variable region (SEQ ID NO: 101; Kabat numbering). In one embodiment, the fusion protein lacks the leader sequence and the His-tag (SEQ ID NOs: 161, 165 and 166).

**[0269]** In some embodiments, the fusion protein comprises a secretory leader sequence, followed by a wild-type MSA, operably coupled via a (Gly<sub>4</sub>Ser)<sub>3</sub> linker domain to a multispecific variable region comprising heavy and light chain variable regions set forth in SEQ ID NOs: 21 and 22, respectively, operably coupled via a (Gly<sub>4</sub>Ser) linker domain to a His-tag (e.g., SEQ ID NO: 97). In some embodiments, the multispecific variable region comprises the amino acid substitution Q100C within the light chain variable region, and the amino acid substitution G44C within the heavy chain variable region (SEQ ID NO: 104; Kabat numbering). In some embodiments, the multispecific variable region comprises the amino acid substitution A43C within the light chain variable region, and the amino acid substitution Q105C within the heavy chain variable region (SEQ ID NO: 105; Kabat numbering). In one embodiment, the fusion protein lacks the leader sequence and the His-tag (SEQ ID NO: 162, 169 and 170).

**[0270]** In some embodiments, the fusion protein comprises the amino acid sequence set forth in SEQ ID NO: 95. In some embodiments, the fusion protein is encoded by the nucleic acid set forth in SEQ ID NO: 83. In some embodiments, the fusion protein comprises the amino acid sequence set forth in SEQ ID NO: 96. In some embodiments, the fusion protein is encoded by the nucleic acid set forth in SEQ ID NO: 84. In some embodiments, the fusion protein comprises the amino acid sequence set forth in SEQ ID NO: 97. In some embodiments, the fusion protein is encoded by the nucleic acid set forth in SEQ ID NO: 86.

**[0271]** In some embodiments, the fusion protein comprises the amino acid sequence set forth in SEQ ID NO: 160. In some embodiments, the fusion protein is encoded by the nucleic acid set forth in SEQ ID NO: 149. In some embodiments, the fusion protein comprises the amino acid sequence set forth in SEQ ID NO: 161. In some embodiments, the fusion protein is encoded by the nucleic acid set forth in SEQ ID NO: 150. In some embodiments, the fusion protein comprises the amino acid sequence set forth in SEQ ID NO: 162. In some embodiments, the fusion protein is encoded by the nucleic acid set forth in SEQ ID NO: 151.

#### Methods of Making Multispecific Variable Regions and Antibodies

**[0272]** The disclosure also provides methods for producing any of the multispecific variable regions, and isolated monoclonal antibodies, or antigen binding fragments thereof, that bind more than one ELR+ CXC chemokine (e.g., at least two, at least three, at least four, at least five, at least six, at least seven), described herein. In some embodiments, the final processed and active form of an ELR+ CXC chemokine protein is used in the methods described herein.

**[0273]** In some embodiments, the methods described herein can involve, or be used in conjunction with, e.g.,

phage display technologies, bacterial display, yeast surface display, eukaryotic viral display, mammalian cell display, and cell-free (e.g., ribosomal display) antibody screening techniques (see, e.g., Etz et al. (2001) *J Bacteriol* 183:6924-6935; Cornelis (2000) *Curr Opin Biotechnol* 11:450-454; Klemm et al. (2000) *Microbiology* 146:3025-3032; Kieke et al. (1997) *Protein Eng* 10:1303-1310; Yeung et al. (2002) *Biotechnol Prog* 18:212-220; Boder et al. (2000) *Methods Enzymology* 328:430-444; Grabherr et al. (2001) *Comb Chem High Throughput Screen* 4:185-192; Michael et al. (1995) *Gene Ther* 2:660-668; Pereboev et al. (2001) *J Virol* 75:7107-7113; Schaffitzel et al. (1999) *J Immunol Methods* 231:119-135; and Hanes et al. (2000) *Nat Biotechnol* 18:1287-1292).

**[0274]** Methods for identifying multispecific variable regions and/or antibodies using various phage display methods are known in the art. In phage display methods, functional variable region domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. Such phage can be utilized to display antigen-binding domains, such as Fab, Fv, or disulfide-bond stabilized Fv antibody fragments, expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage used in these methods are typically filamentous phage such as fd and M13. The antigen binding domains are expressed as a recombinantly fused protein to any of the phage coat proteins pIII, pVIII, or pIX. See, e.g., Shi et al. (2010) *JMB* 397:385-396. Examples of phage display methods that can be used to make the immunoglobulins, or fragments thereof, described herein include those disclosed in Brinkman et al. (1995) *J Immunol Methods* 182:41-50; Ames et al. (1995) *J Immunol Methods* 184:177-186; Kettleborough et al. (1994) *Eur J Immunol* 24:952-958; Persic et al. (1997) *Gene* 187:9-18; Burton et al. (1994) *Advances in Immunology* 57:191-280; and PCT publication nos. WO 90/02809, WO 91/10737, WO 92/01047, WO 92/18619, WO 93/11236, WO 95/15982, and WO 95/20401. Suitable methods are also described in, e.g., U.S. Pat. Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108.

**[0275]** In some embodiments, the methods described herein further comprise prioritizing crossreactivity over affinity using directed co-evolution, described in further detail in the Examples. For example, using yeast surface display methods described above, output of each cycle of selection is exposed to a diverse array of antigens of interest (e.g., ELR+ CXC chemokines) in the following cycle. In some embodiments, methods that improve both the binding and affinity of variable regions and antibodies are used. Specifically, a high degree of genetic diversity in the antibody encoding genes can be created using error-prone PCR amplification. Binding affinity can be increased by allowing mutants to evolve through consecutive cycles of equilibrium-based selection using decreasing concentrations of the antigens of interest (e.g., ELR+ CXC chemokines). Concurrently, crossreactivity is increased by exposing the outputs of each cycle of affinity selection towards a different antigen of interest (e.g., different ELR+ CXC chemokine) in the following cycle of selection. Variants whose affinity and cross-reactivity towards multiple antigens of interest (e.g., ELR+ CXC chemokines) that are higher than their respective parental clones are collected.

**[0276]** A subpopulation of multispecific variable regions and/or antibodies screened using the above methods can be characterized for their specificity and binding affinity for particular antigens (e.g., chemokines, e.g., ELR+ CXC chemokines) using any immunological or biochemical based method known in the art. For example, specific binding of a multispecific variable region or antibody to a chemokine, may be determined for example using immunological or biochemical based methods such as, but not limited to, an ELISA assay, SPR assays, immunoprecipitation assay, affinity chromatography, and equilibrium dialysis as described above. Immunoassays which can be used to analyze immunospecific binding and cross-reactivity of the antibodies include, but are not limited to, competitive and non-competitive assay systems using techniques such as Western blots, RIA, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, and protein A immunoassays. Such assays are routine and well known in the art.

**[0277]** In embodiments where the selected CDR amino acid sequences are short sequences (e.g., fewer than 10-15 amino acids in length), nucleic acids encoding the CDRs can be chemically synthesized as described in, e.g., Shiraishi et al. (2007) *Nucleic Acids Symposium Series* 51(1):129-130 and U.S. Pat. No. 6,995,259. For a given nucleic acid sequence encoding an acceptor antibody, the region of the nucleic acid sequence encoding the CDRs can be replaced with the chemically synthesized nucleic acids using standard molecular biology techniques. The 5' and 3' ends of the chemically synthesized nucleic acids can be synthesized to comprise sticky end restriction enzyme sites for use in cloning the nucleic acids into the nucleic acid encoding the variable region of the donor antibody.

**[0278]** In some embodiments, the antibodies described herein comprise an altered heavy chain constant region that has reduced (or no) effector function relative to its corresponding unaltered constant region. Effector functions involving the constant region of the antibody may be modulated by altering properties of the constant or Fc region. Altered effector functions include, for example, a modulation in one or more of the following activities: antibody-dependent cellular cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), apoptosis, binding to one or more Fc-receptors, and pro-inflammatory responses. Modulation refers to an increase, decrease, or elimination of an effector function activity exhibited by a subject antibody containing an altered constant region as compared to the activity of the unaltered form of the constant region. In particular embodiments, modulation includes situations in which an activity is abolished or completely absent.

**[0279]** An altered constant region with altered FcR binding affinity and/or ADCC activity and/or altered CDC activity is a polypeptide which has either an enhanced or diminished FcR binding activity and/or ADCC activity and/or CDC activity compared to the unaltered form of the constant region. An altered constant region which displays increased binding to an FcR binds at least one FcR with greater affinity than the unaltered polypeptide. An altered constant region which displays decreased binding to an FcR binds at least one FcR with lower affinity than the unaltered form of the constant region. Such variants which display decreased binding to an FcR may possess little or no appreciable

binding to an FcR, e.g., 0 to 50% (e.g., less than 50, 49, 48, 47, 46, 45, 44, 43, 42, 41, 40, 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1%) of the binding to the FcR as compared to the level of binding of a native sequence immunoglobulin constant or Fc region to the FcR. Similarly, an altered constant region that displays modulated ADCC and/or CDC activity may exhibit either increased or reduced ADCC and/or CDC activity compared to the unaltered constant region. For example, in some embodiments, the antibody comprising an altered constant region can exhibit approximately 0 to 50% (e.g., less than 50, 49, 48, 47, 46, 45, 44, 43, 42, 41, 40, 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1%) of the ADCC and/or CDC activity of the unaltered form of the constant region. An antibody described herein comprising an altered constant region displaying reduced ADCC and/or CDC may exhibit reduced or no ADCC and/or CDC activity.

**[0280]** In some embodiments, an antibody described herein exhibits reduced or no effector function. In some embodiments, an antibody comprises a hybrid constant region, or a portion thereof, such as a G2/G4 hybrid constant region (see e.g., Burton et al. (1992) *Adv Immun* 51:1-18; Canfield et al. (1991) *J Exp Med* 173:1483-1491; and Mueller et al. (1997) *Mol Immunol* 34(6):441-452). See above.

**[0281]** In some embodiments, an antibody may contain an altered constant region exhibiting enhanced or reduced complement dependent cytotoxicity (CDC). Modulated CDC activity may be achieved by introducing one or more amino acid substitutions, insertions, or deletions in an Fc region of the antibody. See, e.g., U.S. Pat. No. 6,194,551. Alternatively or additionally, cysteine residue(s) may be introduced in the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved or reduced internalization capability and/or increased or decreased complement-mediated cell killing. See, e.g., Caron et al. (1992) *J Exp Med* 176:1191-1195 and Shopes (1992) *Immunol* 148:2918-2922; PCT publication nos. WO 99/51642 and WO 94/29351; Duncan and Winter (1988) *Nature* 322:738-40; and U.S. Pat. Nos. 5,648,260 and 5,624,821.

**[0282]** It is understood that the above methods can also be used to determine if, e.g., a multispecific variable region does not bind to full length chemokines, e.g., ELR+ CXC chemokines. The above methods can also be used to determine if a multispecific variable region or antibody that specifically binds to more than one ELR+ CXC chemokine also reduces or inhibits the interaction between the chemokines and their cognate receptors (e.g., CXCR1 and CXCR2).

#### Methods of Making Fusion Proteins

**[0283]** The fusion proteins described herein largely may be made in transformed or transfected host cells using recombinant DNA techniques. To do so, a recombinant DNA molecule coding for the polypeptide is prepared. Methods of preparing such DNA molecules are well known in the art. For instance, sequences coding for the polypeptides could be excised from DNA using suitable restriction enzymes. Alternatively, the DNA molecule could be synthesized using

chemical synthesis techniques, such as the phosphoramidate method. Also, a combination of these techniques could be used.

**[0284]** The disclosure also provides a vector capable of expressing the polypeptides in an appropriate host. The vector comprises the DNA molecule that codes for the polypeptides operably coupled to appropriate expression control sequences. Methods of affecting this operative linking, either before or after the DNA molecule is inserted into the vector, are well known. Expression control sequences include promoters, activators, enhancers, operators, ribosomal nuclease domains, start signals, stop signals, cap signals, polyadenylation signals, and other signals involved with the control of transcription or translation. The nucleic acid molecules described above can be contained within a vector that is capable of directing their expression in, for example, a cell that has been transduced with the vector. Accordingly, in addition to polypeptide mutants, expression vectors containing a nucleic acid molecule encoding a mutant and cells transfected with these vectors are among the certain embodiments.

**[0285]** Vectors suitable for use include T7-based vectors for use in bacteria (see, for example, Rosenberg et al., *Gene* 56: 125, 1987), the pMSXND expression vector for use in mammalian cells (Lee and Nathans, *J. Biol. Chem.* 263: 3521, 1988), and baculovirus-derived vectors (for example the expression vector pBacPAKS from Clontech, Palo Alto, Calif.) for use in insect cells. The nucleic acid inserts, which encode the polypeptide of interest in such vectors, can be operably linked to a promoter, which is selected based on, for example, the cell type in which expression is sought. For example, a T7 promoter can be used in bacteria, a polyhedrin promoter can be used in insect cells, and a cytomegalovirus or metallothionein promoter can be used in mammalian cells. Also, in the case of higher eukaryotes, tissue-specific and cell type-specific promoters are widely available. These promoters are so named for their ability to direct expression of a nucleic acid molecule in a given tissue or cell type within the body. Skilled artisans are well aware of numerous promoters and other regulatory elements which can be used to direct expression of nucleic acids.

**[0286]** In addition to sequences that facilitate transcription of the inserted nucleic acid molecule, vectors can contain origins of replication, and other genes that encode a selectable marker. For example, the neomycin-resistance (neo<sup>r</sup>) gene imparts G418 resistance to cells in which it is expressed, and thus permits phenotypic selection of the transfected cells. Those of skill in the art can readily determine whether a given regulatory element or selectable marker is suitable for use in a particular experimental context.

**[0287]** Viral vectors that are suitable for use include, for example, retroviral, adenoviral, and adeno-associated vectors, herpes virus, simian virus 40 (SV40), and bovine papilloma virus vectors (see, for example, Gluzman (Ed.), *Eukaryotic Viral Vectors*, CSH Laboratory Press, Cold Spring Harbor, N.Y.).

**[0288]** The resulting vector having the DNA molecule thereon is used to transform or transfect an appropriate host. This transformation or transfection may be performed using methods well known in the art.

**[0289]** Any of a large number of available and well-known host cells may be used. The selection of a particular host is dependent upon a number of factors recognized by the art.

These include, for example, compatibility with the chosen expression vector, toxicity of the peptides encoded by the DNA molecule, rate of transformation or transfection, ease of recovery of the peptides, expression characteristics, bio-safety and costs. A balance of these factors must be struck with the understanding that not all hosts may be equally effective for the expression of a particular DNA sequence. Within these general guidelines, useful microbial hosts include bacteria (such as *E. coli*), yeast (such as *Saccharomyces*) and other fungi, insects, plants, mammalian (including human) cells in culture, or other hosts known in the art.

**[0290]** Next, the transformed or transfected host is cultured and purified. Host cells may be cultured under conventional fermentation or culture conditions so that the desired compounds are expressed. Such fermentation and culture conditions are well known in the art. Finally, the peptides are purified from culture by methods well known in the art.

**[0291]** Prokaryotic or eukaryotic cells that contain and express a nucleic acid molecule that encodes a polypeptide mutant are also suitable for use. A cell is a transfected cell, i.e., a cell into which a nucleic acid molecule, for example a nucleic acid molecule encoding a mutant polypeptide, has been introduced by means of recombinant DNA techniques. The progeny of such a cell are also considered suitable for use in the methods disclosed herein.

**[0292]** The precise components of the expression system are not critical. For example, a polypeptide can be produced in a prokaryotic host, such as the bacterium *E. coli*, or in a eukaryotic host, such as an insect cell (e.g., an Sf21 cell), or mammalian cells (e.g., COS cells, NIH 3T3 cells, or HeLa cells). These cells are available from many sources, including the American Type Culture Collection (Manassas, Va.). In selecting an expression system, it matters only that the components are compatible with one another. Artisans or ordinary skill are able to make such a determination. Furthermore, if guidance is required in selecting an expression system, skilled artisans may consult Ausubel et al. (*Current Protocols in Molecular Biology*, John Wiley and Sons, New York, N.Y., 1993) and Pouwels et al. (*Cloning Vectors: A Laboratory Manual*, 1985 Suppl. 1987).

**[0293]** The expressed polypeptides can be purified from the expression system using routine biochemical procedures, and can be used, e.g., as therapeutic agents, as described herein.

**[0294]** The fusion proteins may also be made by synthetic methods. For example, solid phase synthesis techniques may be used. Suitable techniques are well known in the art, and include those described in Merrifield (1973), *Chem. Polypeptides*, pp. 335-61 (Katsoyannis and Panayotis eds.); Merrifield (1963), *J. Am. Chem. Soc.* 85: 2149; Davis et al., *Biochem Intl* 1985; 10: 394-414; Stewart and Young (1969), *Solid Phase Peptide Synthesis*; U.S. Pat. No. 3,941,763; Finn et al. (1976), *The Proteins* (3rd ed.) 2: 105-253; and Erickson et al. (1976), *The Proteins* (3rd ed.) 2: 257-527. Solid phase synthesis is the preferred technique of making individual peptides since it is the most cost-effective method of making small peptides. Compounds that contain derivatized peptides or which contain non-peptide groups may be synthesized by well-known organic chemistry techniques.

**[0295]** Other methods of molecule expression/synthesis are generally known in the art to one of ordinary skill.

### Modification of Polypeptides

**[0296]** The polypeptides described herein (e.g., fusion proteins, or antibodies or antigen-binding fragments thereof) can be modified following their expression and purification. The modifications can be covalent or non-covalent modifications. Such modifications can be introduced into the polypeptides by, e.g., reacting targeted amino acid residues of the polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or terminal residues. Suitable sites for modification can be chosen using any of a variety of criteria including, e.g., structural analysis or amino acid sequence analysis of the antibodies or fragments.

**[0297]** In some embodiments, the polypeptides can be conjugated to a heterologous moiety. The heterologous moiety can be, e.g., a heterologous polypeptide, a therapeutic agent (e.g., a toxin or a drug), or a detectable label such as, but not limited to, a radioactive label, an enzymatic label, a fluorescent label, a heavy metal label, a luminescent label, or an affinity tag such as biotin or streptavidin. Suitable heterologous polypeptides include, e.g., an antigenic tag (e.g., FLAG (DYKDDDDK (SEQ ID NO: 180)), polyhistidine (6-His; HHHHHH (SEQ ID NO: 181)), hemagglutinin (HA; YPYDVPDYA (SEQ ID NO: 182)), glutathione-S-transferase (GST), or maltose-binding protein (MBP)) for use in purifying the antibodies or fragments. Heterologous polypeptides also include polypeptides (e.g., enzymes) that are useful as diagnostic or detectable markers, for example, luciferase, a fluorescent protein (e.g., green fluorescent protein (GFP)), or chloramphenicol acetyl transferase (CAT). Suitable radioactive labels include, e.g.,  $^{32}\text{P}$ ,  $^{33}\text{P}$ ,  $^{14}\text{C}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$ , and  $^3\text{H}$ . Suitable fluorescent labels include, without limitation, fluorescein, fluorescein isothiocyanate (FITC), green fluorescent protein (GFP), DyLight™ 488, phycoerythrin (PE), propidium iodide (PI), PerCP, PE-Alexa Fluor® 700, Cy5, allophycocyanin, and Cy7. Luminescent labels include, e.g., any of a variety of luminescent lanthanide (e.g., europium or terbium) chelates. For example, suitable europium chelates include the europium chelate of diethylene triamine pentaacetic acid (DTPA) or tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA). Enzymatic labels include, e.g., alkaline phosphatase, CAT, luciferase, and horseradish peroxidase.

**[0298]** Two proteins (e.g., an antibody and a heterologous moiety) can be cross-linked using any of a number of known chemical cross linkers. Examples of such cross linkers are those which link two amino acid residues via a linkage that includes a “hindered” disulfide bond. In these linkages, a disulfide bond within the cross-linking unit is protected (by hindering groups on either side of the disulfide bond) from reduction by the action, for example, of reduced glutathione or the enzyme disulfide reductase. One suitable reagent, 4-succinimidylsuccinyl- $\alpha$ -methyl- $\alpha$ -(2-pyridyl)dithio) toluene (SMPT), forms such a linkage between two proteins utilizing a terminal lysine on one of the proteins and a terminal cysteine on the other. Heterobifunctional reagents that cross-link by a different coupling moiety on each protein can also be used. Other useful cross-linkers include, without limitation, reagents which link two amino groups (e.g., N-5-azido-2-nitrobenzoyloxysuccinimide), two sulfhydryl groups (e.g., 1,4-bis-maleimidobutane), an amino group and a sulfhydryl group (e.g., m-maleimidobenzoyl-N-hydroxysuccinimide ester), an amino group and a carboxyl group (e.g., 4-[p-azidosalicylamido]butylamine), and an amino

group and a guanidinium group that is present in the side chain of arginine (e.g., p-azidophenyl glyoxal monohydrate).

**[0299]** In some embodiments, a radioactive label can be directly conjugated to the amino acid backbone of the polypeptide. Alternatively, the radioactive label can be included as part of a larger molecule (e.g.,  $^{125}\text{I}$  in meta- $^{125}\text{I}$ iodophenyl-N-hydroxysuccinimide ( $^{125}\text{I}$ mIPNHS) which binds to free amino groups to form meta-iodophenyl (mIP) derivatives of relevant proteins (see, e.g., Rogers et al. (1997) *J Nucl Med* 38:1221-1229) or chelate (e.g., DOTA or DTPA) which is in turn bound to the protein backbone. Methods of conjugating the radioactive labels or larger molecules/chelates containing them to the polypeptides described herein are known in the art. Such methods involve incubating the proteins with the radioactive label under conditions (e.g., pH, salt concentration, and/or temperature) that facilitate binding of the radioactive label or chelate to the protein (see, e.g., U.S. Pat. No. 6,001,329).

**[0300]** Methods for conjugating a fluorescent label (sometimes referred to as a “fluorophore”) to a protein (e.g., an antibody) are known in the art of protein chemistry. For example, fluorophores can be conjugated to free amino groups (e.g., of lysines) or sulfhydryl groups (e.g., cysteines) of proteins using succinimidyl (NHS) ester or tetrafluorophenyl (TFP) ester moieties attached to the fluorophores. In some embodiments, the fluorophores can be conjugated to a heterobifunctional cross-linker moiety such as sulfo-SMCC. Suitable conjugation methods involve incubating a polypeptide, with the fluorophore under conditions that facilitate binding of the fluorophore to the protein. See, e.g., Welch and Redvanly (2003) “Handbook of Radiopharmaceuticals: Radiochemistry and Applications,” John Wiley and Sons (ISBN 0471495603).

**[0301]** In some embodiments, the polypeptides can be modified, e.g., with a moiety that improves the stabilization and/or retention of the polypeptides in circulation, e.g., in blood, serum, or other tissues. For example, the polypeptide can be PEGylated as described in, e.g., Lee et al. (1999) *Bioconjug Chem* 10(6): 973-8; Kinstler et al. (2002) *Advanced Drug Deliveries Reviews* 54:477-485; and Roberts et al. (2002) *Advanced Drug Delivery Reviews* 54:459-476 or HESylated (Fresenius Kabi, Germany; see, e.g., Pavišić et al. (2010) *Int J Pharm* 387(1-2):110-119). The stabilization moiety can improve the stability, or retention of, the polypeptide by at least 1.5 (e.g., at least 2, 5, 10, 15, 20, 25, 30, 40, or 50 or more) fold.

**[0302]** In some embodiments, the polypeptides described herein can be glycosylated. In some embodiments, a polypeptide described herein can be subjected to enzymatic or chemical treatment, or produced from a cell, such that the polypeptide has reduced or absent glycosylation. Methods for producing polypeptides with reduced glycosylation are known in the art and described in, e.g., U.S. Pat. No. 6,933,368; Wright et al. (1991) *EMBO J* 10(10):2717-2723; and Co et al. (1993) *Mol Immunol* 30:1361.

### Pharmaceutical Compositions and Modes of Administration

**[0303]** In certain embodiments, the invention provides for a pharmaceutical composition comprising a fusion protein, or an isolated monoclonal antibody, or antigen binding fragment thereof, described herein, with a pharmaceutically acceptable diluent, carrier, solubilizer, emulsifier, preservative and/or adjuvant.

**[0304]** In certain embodiments, acceptable formulation materials preferably are nontoxic to recipients at the dosages and concentrations employed. In certain embodiments, the formulation material(s) are for s.c. and/or I.V. administration. In certain embodiments, the pharmaceutical composition can contain formulation materials for modifying, maintaining or preserving, for example, the pH, osmolality, viscosity, clarity, color, isotonicity, odor, sterility, stability, rate of dissolution or release, adsorption or penetration of the composition. In certain embodiments, suitable formulation materials include, but are not limited to, amino acids (such as glycine, glutamine, asparagine, arginine or lysine); antimicrobials; antioxidants (such as ascorbic acid, sodium sulfite or sodium hydrogen-sulfite); buffers (such as borate, bicarbonate, Tris-HCl, citrates, phosphates or other organic acids); bulking agents (such as mannitol or glycine); chelating agents (such as ethylenediamine tetraacetic acid (EDTA)); complexing agents (such as caffeine, polyvinylpyrrolidone, beta-cyclodextrin or hydroxypropyl-beta-cyclodextrin); fillers; monosaccharides; disaccharides; and other carbohydrates (such as glucose, mannose or dextrans); proteins (such as serum albumin, gelatin or immunoglobulins); coloring, flavoring and diluting agents; emulsifying agents; hydrophilic polymers (such as polyvinylpyrrolidone); low molecular weight polypeptides; salt-forming counterions (such as sodium); preservatives (such as benzalkonium chloride, benzoic acid, salicylic acid, thimerosal, phenethyl alcohol, methylparaben, propylparaben, chlorhexidine, sorbic acid or hydrogen peroxide); solvents (such as glycerin, propylene glycol or polyethylene glycol); sugar alcohols (such as mannitol or sorbitol); suspending agents; surfactants or wetting agents (such as pluronics, PEG, sorbitan esters, polysorbates such as polysorbate 20, polysorbate 80, triton, tromethamine, lecithin, cholesterol, tyloxapal); stability enhancing agents (such as sucrose or sorbitol); tonicity enhancing agents (such as alkali metal halides, preferably sodium or potassium chloride, mannitol sorbitol); delivery vehicles; diluents; excipients and/or pharmaceutical adjuvants. (Remington's Pharmaceutical Sciences, 18th Edition, A. R. Gennaro, ed., Mack Publishing Company (1995). In certain embodiments, the formulation comprises PBS; 20 mM NaOAC, pH 5.2, 50 mM NaCl; and/or 10 mM NAOAC, pH 5.2, 9% Sucrose. In certain embodiments, the optimal pharmaceutical composition will be determined by one skilled in the art depending upon, for example, the intended route of administration, delivery format and desired dosage. See, for example, Remington's Pharmaceutical Sciences, supra. In certain embodiments, such compositions may influence the physical state, stability, rate of in vivo release and rate of in vivo clearance of the fusion protein, or isolated monoclonal antibody, or antigen binding fragment, described herein.

**[0305]** In certain embodiments, the primary vehicle or carrier in a pharmaceutical composition can be either aqueous or non-aqueous in nature. For example, in certain embodiments, a suitable vehicle or carrier can be water for injection, physiological saline solution or artificial cerebrospinal fluid, possibly supplemented with other materials common in compositions for parenteral administration. In certain embodiments, the saline comprises isotonic phosphate-buffered saline. In certain embodiments, neutral buffered saline or saline mixed with serum albumin are further exemplary vehicles. In certain embodiments, pharmaceutical compositions comprise Tris buffer of about pH 7.0-8.5,

or acetate buffer of about pH 4.0-5.5, which can further include sorbitol or a suitable substitute therefore. In certain embodiments, a composition comprising a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, described herein, can be prepared for storage by mixing the selected composition having the desired degree of purity with optional formulation agents (Remington's Pharmaceutical Sciences, supra) in the form of a lyophilized cake or an aqueous solution. Further, in certain embodiments, a composition comprising a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, described herein, can be formulated as a lyophilizate using appropriate excipients such as sucrose.

**[0306]** In certain embodiments, the pharmaceutical composition can be selected for parenteral delivery. In certain embodiments, the compositions can be selected for inhalation or for delivery through the digestive tract, such as orally. The preparation of such pharmaceutically acceptable compositions is within the ability of one skilled in the art.

**[0307]** In certain embodiments, the formulation components are present in concentrations that are acceptable to the site of administration. In certain embodiments, buffers are used to maintain the composition at physiological pH or at a slightly lower pH, typically within a pH range of from about 5 to about 8.

**[0308]** In certain embodiments, when parenteral administration is contemplated, a therapeutic composition can be in the form of a pyrogen-free, parenterally acceptable aqueous solution comprising a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, described herein, in a pharmaceutically acceptable vehicle. In certain embodiments, a vehicle for parenteral injection is sterile distilled water in which a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, described herein, are formulated as a sterile, isotonic solution, properly preserved. In certain embodiments, the preparation can involve the formulation of the desired molecule with an agent, such as injectable micro spheres, bio-erodible particles, polymeric compounds (such as polylactic acid or polyglycolic acid), beads or liposomes, that can provide for the controlled or sustained release of the product which can then be delivered via a depot injection. In certain embodiments, hyaluronic acid can also be used, and can have the effect of promoting sustained duration in the circulation. In certain embodiments, implantable drug delivery devices can be used to introduce the desired molecule.

**[0309]** In certain embodiments, a pharmaceutical composition can be formulated for inhalation. In certain embodiments, a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, can be formulated as a dry powder for inhalation. In certain embodiments, an inhalation solution comprising a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, can be formulated with a propellant for aerosol delivery. In certain embodiments, solutions can be nebulized. Pulmonary administration is further described in PCT application No. PCT/US94/001875, which describes pulmonary delivery of chemically modified proteins.

**[0310]** In certain embodiments, it is contemplated that formulations can be administered orally. In certain embodiments, a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, that is administered in this fashion can be formulated with or without those carriers customarily used in the compounding of solid dosage forms such as

tablets and capsules. In certain embodiments, a capsule can be designed to release the active portion of the formulation at the point in the gastrointestinal tract when bioavailability is maximized and pre-systemic degradation is minimized. In certain embodiments, at least one additional agent can be included to facilitate absorption of the fusion protein, or isolated monoclonal antibody, or antigen binding fragment. In certain embodiments, diluents, flavorings, low melting point waxes, vegetable oils, lubricants, suspending agents, tablet disintegrating agents, and binders can also be employed.

**[0311]** In certain embodiments, a pharmaceutical composition can involve an effective quantity of the fusion protein, or isolated monoclonal antibody, or antigen binding fragment, in a mixture with non-toxic excipients which are suitable for the manufacture of tablets. In certain embodiments, by dissolving the tablets in sterile water, or another appropriate vehicle, solutions can be prepared in unit-dose form. In certain embodiments, suitable excipients include, but are not limited to, inert diluents, such as calcium carbonate, sodium carbonate or bicarbonate, lactose, or calcium phosphate; or binding agents, such as starch, gelatin, or acacia; or lubricating agents such as magnesium stearate, stearic acid, or talc.

**[0312]** Additional pharmaceutical compositions will be evident to those skilled in the art, including formulations involving a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, in sustained- or controlled-delivery formulations. In certain embodiments, techniques for formulating a variety of other sustained- or controlled-delivery means, such as liposome carriers, bio-erodible microparticles or porous beads and depot injections, are also known to those skilled in the art. See for example, PCT Application No. PCT/US93/00829 which describes the controlled release of porous polymeric microparticles for the delivery of pharmaceutical compositions. In certain embodiments, sustained-release preparations can include semipermeable polymer matrices in the form of shaped articles, e.g. films, or microcapsules. Sustained release matrices can include polyesters, hydrogels, polylactides (U.S. Pat. No. 3,773,919 and EP 058,481), copolymers of L-glutamic acid and gamma ethyl-L-glutamate (Sidman et al., *Biopolymers*, 22:547-556 (1983)), poly (2-hydroxyethyl-methacrylate) (Langer et al., *J. Biomed. Mater. Res.*, 15: 167-277 (1981) and Langer, *Chem. Tech.*, 12:98-105 (1982)), ethylene vinyl acetate (Langer et al., *supra*) or poly-D(-)-3-hydroxybutyric acid (EP 133,988). In certain embodiments, sustained release compositions can also include liposomes, which can be prepared by any of several methods known in the art. See, e.g., Eppstein et al, *Proc. Natl. Acad. Sci. USA*, 82:3688-3692 (1985); EP 036,676; EP 088,046 and EP 143,949.

**[0313]** The pharmaceutical composition to be used for in vivo administration typically is sterile. In certain embodiments, this can be accomplished by filtration through sterile filtration membranes. In certain embodiments, where the composition is lyophilized, sterilization using this method can be conducted either prior to or following lyophilization and reconstitution. In certain embodiments, the composition for parenteral administration can be stored in lyophilized form or in a solution. In certain embodiments, parenteral compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

**[0314]** In certain embodiments, once the pharmaceutical composition has been formulated, it can be stored in sterile vials as a solution, suspension, gel, emulsion, solid, or as a dehydrated or lyophilized powder. In certain embodiments, such formulations can be stored either in a ready-to-use form or in a form (e.g., lyophilized) that is reconstituted prior to administration.

**[0315]** In certain embodiments, kits are provided for producing a single-dose administration unit. In certain embodiments, the kit can contain both a first container having a dried protein and a second container having an aqueous formulation. In certain embodiments, kits containing single and multi-chambered pre-filled syringes (e.g., liquid syringes and lysyringes) are included.

**[0316]** In certain embodiments, the effective amount of a pharmaceutical composition comprising a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, to be employed therapeutically will depend, for example, upon the therapeutic context and objectives. One skilled in the art will appreciate that the appropriate dosage levels for treatment, according to certain embodiments, will thus vary depending, in part, upon the molecule delivered, the indication for which a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, are being used, the route of administration, and the size (body weight, body surface or organ size) and/or condition (the age and general health) of the patient. In certain embodiments, the clinician can titer the dosage and modify the route of administration to obtain the optimal therapeutic effect.

**[0317]** In certain embodiments, the frequency of dosing will take into account the pharmacokinetic parameters of a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, in the formulation used. In certain embodiments, a clinician will administer the composition until a dosage is reached that achieves the desired effect. In certain embodiments, the composition can therefore be administered as a single dose, or as two or more doses (which may or may not contain the same amount of the desired molecule) over time, or as a continuous infusion via an implantation device or catheter. Further refinement of the appropriate dosage is routinely made by those of ordinary skill in the art and is within the ambit of tasks routinely performed by them. In certain embodiments, appropriate dosages can be ascertained through use of appropriate dose-response data.

**[0318]** In certain embodiments, the route of administration of the pharmaceutical composition is in accord with known methods, e.g. orally, through injection by intravenous, intraperitoneal, intracerebral (intra-parenchymal), intracerebroventricular, intramuscular, subcutaneously, intra-ocular, intraarterial, intraportal, or intralesional routes; by sustained release systems or by implantation devices. In certain embodiments, the compositions can be administered by bolus injection or continuously by infusion, or by implantation device. In certain embodiments, individual elements of the combination therapy may be administered by different routes.

**[0319]** In certain embodiments, the composition can be administered locally via implantation of a membrane, sponge or another appropriate material onto which the desired molecule has been absorbed or encapsulated. In certain embodiments, where an implantation device is used, the device can be implanted into any suitable tissue or organ, and delivery of the desired molecule can be via diffusion,



timed-release bolus, or continuous administration. In certain embodiments, it can be desirable to use a pharmaceutical composition comprising a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, in an ex vivo manner. In such instances, cells, tissues and/or organs that have been removed from the patient are exposed to a pharmaceutical composition comprising a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, after which the cells, tissues and/or organs are subsequently implanted back into the patient.

**[0320]** In certain embodiments, a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, can be delivered by implanting certain cells that have been genetically engineered, using methods such as those described herein, to express and secrete the polypeptides. In certain embodiments, such cells can be animal or human cells, and can be autologous, heterologous, or xenogeneic. In certain embodiments, the cells can be immortalized. In certain embodiments, in order to decrease the chance of an immunological response, the cells can be encapsulated to avoid infiltration of surrounding tissues. In certain embodiments, the encapsulation materials are typically biocompatible, semi-permeable polymeric enclosures or membranes that allow the release of the protein product(s) but prevent the destruction of the cells by the patient's immune system or by other detrimental factors from the surrounding tissues.

#### Kits

**[0321]** A kit can include a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, as disclosed herein, and instructions for use. The kits may comprise, in a suitable container, a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, one or more controls, and various buffers, reagents, enzymes and other standard ingredients well known in the art.

**[0322]** The container can include at least one vial, well, test tube, flask, bottle, syringe, or other container means, into which a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, may be placed, and in some instances, suitably aliquoted. Where an additional component is provided, the kit can contain additional containers into which this component may be placed. The kits can also include a means for containing a fusion protein, or isolated monoclonal antibody, or antigen binding fragment, and any other reagent containers in close confinement for commercial sale. Such containers may include injection or blow-molded plastic containers into which the desired vials are retained. Containers and/or kits can include labeling with instructions for use and/or warnings.

#### Methods of Treatment

**[0323]** The compositions described herein are useful in, inter alia, methods for treating or preventing a variety of autoimmune and related disorders, allergy, inflammation, and/or graft or transplant rejection in a subject. The compositions can be administered to a subject, e.g., a human subject, using a variety of methods that depend, in part, on the route of administration. The route can be, e.g., intravenous injection or infusion (IV), subcutaneous injection (SC), intraperitoneal (IP) injection, intramuscular injection (IM), or intrathecal injection (IT). The injection can be in a bolus or a continuous infusion.

**[0324]** Administration can be achieved by, e.g., local infusion, injection, or by means of an implant. The implant can be of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. The implant can be configured for sustained or periodic release of the composition to the subject. See, e.g., U.S. Patent Application Publication No. 20080241223; U.S. Pat. Nos. 5,501,856; 4,863,457; and 3,710,795; EP488401; and EP 430539, the disclosures of each of which are incorporated herein by reference in their entirety. The composition can be delivered to the subject by way of an implantable device based on, e.g., diffusive, erodible, or convective systems, e.g., osmotic pumps, biodegradable implants, electrodiffusion systems, electroosmosis systems, vapor pressure pumps, electrolytic pumps, effervescent pumps, piezoelectric pumps, erosion-based systems, or electromechanical systems.

**[0325]** In some embodiments, a fusion protein, or antibody or antigen-binding fragment thereof, is therapeutically delivered to a subject by way of local administration.

**[0326]** A suitable dose of a fusion protein, or antibody or antigen-binding fragment thereof described herein, which dose is capable of treating or preventing autoimmune and related disorders in a subject, can depend on a variety of factors including, e.g., the age, sex, and weight of a subject to be treated and the particular inducer compound used. For example, a different dose of a whole antibody may be required to treat a subject with autoimmune disease as compared to the dose of a fusion protein required to treat the same subject. Other factors affecting the dose administered to the subject include, e.g., the type or severity of the autoimmune disorder. For example, a subject having rheumatoid arthritis may require administration of a different dosage than a subject with Guillain-Barre syndrome. Other factors can include, e.g., other medical disorders concurrently or previously affecting the subject, the general health of the subject, the genetic disposition of the subject, diet, time of administration, rate of excretion, drug combination, and any other additional therapeutics that are administered to the subject. It should also be understood that a specific dosage and treatment regimen for any particular subject will also depend upon the judgment of the treating medical practitioner (e.g., doctor or nurse). Suitable dosages are described herein.

**[0327]** A pharmaceutical composition can include a therapeutically effective amount of a fusion protein, or antibody or antigen-binding fragment thereof described herein. Such effective amounts can be readily determined by one of ordinary skill in the art based, in part, on the effect of the administered antibody, or the combinatorial effect of the antibody and one or more additional active agents, if more than one agent is used. A therapeutically effective amount of an antibody or fragment thereof described herein can also vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the antibody (and one or more additional active agents) to elicit a desired response in the individual, e.g., reduction in tumor growth. For example, a therapeutically effective amount of a fusion protein can inhibit (lessen the severity of or eliminate the occurrence of) and/or prevent a particular disorder, and/or any one of the symptoms of the particular disorder known in the art or described herein. A therapeutically effective

amount is also one in which any toxic or detrimental effects of the composition are outweighed by the therapeutically beneficial effects.

**[0328]** Suitable human doses of any of the fusion proteins, or antibodies or fragments thereof described herein can further be evaluated in, e.g., Phase I dose escalation studies. See, e.g., van Gorp et al. (2008) *Am J Transplantation* 8(8):1711-1718; Hanouska et al. (2007) *Clin Cancer Res* 13(2, part 1):523-531; and Hetherington et al. (2006) *Anti-microbial Agents and Chemotherapy* 50(10): 3499-3500.

**[0329]** In some embodiments, the composition contains any of the fusion proteins, or antibodies or antigen-binding fragments thereof described herein and one or more (e.g., two, three, four, five, six, seven, eight, nine, 10, or 11 or more) additional therapeutic agents such that the composition as a whole is therapeutically effective. For example, a composition can contain a fusion protein described herein and an anti-inflammatory agent, wherein the fusion protein and agent are each at a concentration that when combined are therapeutically effective for treating or preventing autoimmune and related disorders (e.g., rheumatoid arthritis) in a subject.

**[0330]** Toxicity and therapeutic efficacy of such compositions can be determined by known pharmaceutical procedures in cell cultures or experimental animals (e.g., animal models of any of the cancers described herein). These procedures can be used, e.g., for determining the LD<sub>50</sub> (the dose lethal to 50% of the population) and the ED<sub>50</sub> (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD<sub>50</sub>/ED<sub>50</sub>. A fusion protein, or antibody or antigen-binding fragment thereof that exhibits a high therapeutic index is preferred. While compositions that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue and to minimize potential damage to normal cells and, thereby, reduce side effects.

**[0331]** The data obtained from the cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such fusion proteins, or antibodies or antigen-binding fragments thereof lies generally within a range of circulating concentrations of the antibodies or fragments that include the ED<sub>50</sub> with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For a fusion protein described herein, the therapeutically effective dose can be estimated initially from cell culture assays. A dose can be formulated in animal models to achieve a circulating plasma concentration range that includes the IC<sub>50</sub> (i.e., the concentration of the fusion protein which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography. In some embodiments, e.g., where local administration (e.g., to the eye or a joint) is desired, cell culture or animal modeling can be used to determine a dose required to achieve a therapeutically effective concentration within the local site.

**[0332]** In some embodiments, the methods can be performed in conjunction with other therapies for autoimmune and related diseases. For example, the composition can be administered to a subject at the same time, prior to, or after,

radiation, surgery, targeted or cytotoxic chemotherapy, anti-inflammatory therapy, steroid therapy, chemoradiotherapy, hormone therapy, immunotherapy, immunosuppressive therapy, antithyroid therapy, antibiotic therapy, gene therapy, cell transplant therapy, precision medicine, genome editing therapy, or other pharmacotherapy.

**[0333]** The compositions described herein (e.g., fusion protein compositions) can be used to treat graft rejection and/or a variety of allergy or autoimmune disorders such as, but not limited to, Crohn's disease, multiple sclerosis, myasthenia gravis, rheumatoid arthritis, Goodpasture's syndrome, T-cell mediated hepatitis, graft vs. host disease, autoimmune uveitis, and/or autoimmune diabetes.

**[0334]** In some embodiments, a fusion protein, or an antibody or an antigen-binding fragment thereof described herein can be administered to a subject as a monotherapy. Alternatively, as described above, the fusion protein, or the antibody or fragment thereof can be administered to a subject as a combination therapy with another treatment, e.g., another treatment for an autoimmune or related disease. For example, the combination therapy can include administering to the subject (e.g., a human patient) one or more additional agents that provide a therapeutic benefit to a subject who has, or is at risk of developing, an autoimmune or related diseases. In some embodiments, a fusion protein, or an antibody and the one or more additional active agents are administered at the same time. In other embodiments, the fusion protein, or antibody or antigen binding fragment thereof is administered first in time and the one or more additional active agents are administered second in time. In some embodiments, the one or more additional active agents are administered first in time and the fusion protein, or antibody or antigen binding fragment thereof is administered second in time.

**[0335]** A fusion protein, or an antibody or an antigen-binding fragment thereof described herein can replace or augment a previously or currently administered therapy. For example, upon treating with a fusion protein, or an antibody or antigen-binding fragment thereof, administration of the one or more additional active agents can cease or diminish, e.g., be administered at lower levels. In some embodiments, administration of the previous therapy can be maintained. In some embodiments, a previous therapy will be maintained until the level of the fusion protein, or the antibody reaches a level sufficient to provide a therapeutic effect. The two therapies can be administered in combination.

**[0336]** Monitoring a subject (e.g., a human patient) for an improvement in an autoimmune or related disease, as defined herein, means evaluating the subject for a change in a disease parameter, e.g., a reduction in inflammation. In some embodiments, the evaluation is performed at least one (1) hour, e.g., at least 2, 4, 6, 8, 12, 24, or 48 hours, or at least 1 day, 2 days, 4 days, 10 days, 13 days, 20 days or more, or at least 1 week, 2 weeks, 4 weeks, 10 weeks, 13 weeks, 20 weeks or more, after an administration. The subject can be evaluated in one or more of the following periods: prior to beginning of treatment; during the treatment; or after one or more elements of the treatment have been administered. Evaluation can include evaluating the need for further treatment, e.g., evaluating whether a dosage, frequency of administration, or duration of treatment should be altered. It can also include evaluating the need to add or drop a selected

therapeutic modality, e.g., adding or dropping any of the treatments for an autoimmune or related disease described herein.

**[0337]** As ELR+ CXC chemokines are responsible for inducing neutrophil infiltration to sites of inflammation, in some embodiments a fusion protein or an antibody or an antigen-binding fragment thereof described herein, is administered to prevent or block neutrophil infiltration in a subject with an autoimmune disorder. In some embodiments, the fusion protein or antibody, or antigen-binding fragment thereof, prevents or blocks infiltration of neutrophils into the synovial fluid of arthritic joints. Methods of measuring neutrophil infiltration are known in the art. For example, bodily fluid from a subject (e.g., synovial fluid) is collected, cells are isolated and stained with a neutrophil cell marker (e.g., Ly6G), and assessed via flow cytometry. Exemplary methods are described in Miyabe, Y., Kim, N. D., Miyabe, C. & Luster, A. D. Studying Chemokine Control of Neutrophil Migration In Vivo in a Murine Model of Inflammatory Arthritis. *Methods in enzymology* 570, 207-231 (2016), herein incorporated by reference.

#### EXAMPLES

**[0338]** While the present disclosure has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the disclosure. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the present disclosure. All such modifications are intended to be within the scope of the disclosure.

#### Materials and Methods

##### Cloning of CXC Chemokines for Mammalian Cell Line Expression

**[0339]** Human and murine CXC chemokines undergo proteolysis in vivo resulting in molecules with altered structure and tuned activity. To avoid that in vitro engineered cross-reactive binders might not be able to block the mature form in vivo, the final processed and active form of the protein was cloned and produced. The CXC chemokines were produced in mammalian cell lines thus avoiding refolding procedures while preserving their native structure and activity. CXCL chemokines were cloned as C-terminal fusion of the immunoglobulin fragment crystallizable (Fc) domain (<sup>N</sup>Fc-CXCL<sup>C</sup>) and as N-terminal fusion of the murine serum albumin (SA) protein (<sup>N</sup>CXCL-SA<sup>C</sup>). All mammalian expression vectors were based on gWiz (Genlantis) containing an optimized human cytomegalovirus (CMV) promoter and a Kanamycin antibiotic resistance gene (Kan).

**[0340]** Constructs for expression of <sup>N</sup>Fc-CXCL<sup>C</sup> fusion proteins were generated by using a modified Pfu DNA polymerase-mediated site-directed mutagenesis protocol (Geiser, M., Cebe, R., Drewello, D. & Schmitz, R. Integration of PCR fragments at any specific site within cloning vectors without the use of restriction enzymes and DNA ligase. *Biotechniques* 31, 88-90, 92 (2001)). PfuUltra II Fusion HS DNA Polymerase was obtained from Agilent Technologies, DpnI enzyme from New England Biolabs and the oligonucleotide primers from Integrated DNA Tech-

nologies. The synthetic DNA coding for the active form of three highly diverse human and murine ELR+ CXC chemokines were obtained from GeneArt Gene Synthesis (Thermo Fisher Scientific). Genes were codon-optimized for expression in mammalian cells. A sequence encoding for Gly-Gly dipeptide spacer (G2, <sup>N</sup>GG<sup>C</sup>) followed by a 15 amino acid peptide sequence (AviTag) containing a defined lysine for site-specific biotinylation (<sup>N</sup>GLNDIFEAQKIEWHE<sup>C</sup>) were inserted at the C-terminus of the ELR+ CXC chemokine to obtain <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> synthetic genes. The AviTag sequence for enzymatically biotinylation was placed at the well tolerated C-terminus of the ELR+ CXC chemokines to (i) preserve unaltered the functional N-terminus region, (ii) avoid loss of epitope recognition and (iii) prevent additional structural heterogeneity that could be triggered by performing a chemistry-based amine-reactive succinimidyl esters based biotinylation. The de novo synthesized <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> synthetic sequences were subsequently inserted into a previously modified gWiz expression vector containing a DNA sequence encoding for a secretory leader peptide sequence (<sup>N</sup>MRVPAQLLGLLLLWLPGARC<sup>C</sup>), a Fc domain derived from murine IgG2 heavy-chain constant regions CH2 and CH3, followed by a sequence encoding a hexa-histidine tag (His6; <sup>N</sup>HHHHHH<sup>C</sup>), an eight amino-acid flexible linker (<sup>N</sup>SSGVDLGT<sup>C</sup>) and a Tobacco Etch Virus proteolytic cleavage site (TEV; <sup>N</sup>ENLYFQ:A/V<sup>C</sup>) to obtain the final <sup>N</sup>Fc-His6-linker-TEV-CXCL-G2-AviTag<sup>C</sup> fusion proteins (FIG. 1). The His6-tag was inserted between the Fc domain and the TEV cleavage site for further purification steps. The sequence TEV proteolytic cleavage site allowed for a precisely processed N-terminus of the chemokines that was crucial for their activity. All constructs were verified by DNA sequencing (Macrogen) and termed Fc-CXCL fusion proteins (see Table 1 for information about protein accession number SEQ ID NOs: 31-42 for DNA and amino acid sequences).

TABLE 1

CXCL protein (residues/ accession No.)	Construct for expression	Fusion protein
Groα/hCXCL1 (38-107/P09341)	gWiz-LS-Fc(mIgG2)-His <sub>6</sub> -linker-TEV-hCXCL1 <sup>38-107</sup> -G <sub>2</sub> -AviTag	<sup>N</sup> Fc-hCXCL1 <sup>C</sup>
ENA-78/hCXCL5 (43-114/P42830)	gWiz-LS-Fc(mIgG2)-His <sub>6</sub> -linker-TEV-hCXCL5 <sup>43-114</sup> -G <sub>2</sub> -AviTag	<sup>N</sup> Fc-hCXCL5 <sup>C</sup>
IL-8/hCXCL8 (29-99/P10145)	gWiz-LS-Fc(mIgG2)-His <sub>6</sub> -linker-TEV-hCXCL8 <sup>29-99</sup> -G <sub>2</sub> -AviTag	<sup>N</sup> Fc-hCXCL8 <sup>C</sup>
KC/mCXCL1 (28-96/P12850)	gWiz-LS-Fc(mIgG2)-His <sub>6</sub> -linker-TEV-mCXCL1 <sup>28-96</sup> -G <sub>2</sub> -AviTag	<sup>N</sup> Fc-mCXCL1 <sup>C</sup>
MIP-2/mCXCL2 (31-100/P10889)	gWiz-LS-Fc(mIgG2)-His <sub>6</sub> -linker-TEV-mCXCL2 <sup>31-100</sup> -G <sub>2</sub> -AviTag	<sup>N</sup> Fc-mCXCL2 <sup>C</sup>
LIX/mCXCL5 (48-118/P50228)	gWiz-LS-Fc(mIgG2)-His <sub>6</sub> -linker-TEV-mCXCL5 <sup>48-118</sup> -G <sub>2</sub> -AviTag	<sup>N</sup> Fc-mCXCL5 <sup>C</sup>

**[0341]** Constructs for expression of <sup>N</sup>CXCL-SA<sup>C</sup> fusion proteins were generated by using DNA assembly methods such as Gibson Assembly (New England Biolabs) and In-Fusion Cloning (Clontech Laboratories, Takara Bio) technologies. PfuUltra II Fusion HS DNA Polymerase (Agilent Technologies) and Herculase II Fusion DNA Polymerase (Agilent Technologies) were used for the PCR amplification of the insert and the vector, respectively. DpnI enzyme was obtained from New England Biolabs and the oligonucleotide primers from Integrated DNA Technologies.

**[0342]** The synthetic DNA coding for the active protein form of twelve human and murine (ELR+) CXC chemokines and eight human and murine (ELR-) CXC chemokines were obtained from GeneArt Gene Synthesis (Thermo Fisher Scientific). Genes were codon-optimized for expression in mammalian cells. The de novo synthesized  $^N$ CXCL $^C$  synthetic sequences were subsequently inserted into a previously modified gWiz expression vector containing a DNA sequence encoding for a secretory leader sequence ( $^N$ MRVPAQLLGLLLLWLPGAR $^C$ ), a ten amino-acid flexible linker ( $^N$ GGGGSGGGGS $^C$ ), sequence encoding for mouse serum albumin (SA) followed by a sequence encoding for a five amino-acid flexible spacer ( $^N$ GGGGGS $^C$ ) and a hexa-histidine tag (His $_6$ ;  $^N$ HHHHHH $^C$ ) to obtain  $^N$ CXCL-(G $_4$ G) $_2$ -SA-G $_4$ S-His $_6$  $^C$  fusion proteins. The process of the leader sequence during the secretory pathway allows for a precisely cleaved N-terminus that is crucial for the activity of the chemokines. Genes encoding  $^N$ CXCL(G $_4$ G) $_2$ -SA-G $_4$ S-His $_6$  $^C$  fusion proteins were further sub-cloned into a new gWiz expression vector via Sail-HF (New England Biolabs) and MauBI (Thermo Fisher Scientific) restriction enzymes. All constructs were verified by DNA sequencing (Macrogen) and termed  $^N$ CXCL-SA $^C$  fusion proteins (see Table 2 for information about protein accession number and SEQ ID NOs: 43-82 for DNA and amino-acid sequences).

#### Expression and Purification of Fc Fusion Proteins

**[0343]** Fc fusion proteins  $^N$ Fc-CXCL $^C$  were expressed by transient transfection of suspension-adapted human embryonic kidney (HEK-293) cells. Protein production was performed either in house using FreeStyle 293 Expression System (Thermo Fisher Scientific) or outsourced to the Protein Expression Core Facility (PECF) of the Life Science Faculty of the EPFL, as described previously (Angelini, A. et al. Bicyclic peptide inhibitor reveals large contact interface with a protease target. *ACS Chem Biol* 7, 817-821 (2012); Angelini, A. et al. Chemical macrocyclization of peptides fused to antibody Fc fragments. *Bioconjug Chem* 23, 1856-1863 (2012); Zhu, E. F. et al. Synergistic innate and adaptive immune response to combination immunotherapy with anti-tumor antigen antibodies and extended serum half-life IL-2. *Cancer Cell* 27, 489-501 (2015)). At the end of the 7-day phase production, cells were harvested by centrifugation at 15,000×g for 30 minutes at 4° C. on an Avanti JXN-26 Centrifuge (Beckman Coulter). Any additional cell debris was removed from the medium by filtration through 0.22- $\mu$ m PES membrane filters (Thermo Fisher Scientific) and the clarified medium diluted with  $\frac{1}{10}$  volume 10× PBS pH 7.4.

TABLE 2

CXCL protein (residues/ accession No.)	Construct for expression	Fusion protein
Gro $\alpha$ /hCXCL1 (35-107/P09341)	gWiz-LS-hCXCL1 <sup>35-107</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL1-SA $^C$
Gro $\beta$ /hCXCL2 (35-107/P19875)	gWiz-LS-hCXCL2 <sup>35-107</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL2-SA $^C$
Groy/hCXCL3 (35-107/P19876)	gWiz-LS-hCXCL3 <sup>35-107</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL3-SA $^C$
PF-4/hCXCL4 (32-101/P02776)	gWiz-LS-hCXCL4 <sup>32-101</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL4-SA $^C$
ENA-78/hCXCL5 (44-114/P42830)	gWiz-LS-hCXCL5 <sup>44-114</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL5-SA $^C$
GCP-2/hCXCL6 (43-114/P80162)	gWiz-LS-hCXCL6 <sup>43-114</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL6-SA $^C$
NAP-2/hCXCL7 (59-121/P02775)	gWiz-LS-hCXCL7 <sup>59-121</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL7-SA $^C$
IL-8/hCXCL8 (28-99/P10145)	gWiz-LS-hCXCL8 <sup>28-99</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL8-SA $^C$
MIG/hCXCL9 (23-125/Q07325)	gWiz-LS-hCXCL9 <sup>23-125</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL9-SA $^C$
IP-10/hCXCL10-SA (22-98/P02778)	gWiz-LS-hCXCL10 <sup>22-98</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL10-SA $^C$
I-TAC/hCXCL11-SA (22-94/O14625)	gWiz-LS-hCXCL11 <sup>22-94</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ hCXCL11-SA $^C$
KC/mCXCL1-SA (25-96/P12850)	gWiz-LS-mCXCL1 <sup>25-96</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL1-SA $^C$
MIP-2/mCXCL2-SA (28-100/P10889)	gWiz-LS-mCXCL2 <sup>28-100</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL2-SA $^C$
DCIP-1/mCXCL3-SA (28-100/Q6W5C0)	gWiz-LS-mCXCL3 <sup>28-100</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL3-SA $^C$
Pf-4/mCXCL4-SA (30-105/Q9Z126)	gWiz-LS-mCXCL4 <sup>30-105</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL4-SA $^C$
LIX/mCXCL5-SA (48-118/P50228)	gWiz-LS-mCXCL5 <sup>48-118</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL5-SA $^C$
Nap-2/mCXCL7-SA (48-113/Q9EQI5)	gWiz-LS-mCXCL7 <sup>48-113</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL7-SA $^C$
Mig/mCXCL9-SA (22-126/P18340)	gWiz-LS-mCXCL9 <sup>22-126</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL9-SA $^C$
Ip-10/mCXCL10-SA (22-98/P17515)	gWiz-LS-mCXCL10 <sup>22-98</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL10-SA $^C$
I-Tac/mCXCL11-SA (22-100/Q9JHH5)	gWiz-LS-mCXCL11 <sup>22-100</sup> -(Gly $_4$ Ser) $_2$ -mouse SA-(Gly $_4$ Ser)-His $_6$	$^N$ mCXCL11-SA $^C$

**[0344]** Recombinant Fc fusions were captured on a rProtein A Sepharose Fast Flow resin (GE Healthcare), packed on a glass Econo-Column Chromatography column (Bio-Rad), that was previously equilibrated with 10 column volumes (CVs) of 1×PBS pH 7.4. The filter culture media was passed through the resin at a flow rate of approximately 2.5 mL/min at room temperature. The resin was then extensively washed with 10 CVs of 1×PBS pH 7.4 and the recombinant Fc fusions eluted in a single peak by applying 10 CVs of elution Buffer E (50 mM Glycine-HCl, pH 2.7). 2 CVs of neutralizing Buffer N (1 M Tris-HCl pH 8.5) were then immediately added to the eluted Fc fusion proteins to prevent protein denaturation. Eluted Fc fusions were diluted twice with 1×PBS pH 7.4 and concentrated by using 10000 NMWL Amicon Ultra-15 ultrafiltration devices (Millipore) at 4000× g and 4° C. on a Allegra X14R centrifuge (Beckman Coulter). The concentrated Fc fusion proteins were further subjected to size-exclusion chromatography (SEC) by using a HiPrep 26/10 desalting column (GE Healthcare) connected to an AKTApurifier system (GE Healthcare) equilibrated with Buffer T (50 mM Tris-HCl, 100 mM NaCl, 0.5 mM EDTA, pH 8.0). Purified Fc fusion proteins <sup>N</sup>Fc-CXCL<sup>C</sup> in Buffer T were further concentrated to 2 mg/mL by using 10000 NMWL Amicon Ultra-15 ultrafiltration devices (Millipore) at 4000×g and 4° C. on a Allegra X-14R centrifuge (Beckman Coulter) and cleaved by using recombinant TEV protease (0.5 mg/mL). Fc fusion:TEV at a molar ratio of 100:1 were incubated at 4° C. for up to 24 hours in a cleavage Buffer T supplemented with a 10:1 ratio of reduced (GSH) to oxidized (GSSG) L-glutathione (50 mM Tris-HCl, 100 mM NaCl, 0.5 mM EDTA, 3 mM GSH, 0.3 mM GSSG, pH 8.0) and complete protease inhibitor cocktail (Roche).

**[0345]** The further separation of matured cleaved CXC chemokines from the (i) Fc domain, (ii) un-cleaved Fc-CXCL fusion and (iii) recombinant TEV-His6 protease was performed by loading the cleavage mixture on a Ni Sepharose excel affinity resin (GE Healthcare), packed on a glass Econo-Column Chromatography column (Bio-Rad), that was previously equilibrated with 10 CVs of Buffer X (50 mM sodium phosphate, 500 M NaCl, pH 8.0). The mixture was passed through the resin at a flow rate of approximately 1 mL/min at room temperature and the flow-through containing cleaved <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins collected. The purified <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins were further concentrated by using a 3000 NMWL Amicon Ultra-15 ultrafiltration devices (Millipore) at 4000× g and 4° C. on a Allegra X-14R centrifuge (Beckman Coulter) and subjected to SEC by using a HiLoad 16/600 Superdex 75 prep-grade column (GE Healthcare) equilibrated with biotinylation Buffer R (50 mM Bicine, pH 8.3) on an AKTApurifier system (GE Healthcare). Purified <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins in Buffer R were then concentrated to approximately 100 μM by using 3000 NMWL Amicon Ultra-4 ultrafiltration devices (Millipore) at 4000× g and 4° C. on a Allegra X-14R centrifuge (Beckman Coulter).

**[0346]** Biotinylation of <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins was performed by using BirA enzyme (Avidity) according to manufacturer's guidelines. Briefly, enzymatic reaction included 50 nmol <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> protein in Buffer R, 12 μg of recombinant BirA enzyme (3 mg/mL; Avidity), 50 μM d-biotin, 10 mM ATP pH 7.2 and 10 mM MgOAc for a total volume of 1 mL. To ensure complete biotinylation, the reaction was incubated at 4° C. for 48 hours with gentle

shaking and jumped started every 12 hours by adding 50 μL of Biomix-A (500 mM Bicine, pH 8.3; Avidity) and 50 μL of Biomix-B (100 mM ATP, 100 mM MgOAc, 500 μM d-biotin; Avidity) to the reaction mix. These conditions were sufficient for complete quantitative reaction yielding one product with expected molecular mass ( $\Delta_{\text{mass}}=226$  Da).

**[0347]** Biotinylated <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins were further purified by using either reversed-phase high performance liquid chromatography (RP-HPLC) or SEC. RP-HPLC was performed on a Vydac C18 column (Grace & Co.) connected to a Waters HPLC system (Waters). A flow rate of 1 mL/min and a linear gradient was applied with a mobile phase composed of eluant A (99.9% v/v H<sub>2</sub>O and 0.1% v/v TFA) and eluant B (99.9% v/v ACN and 0.1% v/v TFA). This step efficiently removed unbound small molecules such as free biotin and ATP along with the BirA enzyme. Purified and biotinylated <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins were lyophilized, dissolved in 1×PBS pH 7.4 to a final protein concentration of approximately 100 μM, flash frozen in liquid nitrogen and stored at -80° C. Alternatively, biotinylated <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins were purified by SEC using a Superdex 75 10/300 GL column (GE Healthcare) equilibrated with 1×PBS pH 7.4 and connected to an AKTApurifier system (GE Healthcare).

**[0348]** The final purified and biotinylated proteins were further concentrated by using 3000 NMWL Amicon Ultra-0.5 centrifugal filter units (Millipore) at 14000× g and 4° C. on a Eppendorf 5702R centrifuge (Eppendorf) to a final protein concentration of approximately 100 μM, flash frozen in liquid nitrogen and stored at -80° C. After purification, the yield of pure and biotinylated <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins ranged from 1 to 5 mg/L of culture. Molecular weights were confirmed by reducing sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) using NuPAGE 4-12% Bis-Tris Gels (Thermo Fisher Scientific) in 2-(N-morpholino)ethanesulfonic acid (MES) buffer followed by SimplyBlue SafeStain (Thermo Fisher Scientific) and imaged on the Typhoon Trio imager (GE Healthcare). Biotinylated <sup>N</sup>CXCL-G2-AviTag<sup>C</sup> proteins migrated a single band in SDS-PAGE, with apparent molecular masses of about 8-10 kDa.

#### Mass Spectrometric Analysis

**[0349]** The molecular mass of each ELR+ CXC chemokine before and after biotinylation was determined with electrospray ionization mass spectrometry (ESI-MS) performed on a quadrupole time-of-flight mass spectrometer (Q-TOF) coupled to a C<sup>3</sup> or C<sup>8</sup> reversed phase HPLC column for desalting of protein samples. Both LC-MS Agilent 6520 ESI-Q-TOF (Agilent Technologies) and Waters LCT ESI-Q-TOF (Waters) systems, operated in a positive ionization mode, were used. Data were acquired, processed, and analyzed using the Agilent MassHunter (Agilent Technologies) or the MassLynx (Waters) software package. Mass spectrometry (i) confirmed the corrected mass of the purified biotinylated chemokines and (ii) showed that no un-biotinylated protein remains in the final sample.

Selection of Crossreactive Binders from a Naïve Library of Synthetic scFv Displayed on the Surface of Yeast

**[0350]** Crossreactive protein binders to human and murine ELR+ CXC chemokines based on the synthetic antibody single-chain variable fragment scaffold (scFv) were isolated using standard yeast surface display technology as previ-

ously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). The yeast-displayed synthetic antibody naïve library “G” was constructed using homologous recombination-based methods as previously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015); Van Deventer, J. A., Kelly, R. L., Rajan, S., Wittrup, K. D. & Sidhu, S. S. A switchable yeast display/secretion system. *Protein Eng Des Sel* 28, 317-325 (2015)). The library was constructed to display the synthetic scFv variants on the surface of yeast as C-terminal fusion of the a-agglutinin Aga2 protein ( ${}_{N}CXCL$ -Aga2p<sup>C</sup>).

**[0351]** Yeast surface display vectors were based on pCT-CON backbone and included a secretory leader sequence ( ${}^NMQLLRCFSIFSIVIASVLA^C$ ), a sequence encoding for the Aga2p protein, a sequence encoding for the influenza hemagglutinin epitope tag (HA;  ${}^NYPYDVPDYA^C$ ), a fifteen amino-acid flexible linker ( ${}^NGGGGSGGGGSGGGGS^C$ ), a sequence encoding for the synthetic scFv in the light ( $V_L$ ) to heavy ( $V_H$ ) chain orientation, separated by another fifteen amino-acid flexible linker ( ${}^NGTTAASGSSGSSSGA^C$ ). A sequence encoding for c-myc epitope tag (c-myc;  ${}^NEQKLLSEEDLQ^C$ ) was inserted at the C-terminus of the gene encoding the scFv to obtain  ${}^N$ Aga2p-HA-(G<sub>4</sub>S)3-V<sub>L</sub>-linker-V<sub>H</sub>-c-myc<sup>C</sup> fusion proteins.

**[0352]** Yeast display selection was performed by using an amount of yeast cells at least ten-fold larger than (i) the initial estimated naïve library size ( $1 \times 10^9$  unique clones) or (ii) the number of cells isolated from the previous round of either magnetic bead screening or flow cytometry sorting. The yeast cells display naïve library were grown in SD-CAA medium at 30° C. with shaking (250 rpm) and surface protein expression induced in galactose-containing SG-CAA media for 20 hours at 20° C. with shaking (250 rpm) as previously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). Before positive selection, yeast populations ( $1 \times 10^{10}$ ) underwent three sequential cycles of “negative” selection using uncoated Dynabeads biotin binder magnetic beads (Thermo Fisher Scientific). Ten-fold diversity library depleted of streptavidin-coated beads binders was screened against highly diverse human (hCXCL1, hCXCL5 and hCXCL8) and murine (mCXCL1, mCXCL1 and mCXCL5) biotinylated ELR+ CXC chemokines captured on magnetic beads. Two iterative cycles of magnetic bead selections followed by four cycles of fluorescence-activated cell sorting (FACS) were applied (FIG. 2B).

**[0353]** Complex positive selection schemes, in which ten-fold of the cell output isolated from a pathway was incubated with a diverse ELR+ CXC chemokine target in the following pathway, were performed to force crossreactivity and thus enhance the probabilities of isolating crossreactive protein binders. Each cycle comprised growth of yeast cells, expression of the synthetic antibodies on the surface, binding to the immobilized CXC ELR+ chemokine ligands, washing and expansion of the isolated bound yeast cells as previously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). Cells were washed using ice-cold PBSA buffer (1× PBS pH 7.4 supplemented with 0.1% w/v bovine serum albumin fraction V). For FACS, highly crossreactive protein binders were selected using a two-color labeling scheme

based on fluorescent-conjugated detection reagents for expression (anti-c-myc epitope tag) and binding to ELR+ CXC chemokine (anti-biotin) at recommended dilutions. Notably, highly avidity magnetic and fluorescently labeled reagents (e.g. streptavidin and neutravidin) saturated with diverse biotinylated ELR+ CXC chemokines were used during the all the six selection cycles.

**[0354]** The use of highly avid reagents increased the likelihood of isolating crossreactive low affinity binders from the naïve library by exploiting the multivalent interaction between yeast cells and the preloaded target. Sorting was performed on BD FACSAria I and III sorter instruments (BD Biosciences) and data evaluated using FlowJo v.10.0.7 software (Tree Star). After six cycles of iterative selections, DNA plasmid was extracted from isolated yeast cells using Zymoprep Yeast Plasmid Miniprep II Kit (Zymo Research). Extracted DNA plasmids were further amplified in *Escherichia coli*, purified and used (i) to reveal the amino acid sequence of each selected protein binder by DNA sequencing (Macrogen), (ii) to transform new yeast cells to determine the binding affinity of single protein binder using yeast cell surface titrations, and (iii) as template to prepare mutagenized DNA for further library generation and co-evolution of both binding affinity and crossreactivity, as described below.

#### Single Antibody Clone Binding Affinity Characterization Using Yeast Surface Titrations

**[0355]** The equilibrium dissociation constant ( $K_D$ ) of each individual selected protein binder towards single CXC chemokines was determined by using yeast surface display titrations as described previously (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). Yeast surface display combined to flow cytometry allowed measurement of  $K_D$  directly on the surface of yeast cells without the need for additional sub-cloning, expression and purification steps that were instead necessary to characterize protein binders clones isolated using alternative display technologies (VanAntwerp, J. J. & Wittrup, K. D. Fine affinity discrimination by yeast surface display and flow cytometry. *Biotechnol Prog* 16, 31-37 (2000)). Importantly, the  $K_D$  values measured using such method have been shown to be consistent with values obtained using alternative techniques for examining binding affinities such as Surface Plasmon Resonance (SPR), Bio-Layer Interferometry (BLI) and Kinetic Exclusion Assay (KinExA flow fluorimeter) (Razai, A. et al. Molecular evolution of antibody affinity for sensitive detection of botulinum neurotoxin type A. *J Mol Biol* 351, 158-169 (2005); Traxlmayr, M. W. et al. Strong Enrichment of Aromatic Residues in Binding Sites from a Charge-Neutralized Hyperthermostable Sso7d Scaffold Library. *J Biol Chem* (2016)).

**[0356]** In brief, DNA plasmids encoding single protein binder clones were transformed into genetically modified *Saccharomyces cerevisiae* yeast cells (EBY100 strain) using Frozen-EZ Yeast Transformation II Kit (Zymo Research) and plated on selective SD-CAA solid agar media. Individual colonies were inoculated in 5 mL SD-SCAA cultures, grown to mid-log phase (OD<sub>600</sub>=2-5) in SD-CAA media at 30° C. with shaking (250 rpm). Cells were induced in galactose-containing SG-CAA media for 20 hours at 20° C. with shaking (250 rpm) as previously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast

Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). The binding assays were conducted in 96-well plates (Corning) containing  $1 \times 10^4$  induced cells per well. Non-displaying yeast cells ( $1 \times 10^5$ ) were added to each well and mixed to induced cells to ensure (i) proper cell pelleting and (ii) an excess of soluble CXC chemokine target over total number of yeast displayed protein binders ( $5 \times 10^4$  copies of protein/yeast cell) in solution (Hackel, B. J., Kapila, A. & Wittrup, K. D. Picomolar affinity fibronectin domains engineered utilizing loop length diversity, recursive mutagenesis, and loop shuffling. *Journal of molecular biology* 381, 1238-1252 (2008)). Yeast cells displaying protein binders were incubated with varying concentration of soluble CXC chemokine fusions ( $^N$ CXCL-SA $^S$ ) bearing the His6 tag and the primary chicken anti-c-myc epitope tag (1:1000) antibody (Gallus Immunotech) overnight at 4° C. with shaking (150 rpm). Twelve to sixteen different concentrations of pure  $^N$ CXCL-SA $^C$  fusion proteins, ranging from 10 pM to 10  $\mu$ M, were applied spanning a range of concentrations ten times both above and below the expected  $K_D$  value. After primary incubation, cells were pelleted (2500 $\times$  g for 5 min at 4° C.) and washed twice with 200  $\mu$ L ice-cold PBSA buffer. Secondary labeling was performed with goat anti-chicken and mouse anti-His6 epitope tag antibodies conjugated to Alexa Fluor dyes at recommended dilutions.

**[0357]** The 96-well plates were run on a high-throughput plate sampler iQue Screener (IntelliCyt) or individually analyzed on an Accuri C6 Flow Cytometer (BD Accuri Cytometers). Data were evaluated using FlowJo v.10.0.7 software (Tree Star). To ensure that the differences in binding were not due to variations of number of proteins expressed on the surface of yeast cell, the median fluorescence intensity (MFI $_{BIND}$ ) from binding signal (His6 tag) was normalized to the median fluorescence intensity (MFI $_{DISP}$ ) from display signal (c-myc tag). The normalized (binding/display=MFI $_{BIND}$ /MFI $_{DISP}$ ) median fluorescence intensity as a function of CXC chemokine concentration was used to determine the  $K_D$  values for all clones of interest. Values reported here are the results of three independent experiments and are presented as mean (dots) $\pm$ SE (bars).

#### Co-Evolution of Protein Binding Affinity and Crossreactivity by Yeast Surface Display

**[0358]** Two series of random mutagenesis and FACS-based selections (namely I and II) were applied to improve both the binding affinity and crossreactivity of three cross-reactive clones: CK1, CK2 and CK4. Random mutagenesis libraries were generated by error-prone PCR as previously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). To ensure a mutagenesis rate of approximately 1-2 amino acid mutated residues distributed randomly throughout the entire gene, 1 ng of DNA template encoding the CK1, CK2 and CK4 binders were PCR amplified for 15 cycles using Taq DNA polymerase (New England BioLabs), analogue nucleotides (2  $\mu$ M 8-oxo-dGTP and 2  $\mu$ M dPTP) and flanking oligonucleotide primers (forward: 5'-GGAGGCGGTAGCGGAGGCG-GAGGGTCGGCTAGC-3'; reverse: 5'-GTCCTCTTCAGAAATAAGCTTTTGTTTCGGAT-3'; Integrated DNA Technologies).

**[0359]** The mutagenized PCR products were further purified, re-amplified for additional 30 cycles in the absence of analogue nucleotides and combined with Sall-HF, NheI-HF

and BamHI-HI (New England BioLabs) digested pCT-CON vector at a molar ratio of 2.5:1. Pre-mixed DNA linearized vector and PCR insert (1  $\mu$ m/ $\mu$ L) was electroporated into freshly prepared *Saccharomyces cerevisiae* EBY100 competent cells, where the full constructs are reassembled via homologous recombination (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). Transformed cultures were recovered and expanded in SD-SCAA. Small portions of transformed cells were serially diluted and titrated on SD-SCAA plates to confirm the final reported library sizes (Table 3). Library quality and diversity was further assessed by sequencing twenty colonies of each library. All clones sequenced from the mutagenized libraries were found to be in the expected format. The yeast cells display mutagenized libraries were grown in SD-CAA medium at 30° C. with shaking (250 rpm) and surface protein expression induced in galactose-containing SG-CAA media for 20 hours at 20° C. with shaking (250 rpm) as previously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)).

TABLE 3

Library name	Template	Library size
CK1-lib I	CK1	$1.0 \times 10^8$
CK2-lib I	CK2	$2.0 \times 10^8$
CK4-lib I	CK4	$8.0 \times 10^7$
CK1-lib II	CK19	$3.0 \times 10^8$
CK2-lib II	CK41	$5.0 \times 10^8$
CK4-lib II	CK50	$4.0 \times 10^8$

**[0360]** An amount of yeast cells at least ten-fold larger than the estimated mutagenized libraries size were screened against human (hCXCL1, hCXCL5 and hCXCL8) and murine (hCXCL1, hCXCL2 and hCXCL5) biotinylated ELR+ CXC chemokines using equilibrium-based selection strategies. Six sequential cycles of FACS were applied. Each cycle comprised growth of yeast cells, expression of the binders on the surface, binding to the immobilized CXC ELR+ chemokine ligands, washing and expansion of the isolated bound yeast cells as previously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). Complex selection schemes, in which ten-fold of the cell output isolated from a pathway was incubated with a diverse ELR+ CXC chemokine target in the following pathway, were performed to force crossreactivity and thus enhance the probabilities of isolating crossreactive protein binders. Decreasing concentrations [C] of biotinylated CXC ELR+ chemokines up to ten-fold below the measured  $K_D$  were used for each round of selection ( $[C]=0.1 \times K_D$ ) in order to select for crossreactive clones with improved affinity. Secondary fluorescent-conjugated detection reagents for FACS were constantly alternated to avoid enrichments of clones that could bind to them. Sorting was performed on BD FACSAria I and III sorter instruments (BD Biosciences) and data evaluated using FlowJo v.10.0.7 software (Tree Star). After six cycles of iterative selections, DNA plasmid was extracted from isolated yeast cells and used for further DNA sequencing and single clone characterization as described above.

### Combination of Individual Mutations by Site-Directed Mutagenesis

**[0361]** Individual mutations from different protein binders were combined to further enhance affinity and specificity. A third step of site directed mutagenesis (namely III) was applied to combine mutations derived from different CK1 and CK2 lineage-derived clones. Site-directed mutagenesis was performed by whole plasmid PCR using QuikChange site directed mutagenesis kit (Agilent Technologies) and pairs of complementary primers carrying single point mutations (Integrated DNA Technologies). The DNA sequences encoding CK63, CK66 and CK72 (CK1 lineage) and CK108, CK111 and CK119 (CK2 lineage) were used as templates to generate fifteen (CK131-CK145) and thirteen (CK146-CK158) variants, respectively, each including different combinations of CDR and FWR mutations. All constructs were verified by DNA sequencing (Macrogen).

**[0362]** Single mutants were displayed on the surface of *Saccharomyces cerevisiae* strain EBY100 using Frozen-EZ Yeast Transformation II Kit (Zymo Research) and plated on selective SD-CAA solid agar media. Individual colonies were inoculated in 5 mL SD-SCAA cultures, grown to mid-log phase (OD<sub>600</sub>=2-5) in SD-CAA media at 30° C. with shaking (250 rpm). Cells were induced in galactose-containing SG-CAA media for 20 hours at 20° C. with shaking (250 rpm) as previously described (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). The equilibrium dissociation constant ( $K_D$ ) of each individual clone towards single CXC chemokines was determined by using yeast surface display titrations combined to flow cytometry as described above.

### Cloning of Selected Synthetic scFv Fused to Mouse Serum Albumin Protein for Mammalian Cell Line Expression

**[0363]** Selected crossreactive synthetic single light ( $V_L$ ) and heavy ( $V_H$ ) chain antibody variable fragments (scFv) were cloned and expressed in mammalian cells as C-terminal fusion of the murine serum albumin (SA) protein ( $^N$ SA-scFv $^C$ ). Mammalian expression vectors were based on gWiz (Genlantis). Constructs for expression of  $^N$ SA-scFv $^C$  fusion proteins were generated by using DNA assembly methods such as Gibson Assembly (New England BioLabs) or In-Fusion Cloning (Clontech Laboratories, Takara Bio) technologies. PfuUltra II Fusion HS DNA Polymerase (Agilent Technologies) and Herculase II Fusion DNA Polymerase (Agilent Technologies) were used for the PCR amplification of the insert and the vector, respectively. DpnI enzyme was obtained from New England Biolabs and oligonucleotide primers from Integrated DNA Technologies. The DNA sequences encoding the scFv ( $V_L$ - $V_H$  orientation) CK129, CK138 and CK157 as well as separate  $V_L$  and  $V_H$  domains of CK157 were amplified in a PCR reaction by using the pCT-CON vector as template and following inserted into a previously modified gWiz expression vector containing a DNA sequence encoding for a secretory leader peptide sequence ( $^N$ MDMRVPAQLLGLLLWLPGARC $^C$ ) fol-

lowed by a sequence encoding the mouse serum albumin (SA), a fifteen amino-acid flexible linker ( $^N$ GGGGS $^C$ ). A sequence encoding for a five amino-acid flexible linker ( $^N$ GGGGS $^C$ ) followed by a hexa-histidine tag (His6;  $^N$ HHHHHH $^C$ ) was inserted at the C-terminus of the gene encoding the scFv to obtain the final  $^N$ SA-(G<sub>4</sub>S)<sub>3</sub>-scFv-G<sub>4</sub>S-His6 $^C$ ,  $^N$ SA-(G<sub>4</sub>S)<sub>3</sub>V<sub>L</sub>-G<sub>4</sub>S-His6 $^C$  and  $^N$ SA-(G<sub>4</sub>S)<sub>3</sub>-V<sub>H</sub>-His6 $^C$  fusion proteins (FIG. 6). In a similar fashion, the control scFv ( $V_H$ - $V_L$  orientation) targeting the human carcinoembryonic antigen (CEA) (Graft, C. P., Chester, K., Begent, R. & Wittrup, K. D. Directed evolution of an anti-carcinoembryonic antigen scFv with a 4-day monovalent dissociation half-time at 37 degrees C. *Protein Eng Des Sel* 17, 293-304 (2004)) was fused at the C-terminus of mouse serum albumin. The stability of the each scFv was further improved by connecting the  $V_L$  and  $V_H$  domains via an intermolecular disulfide bond (ds). The addition of stabilizing intermolecular disulfide bridges is reported to increase the percent of monomeric forms by permanently fixing monomer:dimer ratios during the purification steps. Two of the most favorable locations were selected for the introduction of pairs of cysteine residues into each single scFv (dsl: VL100 and VH44; ds2: VL43 and VH105; Kabat numbering system) (Reiter, Y. et al. Stabilization of the Fv fragments in recombinant immunotoxins by disulfide bonds engineered into conserved framework regions. *Biochemistry* 33, 5451-5459 (1994); Jung, S. H., Pastan, I. & Lee, B. Design of interchain disulfide bonds in the framework region of the Fv fragment of the monoclonal antibody B3. *Proteins* 19, 35-47 (1994); Weatherill, E. E. et al. Towards a universal disulphide stabilised single chain Fv format: importance of interchain disulphide bond location and vL-vH orientation. *Protein Eng Des Sel* 25, 321-329 (2012); Kabat, E. A., Wu, T. T., Perry, H., Gottesman, K. and Foeller, C. Sequences of Proteins of Immunological Interest, Edn. Fifth Edition. (1991)) and their relative effects on expression, percent monomer formation and retention of antigen binding compared. Cysteine residues were introduced into each scFv by site-directed mutagenesis using DNA assembly methods such as Gibson-Assembly (New England BioLabs) or In-Fusion Cloning (Clontech Laboratories, Takara Bio) technologies and standard oligonucleotide primers carrying single point mutations (Integrated DNA Technologies). Final genes encoding  $^N$ SA-(G<sub>4</sub>S)<sub>3</sub>-scFv-G<sub>4</sub>S-His6 $^C$ ,  $^N$ SA-(G<sub>4</sub>S)<sub>3</sub>-scFv-ds1-G<sub>4</sub>S-His6 $^C$ ,  $^N$ SA-(G<sub>4</sub>S)<sub>3</sub>-scFv-ds2-G<sub>4</sub>S-His6 $^C$ ,  $^N$ SA-(G<sub>4</sub>S)<sub>3</sub>-V<sub>L</sub>-G<sub>4</sub>S-His6 $^C$  and  $^N$ SA-(G<sub>4</sub>S)<sub>3</sub>-V<sub>H</sub>-G<sub>4</sub>S-His6 $^C$  fusion proteins were further subcloned into a new gWiz expression vector via NotI-HF and XbaI (New England BioLabs) restriction enzymes. All constructs were verified by DNA sequencing (Macrogen, Cambridge, Mass.) and termed  $^N$ CXCL-SA $^C$  fusion proteins (see Table 4 for information about protein accession number and SEQ ID NOS: 83-106 for DNA and amino-acid sequences). The serum albumin-antibody fusion formats were used for all in vitro and in vivo studies.

TABLE 4

Fusion protein (code name)	Construct for expression
$^N$ SA-CK138 $^C$ (SA138)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv ( $V_L$ - $V_H$ ) CK138-(Gly <sub>4</sub> Ser)-His <sub>6</sub>
$^N$ SA-CK157 $^C$ (SA157)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv ( $V_L$ - $V_H$ ) CK157-(Gly <sub>4</sub> Ser)-His <sub>6</sub>



TABLE 4-continued

Fusion protein (code name)	Construct for expression
<sup>N</sup> SA-CK129 <sup>C</sup> (SA129)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv (V <sub>L</sub> -V <sub>H</sub> ) CK129-(Gly <sub>4</sub> Ser)-His <sub>6</sub>
<sup>N</sup> SA-CK138-ds1 <sup>C</sup> (SA138-ds1)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv (V <sub>L</sub> -V <sub>H</sub> ) CK138-ds1 (V <sub>L</sub> 100 <sup>Q&lt;sup&gt;C</sup> /V <sub>H</sub> 44 <sup>Q&lt;sup&gt;C</sup> )-(Gly <sub>4</sub> Ser)-His <sub>6</sub>
<sup>N</sup> SA-CK138-ds2 <sup>C</sup> (SA138-ds2)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv (V <sub>L</sub> -V <sub>H</sub> ) CK138-ds2 (V <sub>L</sub> 43 <sup>A&lt;sup&gt;C</sup> /V <sub>H</sub> 105 <sup>Q&lt;sup&gt;C</sup> )-(Gly <sub>4</sub> Ser)-His <sub>6</sub>
<sup>N</sup> SA-CK157-ds1 <sup>C</sup> (SA157-ds1)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv (V <sub>L</sub> -V <sub>H</sub> ) CK157-ds1 (V <sub>L</sub> 100 <sup>Q&lt;sup&gt;C</sup> /V <sub>H</sub> 44 <sup>Q&lt;sup&gt;C</sup> )-(Gly <sub>4</sub> Ser)-His <sub>6</sub>
<sup>N</sup> SA-CK157-ds2 <sup>C</sup> (SA157-ds2)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv (V <sub>L</sub> -V <sub>H</sub> ) CK157-ds2 (V <sub>L</sub> 43 <sup>A&lt;sup&gt;C</sup> /V <sub>H</sub> 105 <sup>Q&lt;sup&gt;C</sup> )-(Gly <sub>4</sub> Ser)-His <sub>6</sub>
<sup>N</sup> SA-CK157-VL <sup>C</sup> (SA157-VL)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser)-V <sub>L</sub> CK157-His <sub>6</sub>
<sup>N</sup> SA-CK157-VH <sup>C</sup> (SA157-VH)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser)-V <sub>H</sub> CK157-His <sub>6</sub>
<sup>N</sup> SA-CK129-ds1 <sup>C</sup> (SA129-ds1)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv (V <sub>L</sub> -V <sub>H</sub> ) CK129-ds1 (V <sub>L</sub> 100 <sup>Q&lt;sup&gt;C</sup> /V <sub>H</sub> 44 <sup>Q&lt;sup&gt;C</sup> )-(Gly <sub>4</sub> Ser)-His <sub>6</sub>
<sup>N</sup> SA-CK129-ds2 <sup>C</sup> (SA129-ds2)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv (V <sub>L</sub> -V <sub>H</sub> ) CK129-ds2 (V <sub>L</sub> 43 <sup>A&lt;sup&gt;C</sup> /V <sub>H</sub> 105 <sup>Q&lt;sup&gt;C</sup> )-(Gly <sub>4</sub> Ser)-His <sub>6</sub>
<sup>N</sup> SA-sm3e-ds <sup>C</sup> (SActr)	gWiz-LS-mouse SA-(Gly <sub>4</sub> Ser) <sub>3</sub> -scFv (V <sub>H</sub> -V <sub>L</sub> ) sm3E-ds (V <sub>H</sub> 44 <sup>R&lt;sup&gt;C</sup> /V <sub>L</sub> 100 <sup>Q&lt;sup&gt;C</sup> )-(Gly <sub>4</sub> Ser)-His <sub>6</sub>

#### Expression and Purification of Serum Albumin Fusion Proteins

**[0364]** Serum albumin (SA) fusion proteins <sup>N</sup>CXCL-SA<sup>C</sup> and <sup>N</sup>SA-scFv<sup>C</sup> were expressed by transient transfection of suspension-adapted human embryonic kidney (HEK-293) cells. Protein production was performed either in house using FreeStyle 293 Expression System (Thermo Fisher Scientific) or outsourced to the Protein Expression Core Facility (PECF) of the Life Science Faculty of the EPFL, as described previously (Angelini, A. et al. Bicyclic peptide inhibitor reveals large contact interface with a protease target. *ACS Chem Biol* 7, 817-821 (2012); Angelini, A. et al. Chemical macrocyclization of peptides fused to antibody Fc fragments. *Bioconjug Chem* 23, 1856-1863 (2012); Zhu, E. F. et al. Synergistic innate and adaptive immune response to combination immunotherapy with anti-tumor antigen antibodies and extended serum half-life IL-2. *Cancer Cell* 27, 489-501 (2015)). At the end of the 7-day phase production, cells were harvested by centrifugation at 15,000×g for 30 minutes at 4° C. on an Avanti JXN-26 Centrifuge (Beckman Coulter). Any additional cell debris was removed from the medium by filtration through 0.22-µm PES membrane filters (Thermo Fisher Scientific) and the clarified medium diluted with 1/10 volume Buffer A (500 mM sodium phosphate, 5 M NaCl, pH 8.0). Recombinant SA fusions were captured on a Ni Sepharose excel affinity resin (GE Healthcare), packed on a glass Econo-Column chromatography column (Bio-Rad), that was previously equilibrated with 10 CVs of Buffer B (50 mM sodium phosphate, 500 M NaCl, pH 8.0). The medium was passed through the resin at a flow rate of approximately 2.5 mL/min at room temperature. The resin was then extensively washed with 10 CVs of Buffer B and the recombinant SA fusions eluted in a single peak by applying 10 CVs of Buffer C (50 mM sodium phosphate, 500 M NaCl, 500 mM Imidazole, pH 8.0). Eluted SA fusions were following diluted with 10 CVs of Buffer B and concentrated by using 10000 NMWL Amicon Ultra-15 ultrafiltration devices (Millipore) at 4000× g and 4° C. on a Allegra X-14R centrifuge (Beckman Coulter). The concentrated SA fusion proteins were further purified by size exclusion chromatography using a HiLoad 16/600 Superdex 200 prep-grade column (GE Healthcare) equilibrated with 1×PBS pH 7.4 on an

AKTApurifier system (GE Healthcare). Purified SA fusion proteins in 1×PBS pH 7.4 were following concentrated to 5 mg/ml (<sup>N</sup>CXCL-SA<sup>C</sup>) and 2 mg/mL (<sup>N</sup>SA-scFv<sup>C</sup>) final concentration by using 10000 NMWL Amicon Ultra-15 ultrafiltration devices (Millipore) at 4000× g and 4° C. on a Allegra X-14R centrifuge (Beckman Coulter).

**[0365]** Protein concentrations were determined by measuring absorbance at 280 nm using a NanoDrop 2000 spectrophotometer (Thermo Fisher Scientific). Molecular weights were confirmed by reducing sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) using NuPAGE 4-12% Bis-Tris Gels (Life Technologies) in 3-(N-morpholino) propanesulfonic acid (MOPS) buffer followed by SimplyBlue SafeStain (Life Technologies) and imaged on the Typhoon Trio imager (GE Healthcare). All purified SA fusion proteins migrated a single band in SDS-PAGE with an apparent molecular mass of approximately 75 kDa (for <sup>N</sup>CXCL-SA<sup>C</sup>), 80 kDa (<sup>N</sup>SA-V<sub>L</sub><sup>C</sup> or <sup>N</sup>SA-V<sub>H</sub><sup>C</sup>) and 95 kDa (<sup>N</sup>SA-scFv<sup>C</sup>). The monodisperse state of concentrated SA fusion proteins was confirmed by size-exclusion chromatography using a Superdex 200 10/300 GL column (GE Healthcare) connected to an AKTApurifier system and equilibrated with 1×PBS pH 7.4. Purified SA fusion proteins were eluted as a single peak at elution volumes (V<sub>e</sub>) that corresponds to apparent molecular masses ranging between 150 kDa (dimer) and 300 kDa (tetramer) in the case of <sup>N</sup>SA-CXCL<sup>C</sup> fusions while <sup>N</sup>SA-scFv<sup>C</sup> fusions were eluted with V<sub>e</sub> that corresponds to apparent molecular masses of about 95 kDa (monomer). Size exclusion chromatography columns and the FPLC system used for purification of <sup>N</sup>SA-scFv<sup>C</sup> fusions for animal studies were pre-treated with 1M NaOH to remove endotoxins. Purified <sup>N</sup>SA-scFv<sup>C</sup> fusions were further filtered sterile by passing them through a 0.2 µm syringe filters (Pall Life Sciences) and confirmed to contain minimal levels of endotoxin (<0.1 EU/mL) using the QCL-1000 Limulus Amebocyte Lysate (LAL) chromogenic test following the manufacturer's instructions (Lonza).

#### Biotinylation of Serum Albumin Fusion Proteins and Commercial Antibodies

**[0366]** Reactive EZ-link sulfo-NHS-LC-biotin (Thermo Fisher Scientific) was dissolved in 1×PBS pH 7.4 to obtain

a final concentration of 10 mM. Protein conjugates containing biotin were prepared by incubating serum albumin fusion proteins (at concentrations of 2 mg/mL in 1×PBS pH 7.4) with ten-fold molar excess of EZ-link sulfo-NHS-LC-biotin for 30 minutes at room temperature. Excess of unreacted or hydrolyzed biotinylation reagent was removed using size-exclusion chromatography with Superdex 200 10/300 GL (GE Healthcare) connected to an AKTApurifier system (GE Healthcare) and equilibrated with buffer 1×PBS pH 7.4. Fractions corresponded to the expected protein pick were pulled and concentrated to a final concentration of 2 mg/mL using 10000 NMWL Amicon Ultra-4 ultrafiltration devices (Millipore) at 4000× g and 4° C. on a Allegra X-14R centrifuge (Beckman Coulter). Final protein concentrations were measured using a NanoDrop 2000 Spectrophotometer (Thermo Fisher Scientific).

#### Display of CXC Chemokine on Surface of Yeast Cells

**[0367]** The ELR+ and (ELR-) CXC chemokines were displayed on the surface of yeast as N-terminal fusion of the a-agglutinin Aga2 protein (<sup>N</sup>CXCL-Aga2p<sup>C</sup>). Yeast surface display vectors were based on pCT backbone (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). Constructs for surface display of <sup>N</sup>CXCL-Aga2<sup>C</sup> fusion proteins were generated by using Gibson Assembly (New England BioLabs) or In-Fusion Cloning (Clontech Laboratories, Takara Bio) technologies. PfuUltra II Fusion HS DNA Polymerase (Agilent Technologies) and Herculase II Fusion DNA Polymerase (Agilent Technologies) were used for the PCR

amplification of the insert and the vector, respectively. DpnI enzyme was obtained from New England Biolabs and oligonucleotide primers from Integrated DNA Technologies. The synthetic DNA coding for the active protein form of twelve human and murine ELR+ CXC chemokines and eight human and murine (ELR-) CXC chemokines were obtained from GeneArt Gene Synthesis (Thermo Fisher Scientific). The de novo synthesized genes encoding for the active processed form of each CXC chemokine were subsequently inserted into a previously modified yeast display pCT vector containing a DNA sequence encoding for a secretory leader sequence (<sup>N</sup>MKVLIVLLAIFAALPLA-LAQPVISTTVGSAAEGSLDKR<sup>C</sup>), a three amino-acid flexible spacer (<sup>N</sup>GGG<sup>C</sup>), a sequence encoding for c-myc epitope tag (c-myc; <sup>N</sup>EQKLISEEDLQ<sup>C</sup>) followed by a sequence encoding for the Aga2p protein to obtain <sup>N</sup>CXCL-(G<sub>3</sub>)-c-myc-Aga2p<sup>C</sup> fusion proteins. The process of the leader sequence during the secretory pathway allows for a precisely cleaved N-terminus that is crucial for the activity of the mature chemokines. Genes encoding <sup>N</sup>CXCL-(G<sub>3</sub>)-c-myc-Aga2p<sup>C</sup> fusion proteins were further sub-cloned into a new pCT vector via Bpu10I and XhoI (New England BioLabs) restriction enzymes except for MIP-2 for which PstI-HF and XhoI (New England BioLabs) restriction enzymes were used. All constructs were verified by DNA sequencing (Macrogen) and termed <sup>N</sup>CXCL-Aga2p<sup>C</sup> fusion proteins (see Table 5 for information about protein accession number and SEQ ID NOs: 107-146 for DNA and amino-acid sequences).

TABLE 5

CXCL protein (residues/ accession No.)	Construct for expression	Fusion protein
Groα/hCXCL1 (38-107/P09341)	pCHA-LS-hCXCL1 <sup>38-107</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL1-Aga2 <sup>C</sup>
Groβ/hCXCL2 (38-107/P19875)	pCHA-LS-hCXCL2 <sup>38-107</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL2-Aga2 <sup>C</sup>
Groy/hCXCL3 (38-107/P19876)	pCHA-LS-hCXCL3 <sup>38-107</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL3-Aga2 <sup>C</sup>
PF-4/hCXCL4 (32-101/P02776)	pCHA-LS-hCXCL4 <sup>32-101</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL4-Aga2 <sup>C</sup>
ENA-78/hCXCL5 (44-114/P42830)	pCHA-LS-hCXCL5 <sup>44-114</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL5-Aga2 <sup>C</sup>
GCP-2/hCXCL6 (44-114/P80162)	pCHA-LS-hCXCL6 <sup>44-114</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL6-Aga2 <sup>C</sup>
NAP-2/hCXCL7 (59-121/P02775)	pCHA-LS-hCXCL7 <sup>59-121</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL7-Aga2 <sup>C</sup>
IL-8/hCXCL8 (29-99/P10145)	pCHA-LS-hCXCL8 <sup>29-99</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL8-Aga2 <sup>C</sup>
MIG/hCXCL9 (23-125/Q07325)	pCHA-LS-hCXCL9 <sup>23-125</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL9-Aga2 <sup>C</sup>
IP-10/hCXCL10-SA (22-98/P02778)	pCHA-LS-hCXCL10 <sup>22-98</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL10-Aga2 <sup>C</sup>
I-TAC/hCXCL11-SA (22-94/O14625)	pCHA-LS-hCXCL11 <sup>22-94</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> hCXCL11-Aga2 <sup>C</sup>
KC/mCXCL1-SA (28-96/P12850)	pCHA-LS-mCXCL1 <sup>28-96</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> mCXCL1-Aga2 <sup>C</sup>
MIP-2/mCXCL2-SA (31-100/P10889)	pCHA-LS-mCXCL2 <sup>31-100</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> mCXCL2-Aga2 <sup>C</sup>
DCIP-1/mCXCL3-SA (31-100/Q6W5C0)	pCHA-LS-mCXCL3 <sup>31-100</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> mCXCL3-Aga2 <sup>C</sup>
Pf-4/mCXCL4-SA (30-105/Q9Z126)	pCHA-LS-mCXCL4 <sup>30-105</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> mCXCL4-Aga2 <sup>C</sup>
LIX/mCXCL5-SA (48-118/P50228)	pCHA-LS-mCXCL5 <sup>48-118</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> mCXCL5-Aga2 <sup>C</sup>
Nap-2/mCXCL7-SA (48-113/Q9EQI5)	pCHA-LS-mCXCL7 <sup>48-113</sup> -G <sub>3</sub> -c-myc-Aga2	<sup>N</sup> mCXCL7-Aga2 <sup>C</sup>

TABLE 5-continued

CXCL protein (residues/ accession No.)	Construct for expression	Fusion protein
Mig/mCXCL9-SA (22-126/P18340)	pCHA-LS-mCXCL9 <sup>22-126</sup> -G <sub>3</sub> -c-myc- Aga2	<sup>N</sup> mCXCL9-Aga2 <sup>C</sup>
Ip-10/mCXCL10-SA (22-98/P17515)	pCHA-LS-mCXCL10 <sup>22-98</sup> -G <sub>3</sub> -c-myc- Aga2	<sup>N</sup> mCXCL10-Aga2 <sup>C</sup>
I-Tac/mCXCL11-SA (22-100/Q9JHH5)	pCHA-LS-mCXCL11 <sup>22-100</sup> -G <sub>3</sub> -c-myc- Aga2	<sup>N</sup> mCXCL11-Aga2 <sup>C</sup>

**[0368]** The <sup>N</sup>CXCL-Aga2p<sup>C</sup> fusion proteins were displayed on the surface of *Saccharomyces cerevisiae* strain EBY100 using a standard protocol as described previously (Angelini, A. et al. Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). Briefly, EBY100 yeast cells were transformed with pCT vectors encoding <sup>N</sup>CXCL-Aga2p<sup>C</sup> fusion proteins using Frozen-EZ Yeast Transformation II Kit (Zymo Research). Cells were grown to mid-log phase in SD-CAA media at 30° C. and induced in galactose-containing media SG-CAA for 20 hours at 2° C. Staining of C-terminus c-myc epitope tag indicated that all the CXC chemokines are expressed well on the surface of yeast (approximately 105 copies per cell, a standard for yeast surface display). The proper folding of yeast displayed CXC chemokines was assessed by measuring binding of some displayed CXC chemokines to a panel of commercial neutralizing antibodies.

#### Epitope Mapping by Alanine-Scanning Mutagenesis

**[0369]** Functional binding residues were identified by alanine-scanning mutagenesis using yeast surface display technology combined to flow cytometry. Yeast surface display has been shown to provide a simple, flexible and robust method for fine resolution epitope mapping of both full-length or single-domain protein (Chao, G., Cochran, J. R. & Wittrup, K. D. Fine epitope mapping of anti-epidermal growth factor receptor antibodies through random mutagenesis and yeast surface display. *J Mol Biol* 342, 539-550 (2004); Cochran, J. R., Kim, Y. S., Olsen, M. J., Bhandari, R. & Wittrup, K. D. Domain-level antibody epitope mapping through yeast surface display of epidermal growth factor receptor fragments. *J Immunol Methods* 287, 147-158 (2004); Levy, R. et al. Fine and domain-level epitope mapping of botulinum neurotoxin type A neutralizing antibodies by yeast surface display. *J Mol Biol* 365, 196-210 (2007); Mata-Fink, J. et al. Rapid conformational epitope mapping of anti-gp120 antibodies with a designed mutant panel displayed on yeast. *J Mol Biol* 425, 444-456 (2013)). Alanine was chosen as a standard replacement residue for the identification of functional epitopes because it is found commonly in both buried and exposed positions, and it is present in all type of secondary structures. Moreover, alanine does not impose new hydrogen bonding, or lead to steric problems, and is therefore less likely to cause misfolding of the protein (Wells, J. A. Systematic mutational analyses of protein-protein interfaces. *Methods Enzymol* 202, 390-411 (1991); Morrison, K. L. & Weiss, G. A. Combinatorial alanine-scanning. *Curr Opin Chem Biol* 5, 302-307 (2001)). The commonly bound human ELR+ CXC chemokine hCXCL1 (Groa) was selected for alanine-scanning experiments.

**[0370]** Tridimensional structural analysis and literature data were combined to identify Groa residues suitable for mutagenesis (Fairbrother, W. J., Reilly, D., Colby, T. J., Hesselgesser, J. & Horuk, R. The solution structure of melanoma growth stimulating activity. *J Mol Biol* 242, 252-270 (1994); Kim, K. S., Clark-Lewis, I. & Sykes, B. D. Solution structure of GRO/melanoma growth stimulatory activity determined by 1H NMR spectroscopy. *J Biol Chem* 269, 32909-32915 (1994); Poluri, K. M., Joseph, P. R., Sawant, K. V. & Rajarathnam, K. Molecular basis of glycosaminoglycan heparin binding to the chemokine CXCL1 dimer. *J Biol Chem* 288, 25143-25153 (2013); Ravindran, A., Sawant, K. V., Sarmiento, J., Navarro, J. & Rajarathnam, K. Chemokine CXCL1 dimer is a potent agonist for the CXCR2 receptor. *J Biol Chem* 288, 12244-12252 (2013); Sepuru, K. M. & Rajarathnam, K. CXCL1/MGSA is a Novel Glycosaminoglycan (GAG)-binding Chemokine: STRUCTURAL EVIDENCE FOR TWO DISTINCT NON-OVERLAPPING BINDING DOMAINS. *J Biol Chem* 291, 4247-4255 (2016)). Solvent accessibility of hCXCL1 amino acid residues was determined by using both ASAView (Ahmad, S., Gromiha, M., Fawareh, H. & Sarai, A. ASAView: database and tool for solvent accessibility representation in proteins. *BMC Bioinformatics* 5, 51 (2004)) and PyMOL (PyMOL Molecular Graphics System, Version 1.8 Schrödinger, LLC) tools. Structurally buried hydrophobic amino acids (I23, V40, A42, L52, V59, I62 and I63) as well as proline (P20, P31, P33, P54 and P57) and cysteine (C9, C11, C35 and C52) residues that are crucial for overall folding and stability of the chemokine were left unaltered. The wild-type hCXCL1 was displayed on the surface of yeast as the amino terminus fusion of the a-agglutinin Aga2 protein (<sup>N</sup>hCXCL1<sup>WT</sup>-Aga2p<sup>C</sup>). Gene encoding <sup>N</sup>hCXCL1<sup>WT</sup>-(G<sub>3</sub>)-c-myc-Aga2p<sup>C</sup> fusion protein was subcloned into a new pCT vector via Bpu10I and XhoI (New England BioLabs) restriction enzymes. The obtained pCT-hCXCL1<sup>WT</sup>-Aga2 vector was used as the template for the site-directed mutagenesis. Mutagenic oligonucleotides were designed to introduce single point mutations at the desired sites and generate fifty-four hCXCL1 variants (pCT-hCXCL1<sup>ALAn</sup>-Aga2, <sup>N</sup>hCXCL1<sup>ALAn</sup>-Aga2p<sup>C</sup>; see SEQ ID NOs: 147 and 148 for DNA and amino acid sequences).

**[0371]** Binding of wild-type (hCXCL1<sup>WT</sup>) and single alanine mutants (hCXCL1<sup>ALAn</sup>) displayed on the surface of yeast toward soluble SA129, SA138 and SA157\* serum albumin-antibody fusions and two commercial neutralizing antibodies targeting Groa was assessed by using flow cytometry. The wild-type (<sup>N</sup>hCXCL1<sup>WT</sup>-Aga2p<sup>C</sup>) and single alanine mutant (NhCXCL1<sup>ALAn</sup>-Aga2p<sup>C</sup>) fusion proteins were displayed on the surface of *Saccharomyces cerevisiae* strain EBY100 using Frozen-EZ Yeast Transformation II Kit (Zymo Research) as described previously (Angelini, A. et al.

Protein Engineering and Selection Using Yeast Surface Display. *Methods Mol Biol* 1319, 3-36 (2015)). Individual colonies were inoculated in 5 mL SD-SCAA cultures, grown to mid-log phase ( $OD_{600}=2-5$ ) in SD-CAA media at 30° C. with shaking (250 rpm) and induced in galactose-containing SG-CAA media for 20 hours at 20° C. with shaking (250 rpm). The binding assays were conducted in 96-well plates (Corning) containing  $1 \times 10^4$  induced cells per well pre-mixed with  $1 \times 10^5$  non-displaying yeast cells.

**[0372]** The level of expression of single wild-type (hCXCL1<sup>WT</sup>) and alanine mutants (hCXCL1<sup>ALAn</sup>) displayed on the surface of yeast was assessed by staining the C-terminus c-myc epitope tag. Yeast cells displaying wild-type (hCXCL1<sup>WT</sup>) and single alanine mutants (hCXCL1<sup>ALAn</sup>) were then incubated with soluble serum albumin-antibody fusions SA129, SA138 and SA157\* bearing the His6 tag and the primary chicken anti-c-myc epitope tag (1:1000) antibody (Gallus Immunotech) overnight at 4° C. with shaking (150 rpm). The binding epitopes of two commercial mouse derived monoclonal antibodies targeting hCXCL1: Ab275 (clone 20326) and Ab276 (clone 31716) were also determined. High quality epitope maps were achieved by performing the assays at concentrations of soluble serum albumin-antibody fusions and antibodies that were equivalent to their  $K_D$  binding values for the wild-type hCXCL1: 2.5 nM for SA129, 100 nM for SA138, 1.5  $\mu$ M for SA157\*, 0.1 nM for Ab275 and 0.25 nM for Ab276. Concentrations higher or lower than that diminished the sensitivity of the assay and made it difficult to differentiate strong from weak binding signals derived from different mutants. At too high concentrations, all the signals were saturated and showed similar binding whereas at too low concentrations, the noise made it difficult to distinguish strong from weak mutants. After primary incubation, cells were pelleted (2500 $\times$  g for 5 minutes at 4° C.) and washed twice with 200  $\mu$ L of ice-cold PBSA buffer. Secondary labeling was performed with goat anti-chicken and either mouse anti-His6 epitope tag or goat anti-mouse antibodies conjugated to Alexa Fluor dyes at recommended dilutions. The 96-well plates were run on a high-throughput plate sampler iQue Screener (IntelliCyt). Data were evaluated using FlowJo v.10.0.7 software (Tree Star).

**[0373]** To ensure that the differences in binding were not due to variations of number of proteins expressed on the surface of yeast cell, the median fluorescence intensity ( $MFI_{BIND}$ ) from binding signal (His6 tag or goat anti-mouse antibodies) measured for single wild-type (hCXCL1<sup>WT</sup>) and alanine mutants (hCXCL1<sup>ALAn</sup>) was normalized to the median fluorescence intensity ( $MFI_{DISP}$ ) from display signal (c-myc tag). The normalized (binding/display= $MFI_{BIND}/MFI_{DISP}$ ) values obtained for each hCXCL1 variant (hCXCL1<sup>ALAn</sup>) were further normalized for the normalized value obtained for the wild-type (hCXCL1<sup>WT</sup>) and plotted as ( $MFI_{BIND}^{ALAn}/MFI_{DISP}^{ALAn})/(MFI_{BIND}^{WT}/MFI_{DISP}^{WT})$  providing a value, ranging from 0.0 to 1.0, that corresponded to the contribution of each amino acid residues upon binding with the corresponding serum albumin fusion or neutralizing antibody (Table 6). Alanine mutants V26, V28, E39, I41 and L44 exhibited an intense loss of binding when incubated with all soluble serum albumin fusion proteins SA129, SA138, SA157\* and neutralizing antibodies Ab275 and Ab276 indicating possible misfolding of the displayed hCXCL1 variants and were therefore excluded. Values

reported here are the results of three independent experiments and are presented as mean (dots)  $\pm$ SE (bars).

TABLE 6

	Epitope mapping interactions				
	Ab275	Ab276	SA129	SA138	SA157
strong (0.0-0.25)	G17	L15	Q13	L12	N46
	T43	G17	L15	N46	
	N46	I18	I18	G47	
	G47	H19	N46	R48	
	R48	N46	G47		
moderate (0.25-0.5)	K49	K61	R48		
		K65			
	R8	Q16	T14	R8	I18
	L12	K21	G17	T14	H19
	T14	K45	G32	L15	K21
	L15	G47	T43	G32	K29
	Q16	K71	A50	A50	K45
	I18			L67	G47
	G32				I58
	K45				K65
weak (0.5-0.75)	A50				K71
	Q10	T14	N22	Q13	N22
	Q13	N22	K45	I18	
	N22	R48	E64	M66	
	N53	A50			
		I58			
		K60			
Total residues	19	18	14	13	11

#### Yeast Display and Competitive Fluorescent-Based Binding Assay

**[0374]** A competitive flow cytometry-based binding assay was performed to further validate the identified hCXCL1 binding epitopes in different ELR+ CXC chemokines. The assays were conducted in 96-well plates (Corning) containing  $1 \times 10^4$  induced cells per well pre-mixed with  $1 \times 10^5$  non-displaying yeast cells. Yeast cells displaying the ELR+ CXC chemokines hCXCL1, hCXCL5, hCXCL8, mCXCL1 and mCXCL2 were pre-incubated at 4° C. with concentration of soluble un-biotinylated protein serum albumin fusions and neutralizing antibodies (“blocking reagents”) that are equals to 100-times their  $K_D$  values ( $C_B=100 K_D$ ). After 90 minutes, soluble biotinylated protein serum albumin fusions and neutralizing antibodies (“detection reagents”) were added at concentrations that are equals to their  $K_D$  values ( $C_D=K_D$ ).

**[0375]** The incubation time was 30 minutes at 4° C. with shaking (150 rpm). The cells were then pelleted at 2500 $\times$  g for 5 minutes and 4° C. on an Allegra X-14R centrifuge (Beckman Coulter), and washed twice with 200  $\mu$ L ice-cold PBSA buffer. Secondary labeling was performed at 4° C. by using goat anti-chicken and either streptavidin or goat anti-mouse and anti-rat antibodies conjugated to Alexa Fluor 647 at recommended dilutions. After 30 minutes, the cells were pelleted at 2500 $\times$  g for 5 minutes and 4° C. on an Allegra X-14R centrifuge (Beckman Coulter), and washed twice with 200  $\mu$ L ice-cold PBSA buffer. The 96-well plates were run on a high-throughput flow cytometry plate sampler iQue Screener (IntelliCyt). Data were evaluated using FlowJo v.10.0.7 software (Tree Star). To ensure that the differences in binding were not due to variations of number of proteins expressed on the surface of yeast cell, the determined median binding fluorescence intensities ( $MFI$ -

$_{BIND}$ ) were normalized to the median display fluorescence intensities ( $MFI_{DISP}$ ). The obtained normalized binding/display ( $MFI_{BIND}/MFI_{DISP}$ ) values were further normalized to the value obtained in the absence of “blocking reagent” providing a percentage value, ranging from 0 to 100%, that corresponded to the residual binding observed upon blocking with the corresponding un-biotinylated serum albumin fusion or neutralizing antibody. Values reported here are the results of two independent experiments and are presented as mean (dots)  $\pm$ SE (bars).

#### Mammalian Cell Culture and Competitive Fluorescence-Based Binding Assay

**[0376]** The binding of two biotinylated human ELR+ CXC chemokines (hCXCL1 and hCXCL8) to the human CXCR1 and CXCR2 receptors was assessed by using flow cytometry-based binding assay. Human embryonic kidney 293 (HEK293) cells that stably express the human CXCR1 (HEK293-IL8RA) and CXCR2 (HEK293-IL8RB) receptors were used (National Cancer Institute at Frederick, Md.) (Ben-Baruch, A. et al. IL-8 and NAP-2 differ in their capacities to bind and chemoattract 293 cells transfected with either IL-8 receptor type A or type B. *Cytokine* 9, 37-45 (1997)). Transfected HEK293 cells were maintained in DMEM (Thermo Fisher Scientific) supplemented with 10% v/v FBS (Thermo Fisher Scientific), 1% v/v penicillin-streptomycin (Thermo Fisher Scientific), and 0.8 mg/mL G418 (Thermo Fisher Scientific), and grown to approximately 80% confluence in 75 cm<sup>2</sup> flasks in a humidified incubator and an atmosphere of 95% air, 5% CO<sub>2</sub> at 37° C. Receptor expression levels were determined by flow cytometry using fluorescently labeled monoclonal antibodies against human CXCR1 and CXCR2 receptors on an Accuri C6 Flow Cytometer (BD Accuri Cytometers). Cells were treated with Cell Dissociation Buffer Enzyme Free PBS based buffer (Gibson), washed twice with cold 1× PBS pH 7.4 and resuspended in cold Cell Binding Assay (CBA) buffer (1× PBS pH 7.4 supplemented with 1% w/v BSA and 0.1% w/v NaN<sub>3</sub>) to a final density of 1×10<sup>6</sup> cells/mL. Cells were then aliquoted (100  $\mu$ L) in 96-well plates (Corning) and individual wells (1×10<sup>5</sup> cells each) were incubated with various concentrations of biotinylated human ELR+ CXC chemokines (hCXCL1 and hCXCL8) ranging from 0.03 to 300 nM. The incubation time was 30 minutes at 4° C. with shaking (150 rpm). The cells were then pelleted at 600× g for 5 minutes and 4° C. on an Allegra X-14R centrifuge (Beckman Coulter) and washed once with 200  $\mu$ L ice-cold CBA buffer.

**[0377]** Specific binding of biotinylated ELR+ CXC chemokines to CXCR receptors was detected by incubating the cells with Alexa Fluor 647-labeled Streptavidin (1:200; Thermo Fisher Scientific) for 30 minutes at 4° C. with shaking. Cells were then pelleted at 600× g for 5 minutes and 4° C. on an Allegra X-14R centrifuge (Beckman Coulter), and washed twice with 200  $\mu$ L ice-cold CBA buffer. Cells were resuspended in 50  $\mu$ L (2×10<sup>3</sup> cell/ $\mu$ L final concentration) of cold CBA buffer and analyzed by flow cytometry on an iQue Screener (IntelliCyt). Data were evaluated using FlowJo v.10.0.7 software (Tree Star). Median fluorescence intensities (MFI) were normalized to the maximal value obtained, expressed as a percentage and plotted as a function of varying ELR+ CXC chemokine concentration. The maximal effective concentrations ( $EC_{50}$ ) were determined by fitting a sigmoidal dose-response curve on GraphPad Prism

(GraphPad Software). The same assay was used to assess the ability of crossreactive serum albumin-antibody fusions (SA129, SA138 and SA157\*) and commercial neutralizing antibodies (Ab208 and Ab275, R&D Systems) to compete for binding of biotinylated ELR+ CXC chemokines (hCXCL1 and hCXCL8) to their cognate CXCR1 and CXCR2 receptors.

**[0378]** HEK293 cell lines expressing human CXCR1 and CXCR2 receptors were incubated with biotinylated hCXCL1 and hCXCL8 chemokines as “agonist”, at final concentration equal to  $EC_{50}$  values, in the presence of varying concentrations of “antagonists” (SA129, SA138, SA157\*, Ab208 and Ab275), followed by staining with fluorescently labeled streptavidin. Antagonists were serially diluted in 1×PBS pH 7.4 to obtain final concentrations that cover the range from 0.3 nM to 300 nM. Concentrations ranging from 0.03  $\mu$ M to 30  $\mu$ M were used for the antagonist SA157\*. Median fluorescence intensities (MFI) were normalized to the maximal value obtained, expressed as a percentage and plotted as a function of varying concentrations of “antagonists”. The half maximal inhibitory concentration ( $IC_{50}$ ) values were determined by fitting a sigmoidal dose-response curve on GraphPad Prism (GraphPad Software). The  $IC_{50}$  values were further converted to inhibition constants  $K_i$  by using the Cheng-Prusoff equation  $K_i = IC_{50} / ([L] / EC_{50} + 1)$  where [L] is the fixed concentration of “agonist” biotinylated ELR+ CXC chemokine and  $EC_{50}$  is the concentration of “agonist” that results in half maximal activation of the receptor. Values reported here are the results of three independent experiments. The  $K_i$  and  $K_D$  values, specified in units of molar concentration (mol/L or M) were converted to the  $pK_i$  and  $pK_D$  scale using  $pK_i = -\log_{10}(K_i)$  and  $pK_D = -\log_{10}(K_D)$ , respectively. Higher values of  $pK_i$  and  $pK_D$  indicate exponentially greater potency. Data are presented as mean (dots)  $\pm$ SE (bars).

#### Isolation of Neutrophils from Human and Murine Fresh Whole Blood

**[0379]** Human neutrophils were purified directly from human whole blood by immunomagnetic negative selection using EasySep Direct Human Neutrophil Isolation Kit (STEMCELL Technologies). Whole blood from healthy human volunteers was obtained from Research Blood Components, LLC. Blood was collected in sodium-citrate anticoagulant and provided in EDTA vacutainer collection tubes. Murine neutrophils were isolated directly from mouse bone marrow by immunomagnetic negative selection using EasySep Mouse Neutrophils Enrichment Kit (STEMCELL Technologies). The ends of femur and tibia derived from female C57BL/6 mice (Taconic) were cut and the bone marrow cells flushed using a syringe equipped with a 23-gauge needle. Cell clumps and debris were removed by gently passing the cell suspension through a 70  $\mu$ m mesh nylon strainer.

**[0380]** Both human and murine neutrophils were then pelleted at 1000× g for 5 minutes at 4° C. on an Allegra X-14R centrifuge (Beckman Coulter), the supernatant discarded and the cells washed by adding ice-cold PBE buffer (1× PBS pH 7.4 supplemented with 2 mM EDTA, 0.5% w/v BSA, Ca<sup>2+</sup> and Mg<sup>2+</sup> free) to obtain a final cell density of 10<sup>6</sup> cells/mL. The washing step was repeated one time more and the washed cells resuspended at 10<sup>7</sup> cells/mL in ice-cold PBE buffer. Purity of human neutrophils was assessed by using APC-conjugated anti-human CD16 (clone 3G8, BioLegend), FITC-conjugated anti-human CD66b antibody

(clone G10F5; BioLegend) and PE-conjugated anti-human CD45 antibody (clone HI30, BioLegend). Purity of mouse neutrophils was assessed by using APC-conjugated anti-mouse CD11b (clone M1/70; BioLegend) and PE-conjugated anti-mouse Ly-6G/Ly-6C (Gr-1) (clone RB6-8C5; BioLegend). Purified and labeled human and murine neutrophils were further used for calcium signaling experiments.

#### Competitive Flow Cytometry-Based Intracellular Free Calcium Mobilization Assay

**[0381]** The ability of engineered serum albumin fusion antibody to block the capacity of human and murine ELR+ CXC chemokines to signal through CXCR1 and CXCR2 receptors resulting in an increase of the intracellular calcium concentration was tested on both human and murine freshly purified neutrophils, respectively (June, C. H. & Moore, J. S. Measurement of intracellular ions by flow cytometry. *Curr Protoc Immunol Chapter 5*, Unit 5.5 (2004)). Purified human and murine neutrophils in sterile ice-cold PBE buffer were loaded for 30 minutes at 37° C. in the dark with 2 mM cell permeable ratiometric fluorescent dye Indo-1 AM (Thermo Fisher Scientific) resuspended in 100% v/v dry DMSO to obtain a final concentration of 4 μM. Samples of 10<sup>6</sup> cells each were kept aside for autofluorescence measurements and single stained. Indo-1 loaded neutrophils were then pelleted at 1000× g for 5 minutes at 4° C. on a Allegra X-14R centrifuge (Beckman Coulter), the supernatant discarded and the cells washed by adding ice-cold Cell Loading (CL) buffer (1× HBSS, pH 7.4, 0.5% w/v BSA, 1 mM Ca<sup>2+</sup> and 1 mM Mg<sup>2+</sup>) to obtain a final cell density of 10<sup>7</sup> cells/mL. The washing step was repeated one time more and the washed cells were resuspended at 5×10<sup>6</sup> cells/mL in ice-cold CL buffer. Aliquots of 10<sup>6</sup> cells/tube (200 μL) were prepared, individually pre-warmed at 37° C. for 10 minutes and stimulated with varying concentrations of “agonist” ELR+ CXC chemokines ranging from 0.03 to 300 nM.

**[0382]** Samples were analyzed on a BD LSR II flow cytometer (BD Biosciences). Intracellular calcium levels were measured at 405/30 nm (Indo-1 low) and 485/20 nm (Indo-1 high) emission fluorescence after excitation at 355 nm. Baseline fluorescence was recorded for 60 seconds before the addition of “agonist” ELR+ CXC chemokines and fluorescence measured for an additional 240 seconds. The median fluorescence intensities (MFI) at 405/30 nm and 485/20 nm were recorded, the ratio of two wavelengths calculated (Indo-1 ratio) and plotted as a function of time (seconds). Area under the curve (AUC), calculated as an integral over time, was determined using FlowJo v.10.0.7 software (Tree Star). The obtained values were normalized to the maximal response acquired, expressed as percentage of activity. The maximal effective concentrations (EC<sub>50</sub>) were determined by fitting a sigmoidal dose-response curve on GraphPad Prism (GraphPad Software).

**[0383]** The same assay was used to assess the ability of “antagonist” serum albumin-antibody fusions SA129, SA138 and SA157\* to antagonize the ELR+ CXC chemokine-mediated receptors activation and downstream intracellular calcium mobilization. Commercial neutralizing antibodies targeting human CXCL1 (Ab275), CXCL5 (Ab654), CXCL8 (Ab208) and murine CXCL1 (Ab453) and CXCL2 (Ab452) were included as positive controls. Indo-1 loaded neutrophils were incubated with hCXCL1, hCXCL5, hCXCL8, mCXCL1 and mCXCL1 chemokines as “ago-

nist”, at final concentration equal to EC<sub>50</sub> values, in the presence of varying concentrations of “antagonist” serum albumin-antibody fusions and neutralizing antibodies. Antagonists were serially diluted in ice-cold CL buffer to obtain final concentrations that cover the range from 10 pM to 10 μM. Intracellular calcium levels were measured as described above. The obtained values were normalized to the maximal response acquired and expressed as percentage of activity plotted as a function of varying concentrations of “antagonists”. Values reported here are the results of three independent experiments. Data are presented as mean (dots) ±SE (bars). The half maximal inhibitory concentration (IC<sub>50</sub>) values were determined by fitting a sigmoidal dose-response curve on GraphPad Prism (GraphPad Software). The IC<sub>50</sub> values were further converted to inhibition constants K<sub>i</sub> by using the Cheng-Prusoff equation and both pK<sub>i</sub> and pK<sub>D</sub> values determined as described above.

#### Fluorescent Labeling of Serum Albumin Fusion Proteins

**[0384]** Reactive Alexa Fluor 647 succinimidyl ester (Thermo Fisher Scientific) was dissolved in anhydrous dimethylsulfoxide (DMSO, Sigma-Aldrich) to obtain a final concentration of 10 mg/mL. Protein conjugates containing Alexa Fluor 647 were prepared by incubating proteins (at concentrations of 2 mg/mL in 1×PBS pH 7.4 with 1/10 volume 1 M K<sub>2</sub>HPO<sub>4</sub>, pH 9.0) with two-fold molar excess of Alexa Fluor 647 NHS ester (at 10 mg/mL in DMSO) for 20 minutes at room temperature in the dark. Free dye was removed using size-exclusion chromatography with Superdex 200 10/300 GL (GE Healthcare) connected to an AKTA-purifier system (GE Healthcare) and equilibrated with buffer 1× PBS pH 7.4. Fractions corresponded to the expected protein pick were pulled and concentrated to a final concentration of 2 mg/mL using 10000 NMWL Amicon Ultra-4 ultrafiltration devices (Millipore) at 4000× g and 4° C. on a Allegra X-14R centrifuge (Beckman Coulter). Final protein concentrations and degrees of labeling were measured using a NanoDrop 2000 Spectrophotometer (Thermo Fisher Scientific). Dye-to-protein ratios ranged from 1.0 to 1.5.

#### Pharmacokinetic Studies in Mice of Serum Albumin-Antibody Fusions

**[0385]** All animal studies were approved by the Massachusetts Institute of Technology Division of Comparative Medicine and carried out according to the federal, state, and local regulations. Female C57BL/6 mice (Taconic) were maintained under specific pathogen-free conditions and used at 6-8 weeks of age. A single bolus/dose (1 mg) of each Alexa Fluor 647-labeled <sup>N</sup>SA-scF<sup>C</sup> fusions (2 mg/mL) were injected intraperitoneally (i.p.) at 50 mg/kg into 3 mice. At various time points (immediately after injection and at 0.5, 1, 2, 3, 5, 8, 24, 48, 72, 96, 120, 168 hours post injection) blood was collected into heparin-coated capillary tubes (VWR International) and stored at 4° C. in the dark until sample collection was complete. Plasma was obtained after centrifugation (900×g for 5 minutes) and transferred to new capillary tubes. Standard samples were diluted in plasma collected from untreated mice. Serial dilutions (100 μL/well) of the standards (ranging from 0.3 pg/μL to 300 pg/μL) and plasma samples were prepared. Protein fusion concentration was determined by measurement of fluorescent intensity using a Typhoon imager (GE Healthcare) after degree of

labeling correction. Fluorescence intensity was quantified using ImageJ software (NIH).

**[0386]** To calculate  $^{54}\text{SA-scFv}^{\text{C}}$  half-lives, fluorescent measurements were quantified by normalization to a standard curve for each antibody. Starting at the max concentration time point (3 hours for all cases), pharmacokinetic profiles were fit in Graphpad Prism using a two phase non-compartmental model of the following format:  $\text{MFI}(t) = A e^{-\alpha t} + B e^{-\beta t}$ . Where A, B,  $\alpha$  and  $\beta$  represent the systemic clearance rates of a given fusion protein. Fast and slow half-lives,  $t_{1/2,\alpha}$  and  $t_{1/2,\beta}$  were calculated as  $\ln(2)/\alpha$  and  $\ln(2)/\beta$ , respectively. The total clearance (CL) was calculated by dividing the total dose by the AUC from 0 to infinity. Fits for the three mice in each group were averaged to obtain a single pharmacokinetic curve for each  $^{54}\text{SA-scFv}^{\text{C}}$  fusion, from which total clearance rate and standard error were calculated. Values reported here are the results of triplicate and data are presented as mean (dots)  $\pm$ SE (bars).

#### Arthritis Induction and Treatment

**[0387]** All animal studies were approved by the Center for Comparative Medicine (CCM) of the Massachusetts General Hospital (MGH) and carried out according to the federal, state, and local regulations. The inflammatory arthritis serum transfer K/B $\times$ N mice model was used (Kouskoff, V. et al. Organ-specific disease provoked by systemic autoimmunity. *Cell* 87, 811-822 (1996). Mice carrying the KRN T-cell receptor transgene on the C57BL/6 genetic background were mated with NOD mice (Jackson Laboratory) to obtain transgene-positive arthritic K/B $\times$ N mice. The presence of the transgene was determined by allele-specific PCR and confirmed by phenotypic assessment. Serum was collected from K/B $\times$ N arthritic mice as described (Miyabe, Y., Kim, N. D., Miyabe, C. & Luster, A. D. Studying Chemokine Control of Neutrophil Migration In Vivo in a Murine Model of Inflammatory Arthritis. *Methods in enzymology* 570, 207-231 (2016)). Experimental arthritis was induced in recipient C57BL/6 by transferring arthritogenic serum containing autoantibodies to the ubiquitous anti-glucose 6-phosphate isomerase (GPI) protein from transgenic 8- to 10-weeks old K/B $\times$ N mice to healthy C57BL/6 resulting in synovial pannus formation and both bone and cartilage erosions that mimics the disease that develop spontaneously in transgenic mice. Arthritogenic K/B $\times$ N serum (150  $\mu\text{L}$ ) was injected intraperitoneally (i.p.) using 26-gauge needle syringe on days 0 and 2 on healthy wild-type C57BL/6 mice (Jackson Laboratory) and disease progress was monitored every other day for 2 weeks as described in the next section.

**[0388]** For the preventative treatment experiments, 500  $\mu\text{L}$  of 2 mg/mL serum albumin fusions were injected i.p. daily starting on day 0 and treated every day for a total of 14 consecutive days as follows: group 1 (n=10), mice were treated with SA129 (50 mg/Kg in PBS); group 2 (n=10), mice were treated with SA138 (50 mg/Kg in PBS); group 3 (n=10), mice were treated with control serum-albumin fusion (SA $^{\text{CTR}}$ ; 50 mg/Kg in PBS); group 4 (n=10), mice were treated with PBS. For therapeutic treatment, mice were placed into 4 experimental groups so that each group had the same overall clinical score and treated every day for a total of 10 days as follows; Group 1 (n=10), mice were treated with SA129 (50 mg/Kg in PBS); group 2 (n=10), mice were treated with SA138 (50 mg/Kg in PBS); group 3 (n=10), mice were treated with control serum-albumin fusion

(SA $^{\text{CTR}}$ ; 50 mg/Kg in PBS); group 4 (n=10), mice were treated with PBS. Paw thickness and clinical scores were determined every other day as described previously (Miyabe, Y., Kim, N. D., Miyabe, C. & Luster, A. D. Studying Chemokine Control of Neutrophil Migration In Vivo in a Murine Model of Inflammatory Arthritis. *Methods in enzymology* 570, 207-231 (2016)). The clinical arthritis score was calculated for each mouse by summing the scores for the four paws: 0=normal; 1=erythema and swelling of one digit; 2=erythema and swelling of two digits or erythema and swelling of ankle joint; 3=erythema and swelling of more than three digits or swelling of two digits and ankle joint; 4=erythema and severe swelling of the ankle, foot and digits with deformity.

#### Flow Cytometry Analysis and Quantification of Neutrophils in Synovial Fluid

**[0389]** The number of neutrophils that accumulated in the synovial fluid were determined using flow cytometry as previously described (Miyabe, Y., Kim, N. D., Miyabe, C. & Luster, A. D. Studying Chemokine Control of Neutrophil Migration In Vivo in a Murine Model of Inflammatory Arthritis. *Methods in enzymology* 570, 207-231 (2016)). Synovial fluid was obtained from ankle joints of 8- to 10-weeks old C57BL/6 mice (Jackson Laboratory) on day 8 after K/B $\times$ N serum injection for all groups. Retrieved synovial fluid cells were resuspended in sterile 1% v/v FCS/PBS to obtain a final concentration of  $1 \times 10^4$  cells/ $\mu\text{L}$ . For flow cytometry analysis, cells were incubated with anti-Fc $\gamma$ RIII/II antibody (clone 2.4G2; BD Bioscience), and following stained with APC-conjugated anti-murine Ly6G antibody (clone 1A8; BioLegend). Flow cytometry was performed with BD LSRFortessa (BD Bioscience) and analyzed with FlowJo v.10.0.7 software (Tree Star). Neutrophils were identified as Ly6G-positive cells in the granulocyte gate of forward and side scatter plots. Values reported here are the results of triplicate and are presented as mean (dots)  $\pm$ SE (bars).

#### Histology Analysis

**[0390]** Preventative treated mice (n=3 per group) were sacrificed at day 8 after K/B $\times$ N serum injection and paws collected for histology as previously described (Miyabe, Y., Kim, N. D., Miyabe, C. & Luster, A. D. Studying Chemokine Control of Neutrophil Migration In Vivo in a Murine Model of Inflammatory Arthritis. *Methods in enzymology* 570, 207-231 (2016)). Briefly, paws were fixed in 4% v/v formalin solution overnight and decalcified by treatment with 20% EDTA solution for 2 weeks. Samples were then washed with H $_2$ O mQ for at least 10 minutes and embedded in paraffin. Sections of 4  $\mu\text{m}$  thickness were stained with Hematoxylin and Eosin (H&E) staining kit (Wako Pure Chemical Industries), mounted by using Mount-Quick mounting medium (Daido Sangyo Co.) and examined by light microscopy. Values reported here are the results of triplicate and are presented as mean (dots)  $\pm$ SE (bars). Histopathological scoring was performed on H&E stained ankle sections by evaluating both inflammatory cell infiltration and pannus formation as follows. Inflammatory cell infiltration: 0=no change, 1=focal inflammatory cell infiltration, 2=severe and diffuse inflammatory cell infiltration. Pannus formation: 0=no change, 1=pannus formation at one site, 2=pannus formation at two sites, 3=pannus formation at

more than three sites. The score of inflammatory cell infiltration and pannus formation were summed to determine a total histopathological score. Visible clinical signs were scored blinded for the origin and treatment of the mice. Because different batches of serum with different potency have been used in different experiments, the measured clinical score values of each experiment were normalized to the maximal value obtained and expressed as a percentage (clinical score %). Values reported here are the results of two independent experiments and are presented as mean (dots)  $\pm$ SE (bars).

#### Protein Structure Homology Modeling

**[0391]** The protein structure homology models of selected yeast-displayed antibody single-chain variable fragments CK129, CK138 and CK157 have been generated by using protein structure modeling program MODELLER (Sali, A. & Blundell, T. L. Comparative protein modelling by satisfaction of spatial restraints. *J Mol Biol* 234, 779-815 (1993)) and the three-dimensional structure of a highly homologue synthetic antibody fragment as template (PDB ID: 2KH2) (Wilkinson, I. C. et al. High resolution NMR-based model for the structure of a scFv-IL-1 $\beta$  complex: potential for NMR as a key tool in therapeutic antibody design and development. *J Biol Chem* 284, 31928-31935 (2009)). Protein structures and models were rendered using PyMOL (PyMOL Molecular Graphics System, Version 1.8 Schrödinger, LLC).

#### Statistical Analysis

**[0392]** All data are presented as mean (dots)  $\pm$ SE (bars). Statistical comparisons were made between each group using one-way analysis of variance (ANOVA) and GraphPad Prism (GraphPad Software). P values: \*P<0.05, \*\*P<0.01, \*\*\* P<0.001; \*\*\*\* P<0.0001. ns: non-significant.

#### Example 1: Generation of Crossreactive Antibodies that Bind a Diverse Array of ELR+ CXC Chemokines

**[0393]** To evolve highly crossreactive protein binders toward multiple pro-inflammatory ELR+ CXC chemokines,

synthetic single chain variable antibody fragment (scFv) libraries displayed on the surface of yeast were used. Yeast surface display combined with fluorescence-activated cell sorting (FACS) allowed for quantitative selection of protein binders based on both binding affinity and specificity. The synthetic scFv libraries had qualities making them powerful scaffolds for the development of crossreactive binders. Three human (hCXCL1, hCXCL5, and hCXCL8) and three murine (mCXCL1, mCXCL2 and mCXCL5) chemokines were chosen as targets based on their (i) low sequence identity and (ii) proven therapeutic relevance (FIG. 1 and FIG. 2A).

**[0394]** Initially, only one selection pressure was applied, and crossreactivity was prioritized over affinity. To encourage the development of crossreactivity, combinatorial approaches were implemented, in which the output of each cycle of selection was exposed to a diverse array of ELR+ CXC chemokines in the following cycle selection (FIG. 2B). The use of highly avid reagents preloaded with ELR+ CXC chemokines and constant alternation of the detection reagents favored the isolation of weak crossreactive binders while discouraging the enrichment of clones that recognized detection reagents. Subsequent DNA sequences of individual clones revealed eighteen unique antibody clones with varying amino acid compositions and loop lengths within the complementarity-determining regions (CDRs).

**[0395]** Selected antibodies exhibited diverse affinities and specificities for soluble ELR+ CXC chemokines (FIG. 2C, Table 7). Of these clones, only four (CK1-CK4) recognized at least three different ELR+ CXC chemokines. The most abundant and crossreactive of these antibodies, CK3, recognized the biotinylation sequence located at the C-terminus of each chemokine, thus explaining its crossreactivity and similar binding affinities (FIG. 2C). In addition to the generation of crossreactive binders, six bi-specific and eight mono-specific antibody clones were isolated (FIG. 2C). The presence of numerous mono- and bi-specific antibodies can be explained by the use of highly avid reagents during the selection process. Taken together, these data showed that crossreactive antibodies generally occurred at lower frequency and with weaker binding affinities compared with the mono- and bi-specific antibodies (FIG. 2C).

TABLE 7

	Binding affinities - $K_D \pm$ SE (nM)						
	Gro $\alpha$	ENA-78	IL-8	KC	MIP-2	LIX	MBP
CK1	>2000	>2000	>2000	N.B.	N.B.	N.B.	N.B.
CK2	>2000	605 $\pm$ 79	N.B.	481 $\pm$ 80	505 $\pm$ 86	>2000	N.B.
CK3	N.B.	N.B.	N.B.	N.B.	N.B.	N.B.	N.B.
CK3*	562 $\pm$ 88	448 $\pm$ 73	410 $\pm$ 61	589 $\pm$ 75	445 $\pm$ 69	594 $\pm$ 81	522 $\pm$ 79
CK4	39.4 $\pm$ 7.4	>2000	N.B.	744 $\pm$ 93	N.B.	>2000	N.B.
CK5	>2000	N.B.	>2000	N.B.	N.B.	N.B.	N.B.
CK6	1675 $\pm$ 191	1987 $\pm$ 228	N.B.	N.B.	N.B.	N.B.	N.B.
CK7	N.B.	344 $\pm$ 68	N.B.	N.B.	N.B.	>2000	N.B.
CK8	382 $\pm$ 73	N.B.	N.B.	825 $\pm$ 98	N.B.	N.B.	N.B.
CK9	N.B.	N.B.	N.B.	221 $\pm$ 49	278 $\pm$ 41	N.B.	N.B.
CK10	28.9 $\pm$ 4.5	N.B.	N.B.	801 $\pm$ 107	N.B.	N.B.	N.B.
CK11	425 $\pm$ 58	N.B.	N.B.	N.B.	N.B.	N.B.	N.B.
CK12	N.B.	N.B.	N.B.	N.B.	332 $\pm$ 57	N.B.	N.B.
CK13	N.B.	297 $\pm$ 98	N.B.	N.B.	N.B.	N.B.	N.B.
CK14	N.B.	N.B.	N.B.	N.B.	N.B.	269 $\pm$ 57	N.B.
CK15	N.B.	N.B.	N.B.	251 $\pm$ 25	N.B.	N.B.	N.B.



TABLE 7-continued

Binding affinities - $K_D \pm SE$ (nM)							
	Gro $\alpha$	ENA-78	IL-8	KC	MIP-2	LIX	MBP
CK16	N.B.	102 $\pm$ 12	N.B.	N.B.	N.B.	N.B.	N.B.
CK17	N.B.	N.B.	N.B.	N.B.	N.B.	106 $\pm$ 11	N.B.
CK18	N.B.	N.B.	65 $\pm$ 6.1	N.B.	N.B.	N.B.	N.B.

\*= binding affinities measured using biotinylated ELR + CXC chemokines bearing AviTag at C-terminus.  
N.B. = no binding

### Example 2: Use of Two-Pressure Selection Strategies for Molecular Co-Evolution of Antibody Binding Affinity and Crossreactivity

**[0396]** To further improve both the binding affinity and crossreactivity of CK1, CK2 and CK4 clones, two-pressure selection strategies that encouraged the co-evolution of higher affinity and crossreactivity simultaneously were utilized. Specifically, a high degree of genetic diversity in the antibody-encoding genes was created using error-prone PCR amplification. Then, binding affinity was increased by allowing the mutants to evolve through six consecutive cycles of equilibrium-based selection using decreasing concentrations of ELR+ CXC chemokines. Concomitantly, the development of crossreactivity was forced by exposing the outputs of each cycle of affinity selection towards a different ELR+ CXC chemokine in the following cycle of selection. During this iterative process, variants whose affinity and crossreactivity towards ELR+ CXC chemokines was higher than that of their respective parental clones were exclusively collected.

**[0397]** After two iterative evolutionary processes, each comprising six consecutive cycles of selection, the isolated clones were sequenced and assessed for binding affinity and crossreactivity towards ELR+ CXC chemokines. In addition, when distinct mutations were found scattered across

clones and showed improvement, mutations were combined to investigate the possibility of even further crossreactivity and higher affinity. A summary of the overall co-evolutionary approach, including two iterative evolutionary processes of selection for crossreactivity and affinity (I and II), and a third cycle of combinatorial mutagenesis (III), is shown in FIGS. 2D-2F.

**[0398]** Implementing these evolutionary processes in this fashion yielded antibodies with significant improvements in affinity and, in most cases, increased crossreactivity toward multiple ELR+ CXC chemokines. For example, the engineered CK138 clone doubled the number of chemokines recognized (i.e., from three to six) and achieved roughly a 30 to 340-fold improvement in affinity toward these chemokines ( $K_D$  values ranging from  $\frac{5}{8}$  to 193 nM) relative to the parental CK1 clones (FIG. 2D; Table 8). Similarly, the CK157 clone retained its crossreactivity toward five targets and added a 20 to 55-fold improvement in affinity ( $K_D$  values ranging from 16.9 to 57.1 nM) as compared to the initial CK2 clone (FIG. 2E, Table 9). Finally, while CK129 only retained minimal crossreactivity towards two targets, there was a considerable increase in affinity of 50 and 800-fold toward human Gro $\alpha$  ( $K_D=0.79$  nM) and its mouse homologue KC ( $K_D=0.93$  nM), respectively (FIG. 2F; Table 10).

TABLE 8

Binding affinities - $K_D \pm SE$ (nM)						
	Gro $\alpha$	ENA-78	IL-8	KC	MIP-2	LIX
CK1	>2000	>2000	>2000	N.B.	N.B.	N.B.
CK19	1262 $\pm$ 219	895 $\pm$ 72	212 $\pm$ 21	931 $\pm$ 81	>2000	>2000
CK21	>2000	273 $\pm$ 17	144 $\pm$ 8.4	280 $\pm$ 37	>2000	>2000
CK23	>2000	76.4 $\pm$ 5.8	104 $\pm$ 8.2	98.3 $\pm$ 33.4	>2000	>2000
CK63	>2000	42.9 $\pm$ 8.2	15.2 $\pm$ 3.3	53.5 $\pm$ 9.8	>2000	>2000
CK66	594 $\pm$ 39	19.1 $\pm$ 1.6	21.5 $\pm$ 3.6	52.5 $\pm$ 8.1	>2000	>2000
CK72	120 $\pm$ 10	35.1 $\pm$ 2.3	25.8 $\pm$ 3.9	107 $\pm$ 15	63.6 $\pm$ 9.8	>2000
CK138	61.9 $\pm$ 4.1	5.8 $\pm$ 0.9	7.4 $\pm$ 1.1	34.8 $\pm$ 3.2	36.2 $\pm$ 6.5	193 $\pm$ 22
CK140	64.6 $\pm$ 13	4.9 $\pm$ 0.6	8.2 $\pm$ 2.1	32.9 $\pm$ 2.8	33.2 $\pm$ 7.4	197 $\pm$ 10

TABLE 9

Binding affinities - $K_D \pm SE$ (nM)						
	Gro $\alpha$	ENA-78	IL-8	KC	MIP-2	LIX
CK2	>2000	605 $\pm$ 79	N.B.	481 $\pm$ 80	505 $\pm$ 86	>2000
CK41	304 $\pm$ 44	220 $\pm$ 65	N.B.	143 $\pm$ 14	75.4 $\pm$ 19	429 $\pm$ 24
CK43	368 $\pm$ 59	154 $\pm$ 31	N.B.	137 $\pm$ 11	213 $\pm$ 27	762 $\pm$ 98
CK108	110 $\pm$ 24	40.9 $\pm$ 6.4	N.B.	39.8 $\pm$ 7.5	40.6 $\pm$ 6.2	136 $\pm$ 19
CK111	62.9 $\pm$ 8.4	35.3 $\pm$ 2.1	N.B.	30.5 $\pm$ 2.8	23.8 $\pm$ 2.9	97.8 $\pm$ 11
CK119	56.7 $\pm$ 7.2	39.3 $\pm$ 6.4	N.B.	29.8 $\pm$ 2.1	27.5 $\pm$ 3.8	116 $\pm$ 20

TABLE 9-continued

Binding affinities - $K_D \pm SE$ (nM)						
	Gro $\alpha$	ENA-78	IL-8	KC	MIP-2	LIX
CK152	48.4 $\pm$ 6.5	25.4 $\pm$ 2.8	N.B.	17.4 $\pm$ 2.8	21.6 $\pm$ 3.1	66.5 $\pm$ 10
CK155	24.1 $\pm$ 2.2	18.9 $\pm$ 2.5	N.B.	15.9 $\pm$ 2.4	33.5 $\pm$ 5.5	53.7 $\pm$ 8.9
CK157	36.2 $\pm$ 4.3	16.9 $\pm$ 1.7	N.B.	20.6 $\pm$ 4.1	18.2 $\pm$ 3.3	57.1 $\pm$ 3.9

TABLE 10

Binding affinities - $K_D \pm SE$ (nM)						
	Gro $\alpha$	ENA-78	IL-8	KC	MIP-2	LIX
CK4	39.4 $\pm$ 7.4	>2000	N.B.	744 $\pm$ 93	N.B.	>2000
CK50	3.1 $\pm$ 0.5	>2000	N.B.	53.8 $\pm$ 3.5	>2000	>2000
CK56	12.6 $\pm$ 2.5	>2000	N.B.	108 $\pm$ 4.5	>2000	>2000
CK125	1.23 $\pm$ 0.2	>2000	N.B.	1.31 $\pm$ 0.1	>2000	>2000
CK129	0.79 $\pm$ 0.1	>2000	N.B.	0.93 $\pm$ 0.1	>2000	>2000

**[0399]** Importantly, the sequential order in which the ELR+ CXC chemokine targets were exposed to the antibody mutant libraries was critical to the success of the selection process. Among all the possible selection pathways, improvements in both affinity and crossreactivity were observed only when recombinant genetic libraries were screened in order from lowest to highest affinity chemokines (data not shown). However, this was not applicable to the development of CK129, as its parental clone (CK4) already possessed high initial affinity toward hCXCL1 and mCXCL1, but negligible affinity towards the others.

**[0400]** Although reaction conditions that allowed, on average, one to two amino-acid mutations per gene were applied, selected clones from each round of sorting showed higher mutation rates (data not shown). The total number of accumulated mutations within both CDRs and framework regions (FWRs) of variable light ( $V_L$ ) and heavy ( $V_H$ ) chains correlated well with the extent of crossreactivity (data not shown). While the crossreactive antibody CK138 predominantly gathered mutations within the CDRs during the engineering process, CK157 collected numerous mutations within the FWRs (FIGS. 2G and 2H). Both types of mutations were shown to be critical, as reversion of either CDR or FWR mutations to the wild-type amino acids resulted in loss of affinity of CK138 and CK157, respectively, toward ELR+ CXC chemokines (data not shown). Moreover, the FWR mutations were found throughout different clones and cycles of engineering, suggesting strong selection pressure for these residues in conferring high binding crossreactivity and affinity.

**[0401]** Overall, the two-pressure selection approach promoted the evolution of crossreactive binders with improved affinity and revealed the importance of the selection pathway for the achievement of crossreactivity.

#### Example 3: Engineered Antibodies Bind a Larger Array of Human and Murine CXC Chemokines

**[0402]** To assess the extent of crossreactivity of the engineered antibodies, their binding affinity towards all human and murine CXC chemokines were characterized. The chemokine panel included twelve human and mouse ELR+ CXC chemokines (which share 32-90% sequence identity), and eight human and mouse (ELR-) CXC chemokines

(which share 18-70% sequence identity). The ELR+ CXC chemokines share 20-51% sequence identity with the (ELR-) CXC chemokines.

**[0403]** To accurately determine the  $K_D$  values of the antibodies for the different chemokines, two complementary configurations of chemokines and antibodies in the context of yeast surface display were utilized. Specifically, titrations using (i) soluble CXC chemokines with yeast-displayed antibodies, and (ii) soluble antibodies with yeast-displayed CXC chemokines, were performed. Exploring both orientations was necessary as some CXC chemokines are known to form oligomers when present in high concentration in solution, leading to undesired multivalent binding phenomena (Wang, X., Sharp, J. S., Handel, T. M. & Prestegard, J. H. Chemokine oligomerization in cell signaling and migration. *Prog Mol Biol Transl Sci* 117, 531-578 (2013)). The CXC chemokines were expressed as fusions to the N-terminus of mouse serum albumin (SA), and the engineered CK129, CK138 and CK157 binders as single-chain variable fragments (scFv) fused to the C-terminus of SA, which are referred to as SA129, SA138 and SA157\*. SA157\* is denoted with an asterisk as it was produced as separate VL and VH domains and then mixed in equimolar amounts, instead of a single chain with a linker.

**[0404]** In both orientations, similar crossreactivity of the engineered binders towards CXC chemokines that were not included in the selection cycles was observed (FIG. 3A). Importantly, this was not merely due to non-specific polyreactivity of the engineered binders, as no binding was detected toward a panel of unrelated proteins (data not shown). Yeast-displayed CK129, CK138 and CK157 bind 7, 12 and 16 soluble CXC chemokines, respectively (FIG. 3A). Similarly, the soluble SA129, SA138 and SA157\* bind 4, 11 and 14 yeast-displayed CXC chemokines, respectively (FIG. 3A). With a few exceptions, the  $K_D$  values determined using SA129, SA138 and SA157\* antibody-fusions with yeast-displayed CXC chemokines were on average 2- to 5-fold higher than those measured in the opposite arrangement (Table 11). The discrepancy in measured  $K_D$  values and extent of crossreactivity between the two specular orientations was not surprising and may reflect oligomeric CXC chemokines interacting with multiple yeast-displayed antibodies and therefore, mistaking avidity effects as seemingly higher affinity. This phenomenon appeared to be pronounced for (ELR-) CXC chemokines, such as hCXCL10 and hCXCL4, which are known to form highly avid oligomers in solution (Wang, X., Sharp, J. S., Handel, T. M. & Prestegard, J. H. Chemokine oligomerization in cell signaling and migration. *Prog Mol Biol Transl Sci* 117, 531-578 (2013); Swaminathan, G. J. et al. Crystal structures of oligomeric forms of the IP-10/CXCL10 chemokine. *Structure* 11, 521-532 (2003); Zhang, X., Chen, L., Bancroft, D. P., Lai, C. K. & Maione, T. E. Crystal structure of recombinant human platelet factor 4. *Biochemistry* 33, 8361-8366 (1994)).

**[0405]** These data showed that the extent of crossreactivity appeared to correlate both linearly and inversely with binding affinity (FIG. 3C). SA129, which only recognized four chemokines that share significant sequence identity, displayed relatively high affinity for those targets. In contrast, highly crossreactive SA138 and SA157\* had overall lower binding affinities toward a larger array of targets.

determination of residues that were likely critical for the interaction (FIGS. 4A and 4B).

**[0408]** Identification of the epitopes of two commercially available neutralizing antibodies: highly specific Ab275 (binds only hCXCL1) and the crossreactive Ab276 (binds hCXCL1, hCXCL2 and hCXCL3), were also identified. These epitope maps were then compared to the maps

TABLE 11

Binding affinities - $K_D \pm SE$ (nM)						
CK129/SA129		CK138/SA138		CK157/SA157*		
Display						
CK129	CXCL	CK138	CXCL	CK157	CXCL	
Soluble						
	CXCL	SA129	CXCL	SA138	CXCL	SA157*
Gro $\alpha$	1.0 $\pm$ 0.1	2.7 $\pm$ 0.3	41.5 $\pm$ 4.5	96.7 $\pm$ 2.4	61.1 $\pm$ 5.6	1433 $\pm$ 108
Gro $\beta$	13.9 $\pm$ 1.1	43.6 $\pm$ 4.1	267 $\pm$ 38	1591 $\pm$ 315	57.9 $\pm$ 4.8	853 $\pm$ 67
Groy	5.7 $\pm$ 0.5	9.2 $\pm$ 0.9	349 $\pm$ 41	836 $\pm$ 130	53.9 $\pm$ 2.1	1034 $\pm$ 87
ENA-78	>2000	N.B.	5.8 $\pm$ 0.5	33.7 $\pm$ 2.2	26.3 $\pm$ 2.3	2125 $\pm$ 269
GCP-2	N.B.	N.B.	153 $\pm$ 15	>2000	46.6 $\pm$ 3.1	751 $\pm$ 88
NAP-2	N.B.	N.B.	N.B.	40.6 $\pm$ 1.6	N.B.	N.B.
IL-8	N.B.	N.B.	6.9 $\pm$ 0.5	12.7 $\pm$ 0.9	N.B.	N.B.
KC	1.1 $\pm$ 0.1	2.9 $\pm$ 0.3	35.7 $\pm$ 3.3	29.4 $\pm$ 2.8	24.3 $\pm$ 1.9	666 $\pm$ 47
MIP-2	>2000	N.B.	29.1 $\pm$ 4.1	14.7 $\pm$ 0.5	19.9 $\pm$ 1.7	591 $\pm$ 62
DCIP-1	N.B.	N.B.	10.9 $\pm$ 1.1	31.4 $\pm$ 3.1	17.4 $\pm$ 1.4	2647 $\pm$ 264
LIX	>2000	N.B.	176 $\pm$ 21	357 $\pm$ 33	96.9 $\pm$ 6.9	2018 $\pm$ 169
Nap-2	N.B.	N.B.	N.B.	N.B.	13.6 $\pm$ 0.8	528 $\pm$ 53
PF-4	N.B.	N.B.	167 $\pm$ 28	N.B.	112 $\pm$ 5.1	>20000
MIG	N.B.	N.B.	N.B.	N.B.	N.B.	N.B.
IP-10	N.B.	N.B.	N.B.	N.B.	45.5 $\pm$ 3.8	>20000
I-TAC	N.B.	N.B.	N.B.	N.B.	131 $\pm$ 11	>20000
Pf-4	N.B.	N.B.	N.B.	N.B.	17.1 $\pm$ 1.2	1770 $\pm$ 119
Mig	N.B.	N.B.	N.B.	N.B.	N.B.	N.B.
Ip-10	N.B.	N.B.	500 $\pm$ 55	N.B.	44.4 $\pm$ 3.7	N.B.
I-Tac	N.B.	N.B.	N.B.	N.B.	124 $\pm$ 13	N.B.

#### Example 4: Recognition of Functional Epitopes by Crossreactive Antibodies

**[0406]** Next, fine epitope mapping using alanine-scanning mutagenesis was performed to identify the residues that were directly involved in the interactions. hCXCL1 was chosen as the model chemokine over other ELR+ CXC chemokines because (i) it is recognized by all the engineered crossreactive binders and (ii) it is well-characterized biochemically. First, three-dimensional structural analysis and literature data was combined to identify hCXCL1 amino acid suitable to mutagenesis. Structurally buried hydrophobic amino acids, proline and cysteine residues were left unaltered, as they are crucial for overall folding and stability of the chemokine.

**[0407]** Fifty-four predicted solvent-exposed hCXCL1 residues were selected, individually mutated to alanine, expressed on the surface of yeast, and screened for decreased binding affinity to the soluble SA129, SA138 and SA157\* serum-albumin antibody fusions. Five mutants that exhibited an intense loss of binding upon incubation with all the binders were excluded as this phenomenon was likely due to protein misfolding and destabilization of the displayed variants. Next, the binding of the remaining forty-nine hCXCL1 mutants towards soluble SA129, SA138 and SA157\* serum albumin antibody-fusions was assessed. Solvent exposed mutations that eliminated or significantly reduced binding affinity were identified, which allowed for

assigned to the engineered binders. Similarly to Ab275 and Ab276, SA129 and SA138 bind motifs along the functional N- and 40s-loops that are known to be crucial for the binding of hCXCL1 to its cognate receptor, CXCR2. In contrast, SA157\* recognized a distinctive epitope and engaged binding with hCXCL1 residues that are more important for the interaction with the glycosaminoglycans (GAGs). These epitope maps were also consistent with the results from a competitive assay (data not shown).

**[0409]** The residues recognized by the highly crossreactive SA138 and SA157\* are conserved among many different chemokines, thus explaining their wide extent of binding crossreactivity. The epitope-mapping data suggested that the degree of crossreactivity inversely correlated with the number of bound residues. The relatively more specific Ab275, Ab276 and SA129 engaged binding with a larger number of hCXCL1 residues than the more crossreactive SA138 and SA157\* binders. (FIG. 4C). In contrast, the binding specificity of SA138 and SA157\* appeared to be achieved through mostly peripheral long-range weak interactions, and interactions with a few preserved prominent structural conserved residues, such as the hot-spot motif NGF. In contrast, Ab275, Ab276 and SA129 appeared to engage chemokines with much stronger interactions (FIG. 4D).

Example 5: Analysis of Binding of Soluble ELR+ CXC Chemokine Ligands to their Cognate Receptors

**[0410]** To measure the potential therapeutic efficacy of the crossreactive binders, the ability of SA129, SA138 and SA157\* fusions were tested for their ability to inhibit binding of ELR+ CXC chemokines to their cognate CXCR1 and CXCR2. HEK293 cell lines expressing human CXCR1 and CXCR2 were utilized. Cells were incubated with various concentrations of hCXCL1 and hCXCL8 ligands to determine the half-maximal effective concentrations (EC<sub>50</sub>) of the interaction. Next, the ability of SA129, SA138 and SA157\* to antagonize the interactions between hCXCL1 and hCXCL8 ligands and their cognate receptors was examined. The engineered binders inhibited the ability of hCXCL1 and hCXCL8 chemokines to bind CXCR1 and CXCR2 receptors in a dose dependent manner to various extents (data not shown). Further, the determined inhibitory constants (K<sub>i</sub>) correlated well with the previously reported K<sub>D</sub> values (FIG. 5A). These results show that crossreactive SA129, SA138 and SA157\* fusions can markedly interfere with the binding of ELR+ CXC chemokines to both human CXCR1 and CXCR2 in vitro.

**[0411]** Next, the ability of the SA129, SA138 and SA157\* fusions to antagonize the activation of ELR+ CXC chemokine receptors was assessed. An intracellular calcium mobilization assay was utilized, wherein the assay was in the presence of human and mouse derived neutrophils activated with human (hCXCL1, hCXCL5, and hCXCL8) and murine (mCXCL1 and mCXCL2) ELR+ CXC chemokines, respectively. First, the EC<sub>50</sub> of the chemokines on the neutrophils was determined (0.94±0.2 for hCXCL1; 4.8±0.8 for hCXCL5; 1.29±0.4 for hCXCL8; 0.81±0.9 for mCXCL1; 2.5±0.7 for mCXCL2). Then, changes in intracellular calcium levels were monitored upon pre-incubation of ELR+ CXC chemokines with varying concentrations of SA129, SA138 and SA157\* as antagonists. Commercially available neutralizing monoclonal antibodies were used as a positive control. The assays revealed that the engineered binders exhibited inhibitory activity by preventing binding of the human and murine ligands to the receptor in a dose dependent manner (FIGS. 5B and 5C). Again, the calculated K<sub>i</sub> values correlated well with the previously determined K<sub>D</sub> affinities (FIG. 5D). Taken together, these data provided strong evidence that engineered crossreactive antibodies are potent inhibitors of ELR+ CXC chemokine signaling in vitro and ex vivo, and have the potential to suppress CXCR1 and CXCR2 activation in vivo.

Example 6: Effect of Crossreactive Serum Albumin-Antibody Fusions on Neutrophil Infiltration In Vivo and Inflammatory Arthritis in Mice

**[0412]** Given the promising results from the inhibitory assays, the inhibitory potency of the engineered fusions in the murine serum transfer K/B×N model of autoantibody-induced arthritis was tested. This model displays clinical and histopathological similarities to human rheumatoid arthritis (Christensen, A. D., Haase, C., Cook, A. D. & Hamilton, J. A. K/B×N Serum-Transfer Arthritis as a Model for Human Inflammatory Arthritis. *Front Immunol* 7, 213 (2016); Ditzel, H. J. The K/B×N mouse: a model of human inflammatory arthritis. *Trends Mol Med* 10, 40-45 (2004); Kouskoff,

V. et al. Organ-specific disease provoked by systemic autoimmunity. *Cell* 87, 811-822 (1996); Matsumoto, I. et al. How antibodies to a ubiquitous cytoplasmic enzyme may provoke joint-specific autoimmune disease. *Nat Immunol* 3, 360-365 (2002); Ji, H. et al. Arthritis critically dependent on innate immune system players. *Immunity* 16, 157-168 (2002)). The levels of ELR+ CXC chemokines are markedly upregulated in the joints of these arthritic mice and neutrophils, that have upregulated CXCR2 in the joint, are the main effector cells, making K/B×N serum transfer-induced arthritis mice an excellent model to test the therapeutic efficacy of the engineered binders (Chou, R. C. et al. Lipid-cytokine-chemokine cascade drives neutrophil recruitment in a murine model of inflammatory arthritis. *Immunity* 33, 266-278 (2010); Wipke, B. T. & Allen, P. M. Essential role of neutrophils in the initiation and progression of a murine model of rheumatoid arthritis. *J Immunol* 167, 1601-1608 (2001); Jacobs, J. P. et al. Deficiency of CXCR2, but not other chemokine receptors, attenuates autoantibody-mediated arthritis in a murine model. *Arthritis and rheumatism* 62, 1921-1932 (2010)).

**[0413]** Serum albumin-antibody fusions were generated to antagonize circulating small ELR+ CXC chemokines in vivo (FIG. 6). In addition to the SA129 and SA138 fusions described above, an irrelevant SA-fusion (SA<sup>CTR</sup>) was used. The negative control SA<sup>CTR</sup> encodes SA fused to an antibody fragment that targets the human carcinoembryonic antigen (CEA), a protein that does not exist in mice. To ensure complete inhibition of all ELR+ CXC chemokines present in circulation, relatively high doses of the engineered fusion proteins was administered (i.e., 50 mg/kg). When injected into mice, SA129, SA138 and SA<sup>CTR</sup> displayed plasma half-lives between 42-47 hours, considerably longer than small synthetic compounds or antibody fragments, but shorter than full length monoclonal antibodies. Despite the high doses of SA129, SA138 and SA<sup>CTR</sup>, the molecules were well tolerated. Treated mice gained weight and exhibited good body condition. Moreover, no signs of splenomegaly as a consequence of neutropenia were detected.

**[0414]** Initially the ability of crossreactive SA fusions to prevent the manifestation of the inflammatory arthritis in the K/B×N serum transfer model was assessed. Specifically, mice were treated on the same day as the arthritogenic serum was injected and the progression of the disease evaluated by both blinded clinical scores and measurements of ankle thickness. Mice treated with the more crossreactive SA138, which binds all four murine ELR+ CXC chemokines (mCXCL1, mCXCL2, mCXCL3, and mCXCL5), were protected from developing arthritis, with an approximately 80% reduction of clinical score compared with negative controls at the peak of the disease (day 8 after arthritogenic K/B×N serum transfer and disease initiation; FIGS. 7A and 7B). In contrast, the more specific SA129 that recognizes just one murine ELR+ CXC chemokine (mCXCL1) only moderately reduced joint inflammation, with an approximately 30% reduction of clinical score at day 8 (FIGS. 7A and 7B). Mice treated with SA<sup>CTR</sup> showed typical clinical signs of untreated mice that received arthritogenic serum and developed inflammatory arthritis with pronounced joint swelling. There were no differences between mice treated with SA<sup>CTR</sup> or with vehicle (PBS) only (FIGS. 7A and 7B).

**[0415]** Next, the number of synovial fluid neutrophils isolated from the arthritic joints of mice treated with SA129,

SA138 and SA<sup>CTR</sup> fusions was determined. Synovial tissues were harvested at the peak of the disease (day 8 after disease initiation). Mice treated with arthritogenic serum and the broadly crossreactive SA138 had 50- and 70-fold lower levels of infiltrated neutrophils than mice treated with the more specific SA129 and the irrelevant SA<sup>TR</sup>, respectively (FIG. 7C). These data were consistent with previous clinical score measurements and resembled those observed using mice deficient in CXCR2 (CXCR2<sup>-/-</sup>) injected with arthritogenic serum (Chou, R. C. et al. Lipid-cytokine-chemokine cascade drives neutrophil recruitment in a murine model of inflammatory arthritis. *Immunity* 33, 266-278 (2010); Jacobs, J. P. et al. Deficiency of CXCR2, but not other chemokine receptors, attenuates autoantibody-mediated arthritis in a murine model. *Arthritis and rheumatism* 62, 1921-1932 (2010)).

**[0416]** Histological analysis and scoring of inflamed ankle sections were also performed. Inflammatory cell infiltration and pannus formation were absent or minimally present in mice treated with the broadly crossreactive SA138 (FIGS. 7D and 7E). Consistent with previous clinical findings, the joints of mice treated with arthritogenic serum and control

SA<sup>CTR</sup> displayed abundant inflammatory cell infiltration and pannus formation. These pathological changes were present, though less pronounced, in mice treated with the more specific SA129 fusion.

**[0417]** Further, the therapeutic efficacy of crossreactive SA fusion in mice with established arthritis was tested. Arthritic mice were treated 4 days after arthritogenic serum transfer, when joint inflammation had developed. The highly crossreactive SA138 reversed inflammation very quickly and provided a remarkable complete resolution of the disease with an approximately 60% reduction of clinical score and 0.3 mm of ankle thickness over control at the peak of the disease (day 8 after disease initiation; FIGS. 7F and 7G). The specific SA129-treated mice exhibited only a modest reduction of both clinical scores (~25%) and ankle thickness (0.1 mm) at day 8 (FIGS. 7F and 7G). The SA<sup>CTR</sup> and vehicle-treated mice showed no difference in the rate of disease development (FIGS. 7F and 7G). Taken together, these data show that highly crossreactive SA138 fusion efficiently blocked neutrophil infiltration in the synovial tissues, thus preventing and even reversing inflammatory arthritis.

**Table 12: Sequence Summary**

SEQ ID NO	Description	Sequence
1	CK138 V <sub>H</sub> amino acid sequence	EVQLVESDGGGLVQPGGSLRLSCAASGFNLSYYGMHWVRQA PGKGLEWVAYIASYPGYTSYADSVKGRFTISADTSKNTAYL QMNSLRAEDTAVYYCARSGYSYSPYYSWFSAGMNYWGQG ALVTVSS
2	CK138 V <sub>L</sub> amino acid sequence	AIQMTRSPSSLSASVGDRVTITCRASQYHDGSAAWYQQKPG KAPKLLIYGASYLYSGVPSRFSRSGTDFTLTISSLQPEDFA TYYCQQSSYSLITFGQGTKVEIK
3	CK138 V <sub>H</sub> nucleic acid sequence	GAGGTTTCAGCTGGTGGAGTCTGACGGTGGCCTGGTGCAGCCAGGG GGCPCACTCCGTTTGTCTGTGCAGCTTCTGGCTTCAACCTCTCT TACTACGGTATGCACTGGGTGCGTCAGGCCCGGGTAAGGGCCCG GAATGGGTTGCATACATTGCTTCTTACCCTGGCTACACTTCTTAT GCCGATAGCGTCAAGGGCCGTTTCACTATAAGCGCAGACACATCC AAAAACACAGCCTACCTACAAATGAACAGCTTAAGAGCTGAGGAC ACTGCCGTCTACTATTGTGCTCGCTCTGGTTACAGTTACTCTCCG TATTATTCTTGGTTCTCTGCTGGTATGAACTACTGGGGTCAAGGA GCCCTGGTCAACCGTCTCCTCG
4	CK138 V <sub>L</sub> nucleic acid sequence	GCTATCCAGATGACCCGGTCCCCGAGCTCCCTGTCCGCCTCTGTG GGCGATAGGGTCACCATCACCTGCCGTGCCAGTCAGTACCACGAC GGTTCTGCAGCCTGGTATCAACAGAAACCAGGAAAAGCTCCGAAG CTTCTGATTTACGGTGCATCCTACCTCTACTCTGGAGTCCCTTCC CGCTTCTCTGGTAGCCGTTCCGGGACGGATTTCACTCTGACCATC AGCAGTCTGCAGCCGGAAGACTTCGCAACTTATTACTGTGAGCAA TCTTCTTATTCTCTGATCACGTTTCGGACAGGGTACCAAGGTGGAG ATCAA
5	CK138 V <sub>H</sub> CDR1	NLSYYGMH
6	CK138 V <sub>H</sub> CDR2	AYIASYPGYTSY
7	CK138 V <sub>H</sub> CDR3	RSGYSYSPYYSWFSAGMN
8	CK138 V <sub>L</sub> CDR1	QYHDGSA
9	CK138 V <sub>L</sub> CDR2	YGASYL
10	CK138 V <sub>L</sub> CDR3	QSSYSLIT
11	CK157 V <sub>II</sub> amino acid sequence	EVQLVESGGGLVQPGGSLRLSCAASGSNPYYYGGTHWVRQ APGEELEWVASIGSYPGYTDYADSVKGRFTISADTSKNTAY LQMNSLRAEDTAVYYCARHYYWYDATDYWGQGTLVTVS S
12	CK157 V <sub>L</sub> amino acid	DIQMTQSPSSLSASVGDRVTITCRASQSYGGVAWYQQKPGK APKLLIYSASYLYSGVPSRFSRSGTDFTLTISSLQPEDFAT

	sequence	YYCQQPSHLITFGQGTEVEIK
13	CK157 V <sub>H</sub> nucleic acid sequence	GAGGTTTCAGCTGGTGGAGTCTGGCGGTGGCCTGGTGCAGCCAGGG GGCTCACTCCGTTTGTCTGTGCAGCTTCTGGCTCCAACCCCTAC TACTACGGTGGTACGCACTGGGTGCGTCAGGCCCGGGTGAGGAG CTGGAATGGGTTGCATCTATTGGTTCTTACCCTGGCTACACTGAC TATGCCGATAGCGTCAAGGGCCGTTTCACTATAAGCGCAGACACA TCCAAAAACACAGCCTACCTACAAATGAACAGCTTAAGAGCTGAG GACACTGCCGTCTATTATTGTGCTCGCCATTACTACTGGTACGAT GCTACTGACTACTGGGGTCAAGGAACCCTGGTACCGTCTCCTCG
14	CK157 V <sub>L</sub> nucleic acid sequence	GATATCCAGATGACCCAGTCCCCGAGCTCCCTGTCCGCCTCTGTG GGCGATAGGGTCACCATCACCTGCCGTGCCAGTCAGTCTTACGGT GGTGTAGCCTGGTATCAACAGAAACCAGGAAAAGCCCCGAAGCTT CTGATTTACTCTGCATCCTACCTCTACTCTGGAGTCCCTTCTCGC TTCTCTGGTAGCCGTTCCGGGACGGATTTCACTCTGACCATCAGC AGTCTGCAGCCGGAAGACTTCGCAACTTATTACTGTCAGCAACCA TCTCATCTGATCACGTTCCGGACAGGGTACCGAGGTGGAGATCAAA
15	CK157 V <sub>H</sub> CDR1	NPYYYGGTH
16	CK157 V <sub>H</sub> CDR2	ASIGSYPGYTDY
17	CK157 V <sub>H</sub> CDR3	RHYYWYDATD
18	CK157 V <sub>L</sub> CDR1	QSYGGV
19	CK157 V <sub>L</sub> CDR2	YSASYL
20	CK157 V <sub>L</sub> CDR3	QPSHLIT
21	CK129 V <sub>H</sub> amino acid sequence	EVQLVESGGGLVQPGGSLRLSCAASGFMNYSYGSMHWVRQ APGKGLEWVASIYPYSSSTYYADSVKGRFTISADTSKNTAY LQMNSLRAEDTAVYYCARGYGPWYAYSIFALDYWGQGT LTVSS
22	CK129 V <sub>L</sub> amino acid sequence	DIQMTQSPSPLASVSGDRVTITCRASQYGGYVAWYQQKPG KAPKLLIYGASLLYSGVPSRFSGGRSGTDFTLTISSSLQPEDFA TYYCQRGHALITFGQGTKVEIE
23	CK129 V <sub>H</sub> nucleic acid sequence	GAGGTTTCAGCTGGTGGAGTCTGGCGGTGGCCTGGTGCAGCCAGGG GGCTCACTCCGTTTATCCTGTGCAGCTTCTGGCTTCAACATCTCT TCTTACGGTTCTATGCACTGGGTGCGTCAGGCCCGGGTAAGGGC CTGGAATGGGTTGCATCTATTACCCTTACTCTAGCTCTACTTAC TATGCCGATAGCGTCAAGGGCCGTTTCACTATAAGCGCAGACACA TCCAAAAACACAGCCTACCTACAAATGAACAGCTTAAGAGCTGAG GACACTGCCGTCTATTATTGTGCTCGTGGTTACGGTCCGTGGTAC GCTTACTCTTACTTCCGCTTTCGACTACTCGGGTCAAGGAACCCTG GTCACCGTCTCCTCG
24	CK129 V <sub>L</sub> nucleic acid	GATATCCAGATGACCCAGTCCCCGAGCCCCCTGTCCGCCTCTGTG GGCGATAGGGTCACCATCACCTGCCGTGCCAGTCAGTACGGTGGT









		<b>AAAATCCAGTGGCACCAGTGATGATAA</b>
37	<i>LS-Fc-His6-linker-TEV-hCXCL1<sup>38-107</sup>-G2-AviTag</i>	<p> <u>MEVFAQLLQGLLNLNLPGARCEPFRVPIIQNFCPPLEKCPFCAPDILLGGPSVFTF</u>  <u>FFKISQVLMISLSPMVTGVVVDVSEDDFQVQISWFFVNNVEVHTAQQQTTHREGDYN</u>  <u>STLRFVYSALPQQHQDWMSSGKRFKCFVNNPALFSPTEATLSKPRGSPVRAQVYVYL</u>  <u>FFFADEMIKKEFGLLQHLQVLPALAVDWLSNDRISQNYANLAVLQDGGSYF</u>  <u>MYKLRVQKSTWERSLFAQSVVHEGLANRLTTKTIKRSLSGKHHHHHHSSSGVDL</u>  <u>GTENLYFQATELRCQCLQTLQGIHPKNIQSVNVKSPGPHCAQTEVATLKNGRK</u>  <u>ACLNPAAPIVKKIIEKMLNSDKSNGGGLNDFEFAQKIEWHE--</u> </p>
38	<i>LS-Fc-His6-linker-TEV-hCXCL5<sup>43-114</sup>-G2-AviTag</i>	<p> <u>MEVFAQLLQGLLNLNLPGARCEPFRVPIIQNFCPPLEKCPFCAPDILLGGPSVFTF</u>  <u>FFKIKDVLMLISLSPMVTGVVVDVSEDDPDVQIQWVYNNVEVHLAQQLQKREDYN</u>  <u>STLRFVYSALPQQHQDWMSSGKRFKCFVNNPALFSPTEATLSKPRGSPVRAQVYVYL</u>  <u>FFFADEMIKKEFGLLQHLQVLPALAVDWLSNDRISQNYANLAVLQDGGSYF</u>  <u>MYKLRVQKSTWERSLFAQSVVHEGLANRLTTKTIKRSLSGKHHHHHHSSSGVDL</u>  <u>GTENLYFQVRELRCVCLQTTQGVHPKMLSNLQVFAIGPQCSKVEVVASLKNKG</u>  <u>EICLDPEAPFLKKVIQKILDGGNRENGGGLNDFEFAQKIEWHE--</u> </p>
39	<i>LS-Fc-His6-linker-TEV-hCXCL8<sup>29-99</sup>-G2-AviTag</i>	<p> <u>MEVFAQLLQGLLNLNLPGARCEPFRVPIIQNFCPPLEKCPFCAPDILLGGPSVFTF</u>  <u>FFKIKDVLMLISLSPMVTGVVVDVSEDDPDVQIQWVYNNVEVHLAQQLQKREDYN</u>  <u>STLRFVYSALPQQHQDWMSSGKRFKCFVNNPALFSPTEATLSKPRGSPVRAQVYVYL</u>  <u>FFFADEMIKKEFGLLQHLQVLPALAVDWLSNDRISQNYANLAVLQDGGSYF</u>  <u>MYKLRVQKSTWERSLFAQSVVHEGLANRLTTKTIKRSLSGKHHHHHHSSSGVDL</u>  <u>GTENLYFQAKELRCQCIKTYSKPFHPKFIKELRVIESGPHCANTEIVKLSDGR</u>  <u>ELCLDPKENWVQRVVEKFLKRAENSGGGLNDFEFAQKIEWHE--</u> </p>
40	<i>LS-Fc-His6-linker-TEV-mCXCL1<sup>28-96</sup>-G2-AviTag</i>	<p> <u>MEVFAQLLQGLLNLNLPGARCEPFRVPIIQNFCPPLEKCPFCAPDILLGGPSVFTF</u>  <u>FFKIKDVLMLISLSPMVTGVVVDVSEDDPDVQIQWVYNNVEVHLAQQLQKREDYN</u>  <u>STLRFVYSALPQQHQDWMSSGKRFKCFVNNPALFSPTEATLSKPRGSPVRAQVYVYL</u>  <u>FFFADEMIKKEFGLLQHLQVLPALAVDWLSNDRISQNYANLAVLQDGGSYF</u>  <u>MYKLRVQKSTWERSLFAQSVVHEGLANRLTTKTIKRSLSGKHHHHHHSSSGVDL</u>  <u>GTENLYFQANELRCQCLQTMAGIHLKNIQSLKVLPSGPHCIQTEVATLKNGRE</u>  <u>ACLDPEAPLVQKIVQKMLKGVKGGGLNDFEFAQKIEWHE</u> </p>
41	<i>LS-Fc-His6-linker-TEV-mCXCL2<sup>31-100</sup>-G2-AviTag</i>	<p> <u>MEVFAQLLQGLLNLNLPGARCEPFRVPIIQNFCPPLEKCPFCAPDILLGGPSVFTF</u>  <u>FFKIKDVLMLISLSPMVTGVVVDVSEDDPDVQIQWVYNNVEVHLAQQLQKREDYN</u>  <u>STLRFVYSALPQQHQDWMSSGKRFKCFVNNPALFSPTEATLSKPRGSPVRAQVYVYL</u>  <u>FFFADEMIKKEFGLLQHLQVLPALAVDWLSNDRISQNYANLAVLQDGGSYF</u>  <u>MYKLRVQKSTWERSLFAQSVVHEGLANRLTTKTIKRSLSGKHHHHHHSSSGVDL</u>  <u>GTENLYFQASELRCQCLKTLPRVDFKNIQSLSVTPPGPHCAQTEVATLKGQK</u>  <u>VCLDPEAPLVQKIIQKILNKGKANGGGLNDFEFAQKIEWHE--</u> </p>
42	<i>LS-Fc-His6-linker-TEV-mCXCL5<sup>48-118</sup>-G2-AviTag</i>	<p> <u>MEVFAQLLQGLLNLNLPGARCEPFRVPIIQNFCPPLEKCPFCAPDILLGGPSVFTF</u>  <u>FFKIKDVLMLISLSPMVTGVVVDVSEDDPDVQIQWVYNNVEVHLAQQLQKREDYN</u>  <u>STLRFVYSALPQQHQDWMSSGKRFKCFVNNPALFSPTEATLSKPRGSPVRAQVYVYL</u>  <u>FFFADEMIKKEFGLLQHLQVLPALAVDWLSNDRISQNYANLAVLQDGGSYF</u>  <u>MYKLRVQKSTWERSLFAQSVVHEGLANRLTTKTIKRSLSGKHHHHHHSSSGVDL</u>  <u>GTENLYFQATELRCVCLVTTPKINPKLIANLEVIIPAGPQCPTVEVLAKLKNQKE</u> </p>









		<p>GATATCTGACACTTTGACACAAAGACAAATGACATTAATTAACAAAATGGCTGTT          GUTTGACTGATGAAACACAAAGGCAAGGCTACAGGCGGACAAACGAAACAGCTGC          ATGATGACTTTGACACACTTTCGACATGACATGTTTAAACGCTTCTGACAAAGAC          AGCTGCTTCTGACTTAAAGGCTTCAAACTTGTGACTAGATGCAAAAGAGGCTTAA  <u>CCCGGAGGGGGCGGTTCCACCATCACCACCATCACTGATAA</u></p>
<p>48</p> <p><i>gWiz-LS- hCXCL6<sup>43-114</sup> (Gly<sub>4</sub>Ser)<sub>2</sub>- mouse SA- (Gly<sub>4</sub>Ser)- His<sub>6</sub></i></p>		<p><b>ATG</b>AGGGTCCCGGCTGACGCTGCTGGGGCTCTGCGGCTTTCGGCCGCGAGGAGGAA  <u>CGATCT</u>GTGCTGACCGAGCTGCGGGTGCACCTGTCTGAGAGTGACCCTGCGCGTG  <b>AACCCCAAGACCATCGGCAAGCTCCAGGTGTTCCCTGCCGGCCCTCAGTGCAGC</b>  <b>AAGGTGGAAGTGGTGGCCAGCCTGAAAAACGGAAAAACAAGTGTGCTGGACCCC</b>  <b>GAGGCCCCATTCTGAAGAAAGTGATCCAGAAGATCCTGGACAGCGGCAACAAG</b>  <b>AAGAACGGTGGAGGGCGGTAGCGGAGCGGGAGGGTTCG</b>CAAGGACAAUAAAGACAGAC          ATCCDDCATCCCTACAAATCATTCCGACAAACACATTTCAACCGGCTAGTCCGC          AATGCGCTTTCCGAGTAACTCCGACAAATGCGCCATACGATGAGCATGCCAAATTA          GGGTGGAAATACAGAACTTGGCAAGAGCGCTGCTGGATGAGAGCGGCGGCGGCGG          AACTGTGACAAATCCCTTCCGACACTCTCTTTGGAGATAAAGTTGCTGGCCACTCCA          AAGCTGCTGAAZAACTATGCTTAACTGGCTGACTGGCTTACAAZACAAAGAGCCG          GAAACAAACGAATCTTTCTGCAATACAAAATGACAAACCGGACGCTGCCAGCA          TTTGCAAGCGGACAGCGCTGAGGCAATGCGACCTGCTTGAAGCAAAACCCAGCC          AGTTTATGCGACACTATTTGATCAACTTCCCAAGAGCATCTTACTTATG          GCGCTAGAACTTCTTACTTGGTGAAGGAGTACAAAGAGATTCTGAGCCAAATGAT          IGLIUAAGGCTGAAAGAAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG          GAGAAAG          AAGTTTGGAG          TTCTTCAATCTGACTTTTAAAGAAATGACAAATTTGACAAATTTGACAAATTTGAC          GTGACAG          GACTTTCGACTATTTCTGCTGACAAAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG          ACTTGGCTGCAAAACGACTTTTAAAGAAATGAGAGAGAGAGAGAGAGAGAGAGAGAG          CALGAG          GAG          TTGAAAG          CTGCTGAG          GCGGCTGCTGAG          AAGTACCTGCTGAG          TTGAAAG          CCAATCTGAG          CCAATCTGAG          ACATTTCTGAG          CTGAG          AAGTCTGAG          GTGAG          TCTGAG          TTAG  <u>GGAGGGGGCGGTTCCACCATCACCACCATCACTGATAA</u></p>
<p>49</p> <p><i>gWiz-LS- hCXCL7<sup>59</sup></i></p>		<p><b>ATG</b>AGGGTCCCGGCTGACGCTGCTGGGGCTCTGCGGCTTTCGGCCGCGAGGAGGAA  <u>CGATCT</u>GCCGAGCTGCGGGTGCATGTGCATCAAGACCACCAGCGGAATCCACCCC  <b>AAGAATATCCAGTCCCTGGAAGTGATTGGCAAGGGCACCCTGCAACCAGGTG</b></p>





		<pre> TTTCAAAATGC CAGATWTCAGCCDRTATCTGCAUUCGCTTC AACCABAAACCCAAAC ACCTTTATGCGACACTATTTGDAATGAACTTCUUCAGAGGCAATCTTAATTTCTAT GGGACAGAACTTCTTTACTATGCTCGAATACDACAAGACACATTCTGACCCCA TTCT TCTGCGAGAGGCTGACATAGGAAAGCTTGCCTGACCCGSAAGCTTTGATGGCTCTGAA (GAGAAAAG)A1 JUTDTCAG JUTWL DCG JGAGAGAA JUAHHIGC JCUAG. A LKAG AACTTTGAGAGAGAGGCTTTTAAAGGCTATGGGCGAGTACCTGGCTGAGCCGAGAA TTCCCGAATGCTGACTTTTGCAGAAATCACCAATTTGGGACAGACCTGACDAAA CTTACACACCCCTGCTCTD TATGCTCACTTCTCTCCATTCG CDMATGACAC DCTG GAAATTCGCAATACATGCTGAAAGACCGGGGCACTATCTCCAGGAAACCTGCAAG ACTTCCCTGCGATAAACTACCTCTTAAACAAAATCCACTCTCTTTACTGCACTCCAC CATGACACCAATGCTTCTGATCTTCCCTTCCATTTGCTGCTTATCTCTTGGAGAC CAGGAGCTCTGCAAGAACT. A1 GCTGAGGCGCAAGGAA1 GCTCTCC. GGGGACG11 C TTCTATCAATATTCAC CT JSTUAAAGAAATL GAAGGAACTIG1GGAAAG1GCTGCGC1GAAAGGCAAA JUT CCCGGACTCTACCC TATGCTCTCTTGC TCBACTTTCACCCCTTTTC CACAGACCCCT AGGAACTTGGCTCAAAAGCACTTGTGACTCTTCCGAGAGAGCTTTGGGAAATLGGAA TTCTAAATDCTATDCTATCTTCTCTA TCC CACAAAGCAGCTTCTGCTCTCAAC CTACTCTCTCTGAGCTCTGACAAACCTTACGAACTCTCTCTCTCTCTCTCTCTCTCT ACACTCTCTGAGGAL CAGACAC1 GGC TGTG1GGAAAGC1A1GCTCTC. GCAAGC CTGAAACCTGCT AAG1GC JUTAG1GGATGDD1GG JGAAAGGCGAGAA1 GCTCTC1 GCTCTCTCTCT CTTATGAAACATATDCTDCTGAAAGATTTTAAAGTCTGACACCCCTGACCTCTCTCT HJUAATATCTGACACTTCTGAAAGAGAGGAGAAAGCAATL AAGAAACAAACGAACT CTTCCCTTACCTCTCTTACGACAACTTCTGAACTTACACACCTTACGACACTTCTCTG GACACTGAGACTTCTGACACTTCTGAAATACATCTTGGGAGGCTCTCTCTCTCTCTCT GACACTGAGCTCTCTGAGGCTGAAAGCTTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT TTAAAGGAGGGGGCGGTTCACCACATCACCACCATCAGCTGATAA                 </pre>
<p>51</p>	<p><i>gWiz-LS- hCXCL9<sup>23-125</sup> (Gly<sub>4</sub>Ser)<sub>2</sub>- mouse SA- (Gly<sub>4</sub>Ser)- His<sub>6</sub></i></p>	<pre> <b>ATG</b>AGCCCTGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGG <b>CGGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGCGGCGG</b> <b>GGCACCATCCATCTCCAGTCTCTGAAAGGACCTGAAGCAGTTTCGCCCCAGCCCC</b> <b>AGCTGCGGAGAAGATCGAGATTATCGCCACACTGAAAAACGGGGGTGCAGACCTGC</b> <b>CTGAACCCCGACAGCGCGGACGCTGAAAAGAACTGATCAAGAAAATGGGAGAAAACAG</b> <b>GTGTCCCAAGAAGAAGAAGCAGAAGAACGGAAAGAAGCACCAGAAAAAGAAAAGTG</b> <b>CTGAAAAGTGCGGGAAGTCCCAGCGGAGCCGGGCAGAAGAAAACCACAGGTGGAGGGC</b> <b>GGTAGGCGGAGGGCGGAGGGGTCG</b> TAAKACCBKAGCACTCACTTCTCTCTCTCTCTCT AATCATTTGGGAGAAACAATTTCTGAAAGGCTTACTCTCTCTCTCTCTCTCTCTCTCTCT TATCTCTGAAATGCTCATACATGAGCCTTCCCAAAATTAATGCAAGAAATTAAGA CACTTTCCAAAGACCT CTTAAACT HADCTTACT TCT GC1 GAGGGGAL G1 GCAAG1 CT1 TTAAGGAAAGGCTAAGCACT11A JGAAAGC TCT LACTATCT1 GAGUAG1 ACAATGAGAA1 JCTGAACTGAG11 G1 GCAAG1 GAG1 GAG AACCAGAACT TUAATCT CTTTTTAAAGTATCCCGATCT TTCTGAGAAATCACCAGATTTGGCAACAGGCTGACGAAATCTCAAGAAATCTCTCTCT                 </pre>





















		<p>CTLEGGQRIKCVEDYLSAELNRVCLLHESTFVSEHVTKCCSGSLVERRRPQFSAL  TVDEETVYVFFKAEETFTFHSDICTLPEKREKQIKKQFALAEIVKAAFLZTAEQLK  TVMDDFAQFLDPTCKRAADKDTCPFTESPHLVTRQNDALAGGGGSHHHHHHH--</p>
64	<p><i>LS-</i>  <i>hCXCL2</i><sup>35-</sup>  <i>107</i>  <i>(Gly4Ser)</i><sub>2</sub>-  <i>mouse SA-</i>  <i>(Gly4Ser)-</i>  <i>His6</i></p>	<p><u>KNVFAQLLGLLGLLNLIIKARCAPLATELRCQCLQTLQGIHLKNIQSVKVKSPGPH</u>  <b>CAQTEVIATLKNQKACLNPA</b>SPMVKKIIEKMLKNGKSNNGGGSGGGGSEAKKSEI  EIAHYNDLGEQHFKGLVLLAFSQYLQKCSYDERAKLVQEVTFPAKDCVADESA  ANQKSLNHLFGUKLQALFNDRNIGELDUCQIAGEFANRQELQKDDNFSLP  FFERPEAEAMCTPFPENPTTFMGNYLREYAFWHPYFAYEELLYAEQYNEELTQ  CCAEADKESCLTPKLDGVKEXALVSSVQRMGCSMGEFQBRATYAWAVARLSQ  TFENADFAELKLAELTKVYRACUNODLLECAULMAELAKYKQENQATLSKLL  QTCDDKPLKKAACLSSEVERPTMPAULPALASDFVEDQEVCKNYAAKQVFLGT  FLYETSPFPDYSVSLLEKLAHYEATLEKCCAEANPFPACYGTVLAEFQPLVVEE  PKNLVKTNCULYERLQENQQAELVRYIQKAPQVSTFTLVFAAPHLCKVDTKCT  CTLEGGQRIKCVEDYLSAELNRVCLLHESTFVSEHVTKCCSGSLVERRRPQFSAL  TVDEETVYVFFKAEETFTFHSDICTLPEKREKQIKKQFALAEIVKAAFLZTAEQLK  TVMDDFAQFLDPTCKRAADKDTCPFTESPHLVTRQNDALAGGGGSHHHHHHH--</p>
65	<p><i>LS-</i>  <i>hCXCL3</i><sup>35-</sup>  <i>107</i>  <i>(Gly4Ser)</i><sub>2</sub>-  <i>mouse SA-</i>  <i>(Gly4Ser)-</i>  <i>His6</i></p>	<p><u>KNVFAQLLGLLGLLNLIIKARCAPLATELRCQCLQTLQGIHLKNIQSVNVRSPGPH</u>  <b>CAQTEVIATLKNQKACLNPA</b>SPMVQKIIEKILKNGSTNNGGGSGGGGSEAKKSEI  EIAHYNDLGEQHFKGLVLLAFSQYLQKCSYDERAKLVQEVTFPAKDCVADESA  ANQKSLNHLFGUKLQALFNDRNIGELDUCQIAGEFANRQELQKDDNFSLP  FFERPEAEAMCTPFPENPTTFMGNYLREYAFWHPYFAYEELLYAEQYNEELTQ  CCAEADKESCLTPKLDGVKEXALVSSVQRMGCSMGEFQBRATYAWAVARLSQ  TFENADFAELKLAELTKVYRACUNODLLECAULMAELAKYKQENQATLSKLL  QTCDDKPLKKAACLSSEVERPTMPAULPALASDFVEDQEVCKNYAAKQVFLGT  FLYETSPFPDYSVSLLEKLAHYEATLEKCCAEANPFPACYGTVLAEFQPLVVEE  PKNLVKTNCULYERLQENQQAELVRYIQKAPQVSTFTLVFAAPHLCKVDTKCT  CTLEGGQRIKCVEDYLSAELNRVCLLHESTFVSEHVTKCCSGSLVERRRPQFSAL  TVDEETVYVFFKAEETFTFHSDICTLPEKREKQIKKQFALAEIVKAAFLZTAEQLK  TVMDDFAQFLDPTCKRAADKDTCPFTESPHLVTRQNDALAGGGGSHHHHHHH--</p>
66	<p><i>LS-</i>  <i>hCXCL4</i><sup>32-</sup>  <i>101</i>  <i>(Gly4Ser)</i><sub>2</sub>-  <i>mouse SA-</i>  <i>(Gly4Ser)-</i>  <i>His6</i></p>	<p><u>KNVFAQLLGLLGLLNLIIKARCAPLATELRCQCLQTLQGIHLKNIQSVNVRSPGPH</u>  <b>HCPTAQLIATLKNRGIKICLDLQAPLYKKI</b>IKKLLSEGGGGSGGGGSEAKKSEI  EIAHYNDLGEQHFKGLVLLAFSQYLQKCSYDERAKLVQEVTFPAKDCVADESA  ANQKSLNHLFGUKLQALFNDRNIGELDUCQIAGEFANRQELQKDDNFSLP  FFERPEAEAMCTPFPENPTTFMGNYLREYAFWHPYFAYEELLYAEQYNEELTQ  CCAEADKESCLTPKLDGVKEXALVSSVQRMGCSMGEFQBRATYAWAVARLSQ  TFENADFAELKLAELTKVYRACUNODLLECAULMAELAKYKQENQATLSKLL  QTCDDKPLKKAACLSSEVERPTMPAULPALASDFVEDQEVCKNYAAKQVFLGT  FLYETSPFPDYSVSLLEKLAHYEATLEKCCAEANPFPACYGTVLAEFQPLVVEE  PKNLVKTNCULYERLQENQQAELVRYIQKAPQVSTFTLVFAAPHLCKVDTKCT  CTLEGGQRIKCVEDYLSAELNRVCLLHESTFVSEHVTKCCSGSLVERRRPQFSAL  TVDEETVYVFFKAEETFTFHSDICTLPEKREKQIKKQFALAEIVKAAFLZTAEQLK  TVMDDFAQFLDPTCKRAADKDTCPFTESPHLVTRQNDALAGGGGSHHHHHHH--</p>
67	<p><i>LS-</i>  <i>hCXCL5</i><sup>44-</sup>  <i>114</i></p>	<p><u>KNVFAQLLGLLGLLNLIIKARCAPLATELRCQCLQTLQGIHLKNIQSVNVRSPGPH</u>  <b>VEVVASLKNQKEICLDPEAPFLKVIQKIL</b>DGGNKENGGGGGSGGGGSEAKKSEI  EIAHYNDLGEQHFKGLVLLAFSQYLQKCSYDERAKLVQEVTFPAKDCVADESA  ANQKSLNHLFGUKLQALFNDRNIGELDUCQIAGEFANRQELQKDDNFSLP  FFERPEAEAMCTPFPENPTTFMGNYLREYAFWHPYFAYEELLYAEQYNEELTQ  CCAEADKESCLTPKLDGVKEXALVSSVQRMGCSMGEFQBRATYAWAVARLSQ  TFENADFAELKLAELTKVYRACUNODLLECAULMAELAKYKQENQATLSKLL  QTCDDKPLKKAACLSSEVERPTMPAULPALASDFVEDQEVCKNYAAKQVFLGT  FLYETSPFPDYSVSLLEKLAHYEATLEKCCAEANPFPACYGTVLAEFQPLVVEE  PKNLVKTNCULYERLQENQQAELVRYIQKAPQVSTFTLVFAAPHLCKVDTKCT  CTLEGGQRIKCVEDYLSAELNRVCLLHESTFVSEHVTKCCSGSLVERRRPQFSAL  TVDEETVYVFFKAEETFTFHSDICTLPEKREKQIKKQFALAEIVKAAFLZTAEQLK  TVMDDFAQFLDPTCKRAADKDTCPFTESPHLVTRQNDALAGGGGSHHHHHHH--</p>

	<i>(Gly<sub>4</sub>Ser)<sub>2</sub>-mouse SA-(Gly<sub>4</sub>Ser)-His<sub>6</sub></i>	<p>           QDKS LRTLEFGDSE LCAI ENLRSNYGHELA I-GCTTKQEPERNGEUFILQ-BSGDDNPS LFF F            ERPEAEAMCTSPKAMN TTFYNOHYLWVAVRRHI YFYAPELLYYASQTHEIL LQQC            ABADYKESGLTFPKLDQVREKALVSSVRQRMKCS SMQKFCERAFKAWAVARI SQTF            FNAQVAEI TALE TDLTVVWVFCORGDLELCAADPRAEALAKYKCBHQATISSRLQY            GGRFVL LKKARULSKVERHTHPADLPA LAADYVLLN<sub>2</sub>EVCKNITABAKUYVLLNTVY            YENYRSHFDYGVSLLELRI AKRYEATIEKOCCEANPPACVGTVL ASFPQPLVEEERK            NIVKTNCDLXEKLGSEYGFQNA LLVNYTQKAPQVSTPTLVEAARNLGRVGTKCC            LPEDQPLFCVEDYLSA IINRVCLLBEKTFVYSGEVTKCCSGSIVERRPCPSALTY            DETYVPEKFTAEFTTFASPTCITLPEAKENQIKKQYALASL VAILVVALDABQKTY            MDLPAQFLDTCKAADKCTCFSTEGPNLVTECKDALA <u>GGGGS</u>HHHHHHH         </p>
68	<i>LS-hCXCL6<sup>43-114</sup>- (Gly<sub>4</sub>Ser)<sub>2</sub>- mouse SA- (Gly<sub>4</sub>Ser)- His<sub>6</sub></i>	<p>           RRYVLAQ LQLLL LLLPQAFVLT<del>ELR</del>CTCLRVTLRVNPKTIGKLVQVFPAGPQCS  <b>KVEVVASLKNKGQVCLDPEAPFLKKVIQKILD</b>SGNKKNGGGGGGGGGSSBAHKSE            LAHRYNDLGEQRKQVGLV LAFSQYLQKCSYDENAKLVQEVITUPAKCQVADPSAA            NCDKSLHTLFGDKLCA IINLPRHYGS LADGCTKQKPEPNECV LQHEFENPILAPP            FEFPEAEAMCTSPKAMN TTFYNOHYLWVAVRRHI YFYAPELLYYASQTHEIL LQQC            CAEADKESGLTFPKLDQVREKALVSSVRQRMKCS SMQKFCERAFKAWAVARI SQTF            FNAQVAEI TALE TDLTVVWVFCORGDLELCAADPRAEALAKYKCBHQATISSRLQY            TCCDRELLPKARCLSEVENDTMRADIPALAADYVLLN<sub>2</sub>EVCKNITABAKUYVLLNTVY            LYEYSPRSHFDYGVSLLELRI AKRYEATIEKOCCEANPPACVGTVLASFPQPLVEEERK            NIVKTNCDLXEKLGSEYGFQNA LLVNYTQKAPQVSTPTLVEAARNLGRVGTKCC            LLEPQPLFCVEDYLSA IINRVCLLBEKTFVYSGEVTKCCSGSIVERRPCPSALTY            DETYVPEKFTAEFTTFASPTCITLPEAKENQIKKQYALASL VAILVVALDABQKTY            MDLPAQFLDTCKAADKCTCFSTEGPNLVTECKDALA <u>GGGGS</u>HHHHHHH--         </p>
69	<i>LS-hCXCL7<sup>59-121</sup>- (Gly<sub>4</sub>Ser)<sub>2</sub>- mouse SA- (Gly<sub>4</sub>Ser)- His<sub>6</sub></i>	<p>           RRYVLAQ LQLLL LLLPQAFVLT<del>ELR</del>CTCLRVTLRVNPKTIGKLVQVFPAGPQCS  <b>EVIATLKDGRKICLDPDAPRIKKIVQKKL</b>GGGGGGGGGGSSBAHKSE LAHRYNDLQ            EQHFKGLVLLIAE SQLLQKCS IIRBAKLVQEVITUPAKICVADPSAANCLNS LMTL            FQDFLCAIENLRFENYDELADGCTTKQEPERNGEUFILQ-BSGDDNPS LFF F            ERPEAEAMCTSPKAMN TTFYNOHYLWVAVRRHI YFYAPELLYYASQTHEIL LQQC            CAEADKESGLTFPKLDQVREKALVSSVRQRMKCS SMQKFCERAFKAWAVARI SQTF            FNAQVAEI TALE TDLTVVWVFCORGDLELCAADPRAEALAKYKCBHQATISSRLQY            TKLADLTVVWVFCORGDLELCAADPRAEALAKYKCBHQATISSRLQY LCCDKPILK            KAHCTSEVENDTMRADIPALAADYVLLN<sub>2</sub>EVCKNITABAKUYVLLNTVY            DYSVST LLRLAKRYEATIEKOCCEANPPACVGTVLASFPQPLVEEERK NIVKTNCD            LYEYSPRSHFDYGVSLLELRI AKRYEATIEKOCCEANPPACVGTVLASFPQPLVEEERK            NIVKTNCDLXEKLGSEYGFQNA LLVNYTQKAPQVSTPTLVEAARNLGRVGTKCC            LPEDQPLFCVEDYLSA IINRVCLLBEKTFVYSGEVTKCCSGSIVERRPCPSALTY            DETYVPEKFTAEFTTFASPTCITLPEAKENQIKKQYALASL VAILVVALDABQKTY            MDLPAQFLDTCKAADKCTCFSTEGPNLVTECKDALA <u>GGGGS</u>HHHHHHH--         </p>
70	<i>LS-hCXCL8<sup>28-99</sup>- (Gly<sub>4</sub>Ser)<sub>2</sub>- mouse SA- (Gly<sub>4</sub>Ser)- His<sub>6</sub></i>	<p>           RRYVLAQ LQLLL LLLPQAFVLT<del>ELR</del>CTCLRVTLRVNPKTIGKLVQVFPAGPQCS  <b>ANTE IIVKLS</b>DGRELCLDPKENVQVVEKFLKRAENSGGGGGGGGGSSBAHKSE            LAHRYNDLGEQRKQVGLV LAFSQYLQKCSYDENAKLVQEVITUPAKCQVADPSAA            NCDKSLHTLFGDKLCA IINLPRHYGS LADGCTKQKPEPNECV LQHEFENPILAPP            FEFPEAEAMCTSPKAMN TTFYNOHYLWVAVRRHI YFYAPELLYYASQTHEIL LQQC            CAEADKESGLTFPKLDQVREKALVSSVRQRMKCS SMQKFCERAFKAWAVARI SQTF            FNAQVAEI TALE TDLTVVWVFCORGDLELCAADPRAEALAKYKCBHQATISSRLQY            ICCFST LKKARULSKVERHTHPADLPA LAADYVLLN<sub>2</sub>EVCKNITABAKUYVLLNTVY            LYEYSPRSHFDYGVSLLELRI AKRYEATIEKOCCEANPPACVGTVLASFPQPLVEEERK            NIVKTNCDLXEKLGSEYGFQNA LLVNYTQKAPQVSTPTLVEAARNLGRVGTKCC         </p>

		<p>ILFPPQRRLPQVDEYLSA ILNRVILIMHSTPVSEHVTNDCDSGLVGRRRPCFSALT                  VDETYPVPEPKAETFTFHSDDICTLPEKKAQILNKQDTALAEVYKHKSPATAEQKAE                  VMDDFAQFLDTCCKAARDSTCFSTROPMLVTRCKDALA <u>GGGGSHHHHHH</u>---</p>
71	<p><i>LS-</i>  <i>hCXCL9<sup>23-</sup></i>  <i>115<sub>-</sub></i>  <i>(Gly<sub>4</sub>Ser)<sub>2-</sub></i>  <i>mouse SA-</i>  <i>(Gly<sub>4</sub>Ser)-</i>  <i>His<sub>6</sub></i></p>	<p><u>KNVFAQLLGLLILNLIICARCTPVVRKGRCSCTSTNOGTIHLQSLKDLKQFAPSP</u>  <b>SCEKIEIIATLNKGVQTCLNPD SADVKELIKKWEKQVSQKKKQKNGKKHKQKKV</b>  <b>LKVRKSRQSRQKKTGGGGSGGGGS</b>EAHYSEIARFYKNDI EQQHFVGLVLLAFASQ                  LLQFUSYDERHAEVYQRYIVAYAKI QVADPSSANNQNSDEL LKQDNLCAI PHLKDN                  YGELLADQCTKQEPPEPNECFLOREDDNPFLEFFERPEAEAMCTSPKRNPTTFMGR                  YIHEVAREWPFYFAPFELLNYAEQYNECLTQCCAEADRESCTIPKLDGVKKAIV                  SSYVQPMBUSSNQKFCCKAKAWAVARLSQ LFFHADFAALITKALIDLLKVNKAC                  CRDYLIECADDFAEELAKYMCENQATLSSVLTQCCNKTPLKAAHCLSEVERDTHP                  ADLEAIADDFVEDQEVQDNYAERKDYFLCTFHYDNGRRHPDYQVGLDEPLASSY                  EATLEKCCAEANNPACYCTVLABFQPLVSEEPKHVKTNDIYFKLQBYCTQRAI                  LVRYIQEAPQVSTFLLVEAARHLGRVGLKCCCLPKDQQLI QVVDILSALLNPVC                  LLHEKTPVDEHVTKCCQDGLVKKRQCFSAITVDETYVPEKEDRAETTFPADACT                  LPEKQKQIARQTAIAELVHVKPKATAEQEKTYMDNFAQFLDTCCKAARDSTCF                  TEGPRLVTRCKDALA <u>GGGGSHHHHHH</u>---</p>
72	<p><i>LS-</i>  <i>hCXCL10<sup>22-</sup></i>  <i>98<sub>-</sub></i>  <i>(Gly<sub>4</sub>Ser)<sub>2-</sub></i>  <i>mouse SA-</i>  <i>(Gly<sub>4</sub>Ser)-</i>  <i>His<sub>6</sub></i></p>	<p><u>KPYFAQLLGLLILNLIICARCTVPLSRTVRCCTCISISINQPVNPRSLEKLEIIPASQ</u>  <b>FCPRVEIIATMKKKGKRCCLNPESKAIKNLLKAVSKERSKRSPGGGGSGGGGS</b>                  ANKSEIARRYNDLQEQWFKQLVCLAFSQVLOKCSYDERAMVQEVTFDAKTCVA                  USSAANKDPSLHILFQKLLCAIPNLREHYGELAUDCTYQEPBRNECFLQKDDN                  PSLPFFERPEAEAMCTSPKRNPTTFMGRYIHEVAREWPFYFAPFELLYAEQYNE                  LLQFUSYDERHAEVYQRYIVAYAKI QVADPSSANNQNSDEL LKQDNLCAI PHLKDN                  YGELLADQCTKQEPPEPNECFLOREDDNPFLEFFERPEAEAMCTSPKRNPTTFMGR                  YIHEVAREWPFYFAPFELLYAEQYNECLTQCCAEADRESCTIPKLDGVKKAIV                  SSYVQPMBUSSNQKFCCKAKAWAVARLSQ LFFHADFAALITKALIDLLKVNKAC                  CRDYLIECADDFAEELAKYMCENQATLSSVLTQCCNKTPLKAAHCLSEVERDTHP                  ADLEAIADDFVEDQEVQDNYAERKDYFLCTFHYDNGRRHPDYQVGLDEPLASSY                  EATLEKCCAEANNPACYCTVLABFQPLVSEEPKHVKTNDIYFKLQBYCTQRAI                  LVRYIQEAPQVSTFLLVEAARHLGRVGLKCCCLPKDQQLI QVVDILSALLNPVC                  LLHEKTPVDEHVTKCCQDGLVKKRQCFSAITVDETYVPEKEDRAETTFPADACT                  LPEKQKQIARQTAIAELVHVKPKATAEQEKTYMDNFAQFLDTCCKAARDSTCF                  TEGPRLVTRCKDALA <u>GGGGSHHHHHH</u></p>
73	<p><i>LS-</i>  <i>hCXCL11<sup>22-</sup></i>  <i>94<sub>-</sub></i>  <i>(Gly<sub>4</sub>Ser)<sub>2-</sub></i>  <i>mouse SA-</i>  <i>(Gly<sub>4</sub>Ser)-</i>  <i>His<sub>6</sub></i></p>	<p><u>KRYFAQLLGLLILNLIICARCTFPMFKRGRCLCIGPGVKAVKVADIEKASIMYPSN</u>  <b>NCDKIEVIITLKENKGQRCLNPKSKQARLI IKKVERKNFGGGSGGGGS</b>EAHYG                  EIAKRYNDLQEQWFKQLVCLAFSQVLOKCSYDERAMVQEVTFDAKTCVADELA                  ANCISSLHTLFOKLLCAIPNLREHYGELAUDCTYQEPBRNECFLQKDDNPSLP                  PFERPEAEAMCTSPKRNPTTFMGRYIHEVAREWPFYFAPFELLYAEQYNECLTQ                  CCADAEHESCLIPHLFQVKKKALVSSVQPMBUSSNQKFCCKAKAWAVARLSQ                  TFFHADFAALITKALIDLLKVNKACCRDYLIECADDFAEELAKYMCENQATLSSVLT                  QCCNKTPLKAAHCLSEVERDTHPADLEAIADDFVEDQEVQDNYAERKDYFLCT                  FHYDNGRRHPDYQVGLDEPLASSY EATLEKCCAEANNPACYCTVLABFQPLVSE                  EEPKHVKTNDIYFKLQBYCTQRAILVRYIQEAPQVSTFLLVEAARHLGRVGLKCC                  CLPKDQQLI QVVDILSALLNPVC LLHEKTPVDEHVTKCCQDGLVKKRQCFSAI                  TVDETYVPEKEDRAETTFPADACTLPEKQKQIARQTAIAELVHVKPKATAEQEK                  TYMDNFAQFLDTCCKAARDSTCFSTECENLVTRCKDALA <u>GGGGSHHHHHH</u>---</p>
74	<i>LS-</i>	<p><u>KNVFAQLLGLLILNLIICARCTAPIANELRCQCLQTMAGIHLKNIQSLKVLPSGPH</u></p>

	<p><i>mCXCL1</i><sup>25-96</sup> <i>(Gly4Ser)</i><sub>2</sub>- <i>mouse SA-</i> <i>(Gly4Ser)-</i> <i>His6</i></p>	<p><b>CTQTEVIATLKNGREACLDPEAPLVQKIVQKMLKGVPKGGGGSGGGGS</b>EAHKS E IAHRYNDLGEQHFVKGLVLLAFSQYLQKCSYDERAAKLVQEVTFDFAKTCVADDEGA ANCDKSLHTLFDKLCALPHLPHENYGLADCCTRQDEPERNECF LQHKDGNF SLF PFEERFSAHMCCTGFKENFTTFMCHYLAEVARRRPFYFYAPPELLYQAEQYNEILLTQC CCAEADKESCLITKLDGVLEAAIVSSYVQRMKCSNMQKFFTEPAFSAWAVARLSQIT TFNADPFAEITKLAIDLTGVNKECCWGDILLECADRARAIAKYMENQATISSALQ TCCDAPLAKKARCLSEVENDTNPADLFAAADFVEDQEVCKNYASAKDVF LST FLNEYSPRHPDYGVSLLLRLAKKYEALTEKCCAEANPPACVCTVLAHFQPLVERE PKNLVKTACULYKALDGEYQQAHLVRYTQKXRPQVSTFLVFAARNLGRVGTAC CTLEFEDQRLFCVEDYLSALNRPVCLLNEKTPVSEHVTKCCSGSLVERRRPFCFSAI TVDETYVPRFPAEFTTFHSDICTLPEKKEKQIKKQFALAPLVKHKPKATAEQLK TVNDDFAQFLDCCCKAARPKDTFSTGCPNLVTRCKDALLA <u>GGGGSHHHHHHH</u>---</p>
<p>75</p>	<p><i>LS-</i> <i>mCXCL2</i><sup>28-100</sup> <i>(Gly4Ser)</i><sub>2</sub>- <i>mouse SA-</i> <i>(Gly4Ser)-</i> <i>His6</i></p>	<p><b>MEVFAQLLGLLLEWLEFARAVVASELRCQCLKTLPRVDFKNIQSLSVTPPGPH</b> <b>CAQTEVIATLKGQKVCVDPEAPLVQKI IQKILNKGKANGGGGSGGGGS</b>EAHKS EIAHRYNDLGEQHFVKGLVLLAFSQYLQKCSYDERAAKLVQEVTFDFAKTCVADDEGA ANCDKSLHTLFDKLCALPHLPHENYGLADCCTRQDEPERNECF LQHKDGNF SLF PFEERFSAHMCCTGFKENFTTFMCHYLAEVARRRPFYFYAPPELLYQAEQYNEILLTQC CCAEADKESCLITKLDGVLEAAIVSSYVQRMKCSNMQKFFTEPAFSAWAVARLSQIT TFNADPFAEITKLAIDLTGVNKECCWGDILLECADRARAIAKYMENQATISSALQ TCCDAPLAKKARCLSEVENDTNPADLFAAADFVEDQEVCKNYASAKDVF LST FLNEYSPRHPDYGVSLLLRLAKKYEALTEKCCAEANPPACVCTVLAHFQPLVERE PKNLVKTACULYKALDGEYQQAHLVRYTQKXRPQVSTFLVFAARNLGRVGTAC CTLEFEDQRLFCVEDYLSALNRPVCLLNEKTPVSEHVTKCCSGSLVERRRPFCFSAI TVDETYVPRFPAEFTTFHSDICTLPEKKEKQIKKQFALAPLVKHKPKATAEQLK TVNDDFAQFLDCCCKAARPKDTFSTGCPNLVTRCKDALLA <u>GGGGSHHHHHHH</u>---</p>
<p>76</p>	<p><i>LS-</i> <i>mCXCL3</i><sup>28-100</sup> <i>(Gly4Ser)</i><sub>2</sub>- <i>mouse SA-</i> <i>(Gly4Ser)-</i> <i>His6</i></p>	<p><b>MEVFAQLLGLLLEWLEFARAVVASELRCQCLNTLPRVDFETIQSLTVTPPGPH</b> <b>CTQTEVIATLKDQGEVCLNPQGPRLQII IKKILKSGKSSGGGGSGGGGS</b>EAHKS EIAHRYNDLGEQHFVKGLVLLAFSQYLQKCSYDERAAKLVQEVTFDFAKTCVADDEGA ANCDKSLHTLFDKLCALPHLPHENYGLADCCTRQDEPERNECF LQHKDGNF SLF PFEERFSAHMCCTGFKENFTTFMCHYLAEVARRRPFYFYAPPELLYQAEQYNEILLTQC CCAEADKESCLITKLDGVLEAAIVSSYVQRMKCSNMQKFFTEPAFSAWAVARLSQIT TFNADPFAEITKLAIDLTGVNKECCWGDILLECADRARAIAKYMENQATISSALQ TCCDAPLAKKARCLSEVENDTNPADLFAAADFVEDQEVCKNYASAKDVF LST FLNEYSPRHPDYGVSLLLRLAKKYEALTEKCCAEANPPACVCTVLAHFQPLVERE PKNLVKTACULYKALDGEYQQAHLVRYTQKXRPQVSTFLVFAARNLGRVGTAC CTLEFEDQRLFCVEDYLSALNRPVCLLNEKTPVSEHVTKCCSGSLVERRRPFCFSAI TVDETYVPRFPAEFTTFHSDICTLPEKKEKQIKKQFALAPLVKHKPKATAEQLK TVNDDFAQFLDCCCKAARPKDTFSTGCPNLVTRCKDALLA <u>CCCGSHHHHHHH</u>---</p>
<p>77</p>	<p><i>LS-</i> <i>mCXCL4</i><sup>30-105</sup> <i>(Gly4Ser)</i><sub>2</sub>- <i>mouse SA-</i> <i>(Gly4Ser)-</i></p>	<p><b>MEVFAQLLGLLLEWLEFARAVVASELRCQCLNTLPRVDFETIQSLTVTPPGPH</b> <b>VIKAGRHCAPVQLIATLKNGRKICLDRQAPLYKKVIRKILES</b>GGGGSGGGGS EAHKS EIAHRYNDLGEQHFVKGLVLLAFSQYLQKCSYDERAAKLVQEVTFDFAKTCVAD DEGAANCDKSLHTLFDKLCALPHLPHENYGLADCCTRQDEPERNECF LQHKDGNF SLF PFEERFSAHMCCTGFKENFTTFMCHYLAEVARRRPFYFYAPPELLYQAEQYNEILLTQC CCAEADKESCLITKLDGVLEAAIVSSYVQRMKCSNMQKFFTEPAFSAWAVARLSQIT TFNADPFAEITKLAIDLTGVNKECCWGDILLECADRARAIAKYMENQATISSALQ TCCDAPLAKKARCLSEVENDTNPADLFAAADFVEDQEVCKNYASAKDVF LST FLNEYSPRHPDYGVSLLLRLAKKYEALTEKCCAEANPPACVCTVLAHFQPLVERE PKNLVKTACULYKALDGEYQQAHLVRYTQKXRPQVSTFLVFAARNLGRVGTAC CTLEFEDQRLFCVEDYLSALNRPVCLLNEKTPVSEHVTKCCSGSLVERRRPFCFSAI TVDETYVPRFPAEFTTFHSDICTLPEKKEKQIKKQFALAPLVKHKPKATAEQLK TVNDDFAQFLDCCCKAARPKDTFSTGCPNLVTRCKDALLA <u>CCCGSHHHHHHH</u>---</p>

	<i>His6</i>	<p>IGTFLYEYSPRRRFPQYSVSLLLRLAKYNEBATLEKCCA SANPPAC YCTVLAEEFQF I  VEEPRAIYVFNODLYEKI CEYVGFQNAL LVRYTQKAPQVSEFTLVEAAENI DRVQ  TRQWTLBPQRLPCVBYLSA ELNRVCLLHEETPVSEHVTRQDSSGLVERRRPF  SADTVDEL YVPEEFKARTFTFHSQICOTLPEKKAQLEKQATALAEVYKHKRDATAE  QLATVMDDEA QF LUL DCKAAHKDICE STGDFNLY LKDKDALA <u>GGGGSNNHHHHH</u>—  —</p>
78	<p><i>LS-</i>  <i>mCXCL5<sup>48-</sup></i>  <i>118_</i>  <i>(Gly4Ser)<sub>2-</sub></i>  <i>mouse SA-</i>  <i>(Gly4Ser)-</i>  <i>His6</i></p>	<p><u>MEVFAQQLLQELLELNLPGAE</u> <b>A</b>TELRCVCLTVTPKINPKLIANLEVIPAGPQCPT  <b>VEVIARLKNQKEVCLDPEAPVIKKIIQKILGSDKKKAGGGSSGGGSS</b>EAHKSEI  AHRYNDLGEYGFQNAL LVRYTQKAPQVSEFTLVEAAENI DRVQ  DUKSLH LFPQCKLCA LFN LMAHYCRLADCC LKQKPEPHECFL QHKDNNLSLWFA  ERFEAEANOTSEVENPTTFMGHYLAEVAFRHPYFYAPEL LY YARQYNE L TQCCAEASK  AEASRESCITTFE LDVYKEKALVSYVQFMKCSMCEPQPRAEKAVAVARLSQTF  PNADFPALTKLATD LTKVNRKCCGSD LLECADDRAEALAFYKCEHQAC LGGKLOT  GDDKPL LKKAHC LSEVCHDIMPADLFAI AADFVEQEVCLNXYAAAEVFL E LFL  YRYSRRHPDYSVSL LRLAKYNEATLEKCCA SANPPAC YCTVLAEEFQF I  ELVKTNCDLYEYGFQNAL LVRYTQKAPQVSEFTLVEAAENI DRVQ  LPELQRLPCVBYLSA ELNRVCLLHEETPVSEHVTRQDSSGLVERRRPFSA LTV  DETYVPEEFKARTFTFHSQICOTLPEKKAQLEKQATALAEVYKHKRDATAEQ LATV  MDFAQPLDTCCKAAADTCVSTGDFNLYLVRKDDALA <u>GGGGSNNHHHHH</u>—  —</p>
79	<p><i>LS-</i>  <i>mCXCL7<sup>48-</sup></i>  <i>113_</i>  <i>(Gly4Ser)<sub>2-</sub></i>  <i>mouse SA-</i>  <i>(Gly4Ser)-</i>  <i>His6</i></p>	<p><u>MEVFAQQLLQELLELNLPGAE</u> <b>I</b>ELRCRCTNTISGIPFNSISLVNVYRPGVHCADV  <b>EVIATLKNQKTCCLDPNAPGVKRIVMKILEGYGGGSSGGGSS</b>EAHSEGIARHYH  DLSEQHPKGLVETRFY QYLQK SYDENKVLVQEVYDFAKTTCVADSSRANCKYI  H L LFSUKLCA L NLRKHYGLADCC LKQKPEPHECFL QHKDNNLSLWFA  EAMOTSEVENPTTFMGHYLAEVAFRHPYFYAPEL LY YARQYNE L TQCCAEASK  ESCLTFEFDGVKCALVSYVQFMKCSMCEPQPRAEKAVAVARLSQTFPNADF  AE L LKLATD LTKVNRKCCGSD LLECADDRAEALAFYKCEHQAC LGGKLOT  LLEVAHCLSEVEVDIMPADLFAI AADFVEQEVCLNXYAAAEVFL E LFL  EHEFYVSVLL L LAKKIYATLEKCCA SANPPAC YCTVLAEEFQF I  NCLLYEYGFQNAL LVRYTQKAPQVSEFTLVEAAENI DRVQ  KLPVVEPYLQAL LRFVCL LHEE L VGRV LKCCGSEVLEK SPQYSA LTVK LTV  EHEFYAETTFYVQD LQTLPEYKQLEKQATALAEVYKHKRDATAEQ LATV  QELFTQCKAAADTCVSTGDFNLYLVRKDDALA <u>GGGGSNNHHHHH</u>—  —</p>
80	<p><i>LS-</i>  <i>mCXCL9<sup>22-</sup></i>  <i>126_</i>  <i>(Gly4Ser)<sub>2-</sub></i>  <i>mouse SA-</i>  <i>(Gly4Ser)-</i>  <i>His6</i></p>	<p><u>MEVFAQQLLQELLELNLPGAE</u> <b>T</b>LVIARNARCSCI STSRGTIHYKSLKDLKQFAPSP  <b>NCNKTEI IATLKNQDQTCCLDPDSANVKKLMKEWEKKI SQQKKQKRGKKHQKNMK</b>  <b>NRKP KTPQSRRRSRKTTGGGSSGGGSS</b>EAHSEGIARHYH  SQYLQKGSYDERAKLVQEVYDFANTCVADSSRANCKR LVTFFQDLCA LFNLE  ENYQALADGAL KQKPEPHECFL QHKDNNLSLWFA  QRYLMEVARRHPYFYAPEL LY YARQYNE L TQCCAEASK  LVSSVNRHRCGSRQKFGERAFKAVARLSQTFPNADF AE L LKLATD LTKVNRK  ECCEGLLECALDRAELAFYKCEHQAC LGGKLOT  NPADLFAI AADFVEQEVCLNXYAAAEVFL E LFL  KXEA L LKLATD LTKVNRKCCGSD LLECADDRAEALAFYKCEHQAC LGGKLOT  ALVYKTNCDLYEYGFQNAL LVRYTQKAPQVSEFTLVEAAENI DRVQ  VCLLSEKIPVSEWV LKCCSSGLVRRPFCYCALYDETYVPEEFKARTFTFHSQI  CTLPEYKQLEKQATALAEVYKHKRDATAEQ LATV  KSLRQVNLVTRKDDALA <u>GGGGSNNHHHHH</u>—  —</p>















	<p>(Gly<sub>4</sub>Ser)-His<sub>6</sub></p>	<p>GAGCACTCAATAEAAATTTCTCAATCACTCTTTTCCACADTCCTCAGAACGAAAGC          TCCCTGACCCGCAAGCTTCATGGTTGTGAAAGCCGAAGCCATTCCTCCCTTCTCTG          CDTTACACAAATTAAGTCTTTTACTATTTACAACTTTCCACACAGAGCCTTTTAAA          GCAATGAGCACTTGCTTCTCTTCAACCAAGCAGTTTCCCAATTTTCACTTTGACAAA          ATCAACAAAATTTGGAAACAGAAATTTACCAAAATTTCAAAATTTGTTCTTTGAA          GACCTTCTGAAATTCCTCGAGATGACAGGCGGGAATTTGCGAACTTACATTTGTA          AACCAACCTGATATTCTCCAGCAACTGGCAGACTTTCCTGCGATTAACCACTTTCTG          AAATTAACCCCTTTCTCTTACTGACCTTTACCATCAATTTCTGCTTCTCTGAACTT          CCTTCGATTTGCTGCTTAATTTATTTGAGGAAACAGGAGTGTGCGAAGAACTATGCT          GACCCCAATGATCTCTTTCTCTCAATCTTCTTCTGATCAATATTTCAAATGACAC          CCTTAAATTTCTGATATTCTCTTCTCTGAGACTTTGCAATTTAAATTTGAAATGCACT          CTGGAAAAGTTCCTGGCTGAAAGCCAACTCTCTCTGAACTGCTTCTGCGAACTTTC          CCTGAAATTTGAGCCCTTCTCTGCAACAAGCTTACAACCTTTCTCTGAAAGCAACTG          GAAATTTGAGCAAGATTTCTGAAAGATTTCAAAATTTCTGAAAGCAACTTCTGAAAG          TACACCTTTGAAAGCAACTTTCAACTTTCAAACTTCTGAAAGCAACTTCTGAAAGCA          AACCTTAAAGAGTGGGCAAGCTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCA          CDTTCTCTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCA          CAAAGCAAGCTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAG          GAAAGCAAGCTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAG          CACTTTTAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCT          AAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCA          CDTTAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAA          CTTAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAA          CCAAAATTTGAGCAAGCTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACT          CCAAAATTTGAGCAAGCTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACT          CCAAAATTTGAGCAAGCTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAAAGCAACT  <u>GGAGGGGGTAGCGGAGGCGGAGGGTGGATATCCAGATGACCCAGTCCCCGAGC</u>  <u>TCCCTGTCCGCTCTGTGGGCGATAGGGTCACCATCACCTGCCGTGCCAGTCCAG</u>  <u>TCTTACCGGTGGTGTAGCTTGGTATCAACAGAAACCAGGAAAAGCCCCGAAGCTT</u>  <u>CTGATTTACTCTGCATCCTACTCTACTCTGGAGTCCCCTTCTCGCTTCTCTGGT</u>  <u>AGCCGTTCGGGACGGATTTCACTCTGACCATCAGCAGTCTGCAGCCGGAAGAC</u>  <u>TTCGCAACTTATTACTGTGACCAACCATCTCATCTGATCAGCTTCGGAATCCGCT</u>  <u>ACCGAGGTGGAGATCAAAGGTACTACTGCCGCTAGTGGTAGTAGTGGTGGCAGT</u>  <u>AGCAGTGGTGGCAGGTTTCACTGAGCTGGTGGAGTCTGGCGGTGGCCCTGGTGCAGCA</u>  <u>GGGGGCTCACTCCGTTTTGTCTGTGCAGCTTCTGGCTCCAACCCCTACTACTAC</u>  <u>GGTGGTACGCACTGGGTGCGTCAGGCCCCGGGTGAGTGCCTGGAATGGGTTGCA</u>  <u>TCTATTGGTTCTTACCCTGGCTACACTGACTATGCCGATAGCGTCAAGGGCCGT</u>  <u>TTCACTATAAGCGCAGACACATCCAAAAACACAGCCTACCCTACAAATGAACAGC</u>  <u>TTAAGAGCTGAGGACACTGCCGTCTATTATTGTGCTCGCCATTACTACTGGTAC</u>  <u>GATGCTACTGACTACTGGGGTCAAGGAACCCTGGTCACCGTCTCCTCGGGAGGG</u>  <u>GGCGGTTCCACCATCACCACTCACTGATAG</u></p>
<p>89</p>	<p>gWiz-LS-  mouse SA-  (Gly<sub>4</sub>Ser)<sub>3</sub>-  scFv (V<sub>L</sub>-  V<sub>H</sub>) CK157-  ds2  (V<sub>L</sub>43<sup>A&gt;C</sup> /</p>	<p><u>ATG</u><u>TCATATGAGCAAGTCCCTGCTTCACTTCCCTCCCTGCTGCTGCTGCTGCTGCT</u>  <u>CCCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT</u>  <u>GGAGGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCA</u>  <u>AAATGCTTATACGATGAGCCTGCAAAATTTAGTTCAGCAAGCAAGCAAGCAAGCA</u>  <u>AAGAAGLCTGCTGAAAGCAAGCTTCTGAAAGCAACTTCTGAAAGCAACTTCTGAA</u>  <u>CTTTTCTGAGATAAATTTCTCTGCAATTTGAAAGCAACTTCTGAAAGCAACTTCTG</u>  <u>CTGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT</u>  <u>CAATTAACATONTAACCCCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG</u>  <u>ATGCTCAGCTCTCTTAAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAG</u></p>













		<p>CCCTGCGATTTCCTCCCTTATCTTCTTTGACCGAGCCGGAACTCTTCCAAACAATTAACCT GACCGCAAGGATGTCTTCCCTCCGGACGCTTCCTCTATATGATATTCAGLACAGAC CCTTATTAAGTTATATGATGTTTCTCTTCACTTCCAAACATGAAACCTACT CTSSAAAGTGTCTGCTGAAAGCCTATCCTTCTGCTATCCCTGCGGACAGCTCTT GCTAAALCTTCACTCTCTCTTTGTAAGAAAGCTTAAAGAACTTCTTCAAAAACCACTT GATTTCTGAAAGCTTCTGAAAGTATGAACTCCAAACAGCTCTCTCTCTCTCTCT TAGACCGCGAAGCAGCTTCAAGTTCTTACCGCCAACTTCTCTGCGAGGCTCTGAGAA AACTTACCAAGCTCTCCCACTAACTCTCTTACAGCTTCTCTCAAACTCTCACAGCTCT CCTTCTCTGAGAGGAGCTATCTTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT GCAACCACTCTCACTTCT GAAAGGCGCTCATCT GAGCTTAAAGCTTCAAGCT AAAGCAGGCAAGCTTAAAGCAAGCAAGCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT CCCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCA CTCTCTATATCT CCTAAAGCTTCT <u>GGTGGAGGAGGCTCTGGT</u> <u>GGAGGGGTTAGCGGAGGCGGAGGGTCCCAAGTTAAACTGGAACAGTCCGGTGT</u> <u>GAAGTTGTCAAACCAGGTGCTTCCTGGAAGTTGCTCTGTAAGCCTCTGGTTTT</u> <u>AACATCAAGGATTCGTATATGCATTGGTGGAGACAAGGGCCAGGACAATGTTTG</u> <u>GAATGGATTGGCTGGATTGATCCAGAGAATGGTGATACCGAGTACGCTCCTAAA</u> <u>TTTCAGGGAAAGGCTACTTTTACTACCGACACTTCCGCTAATACCGCATACTTG</u> <u>GGCTTATCTTCTCTTCTGAGACCAGAGGACACTGCCGTATACTACTGCAACGAAGGG</u> <u>ACACCAACTGGTCTCTTACTATTTCTGACTACTGGGGACAAGGTACCTTAGTTACT</u> <u>GTCTCTAGCGGTGGCGGAGGTTGAGGCGGTTGAGGGTCTGGAGGTGGCGGTAGT</u> <u>GAAATGTGCTGACCAATCTCCAAGCTCCATGTCTGTTTTCTGTTGGCGATAGA</u> <u>GTAACCATCGCTTGTAGCGCATCTCTAGTGTCCATATATGCACTGGCTTCAA</u> <u>CAGAAGCCAGGTAAGGCCCCAAGTTGTTGATTATTTGACATCCAACCTTGGCT</u> <u>TCTGGAGTGCCTTCAAGGTTTTCTGTTCCGGCTCAGGAACCGATTATAGTTTG</u> <u>ACTATTAGCTCAGTGCAGCCAGAGGATGCTGCAACCTACTATTGCCAGCAAAGG</u> <u>TCCTCATATCCACTGACTTTCGGGCTGGAACGAAGTTGGAATCAAGGGAGGG</u> <u>GGCGGTTCCACCATCACCACCTCACTGATAG</u></p>
95	<p><i>LS-mouse SA-(Gly<sub>4</sub>Ser)<sub>3</sub>-scFv (V<sub>L</sub>-V<sub>H</sub>) CK138-(Gly<sub>4</sub>Ser)-His<sub>6</sub></i></p>	<p>MNRYFAQLIGLLLDLFLGARGGAKSEIANKYNQLAEGSNFKSLVLLAFLSQYLQ KCYDBHAKLVQEVDFAKKVAIGSNAKDFSLHTLFLCHLQDENLRENYCE LADCTKQEFREUECFQKEDNPALFPVERFEAEKCTTFAENPCTFMQHYLB EVAKNEPVTATDLALYTAQYKELHQCARRADESGCLPALDGPKKALVCCV KQMKCSMKQKFEFAFKAVAVFLQCTFENAGFARTTBLATDLITVVKEGCCEG DLTECADDAAELANVMCENQFTLSKLOTCCDKPLRLALHCLSEVEHDTPADL FALPADEFVGDQEVCKNYRAKIDVFLCTFLNEYSKRNDNSVSLLDLARKYEAT LRLDCAEAREPACYGTYLAEPQPLVEEFPNLYKINODLYEALGEXGQRA...LVR YTKSAPQVSTPTLVFAAPNLGRVTKCCTLPEDQRLDQVEDYLCAALNRPVCLLE EKTFVSHVTKCCQSSLVERRPQFJALTVDETYVPRPEKATFPDRBDCITLER KPKQLRQTA...AELVREKPKALAEQLKIWHDFVAQLK...DOKAABELDFCSFELG FH...VTRCDA...<u>GGGGSGGGSGGGSSAAAIQMTTRSPSSLSASVGDRTITCRA</u> <u>SQYHDGSAAWYQOKPKAPKLLIYGASYLYSGVPSRFSGRSGTDFTLTISLQ</u> <u>PEDFATYYCQSSYSLITFGQGTKVEIKGTTAASGSSGGSSGAEVQLVESDGG</u> <u>LVQPGGSLRLSCAASGFNLSYYGMHWVRQAPGKLEWVAYIASYPGYTSYADSV</u> <u>KGRFTI SADTSKNTAYLQMNSLRAEDTAVYYCARSGYSPYYSWFSAGMNYWG</u> <u>QGALVTVSSGGGSHNNNNH--</u></p>

<p>96</p> <p><i>LS-mouse</i> <i>SA-</i> <i>(Gly<sub>4</sub>Ser)<sub>3</sub>-</i> <i>scFv (V<sub>L</sub>-</i> <i>V<sub>H</sub>) CK157-</i> <i>(Gly<sub>4</sub>Ser)-</i> <i>His<sub>6</sub></i></p>		<p>MMGLVFAQLLGLLLEWLFQKCFARAKSETAHRVINDLSEQRFKGLVLEAFKQYLG KCSYGEHAALVQEVTDFAITTCVADESAENCKSLHTLFPDRALCAIPNLRENYS LADGCTKQEDPERNECFLQHFQONPILPFERPEAEAMCTSYKENGCTTFMCHYLE EVARRRPYFYAPPELLYYAEQTHEILITQCCAEADKESCLTFYKLDGVEEMALVSSV KQRNKCSSPAQKFGEPFKAWAVARLSQTEPHAFAMLELALATGLIEVHKEDCG DLLESCADPAELAKYMCENQATISKALQTCCKKFLKARGLSEVERHTMPADI PALAADFVEUQEVDCHYAEAADVFLGTFLEYGRRRPPYSYGLLRLAKKYEAT LEKCCABANPPFACTGTVLAEPQFVVEEPNLYKTNODLYEYLGQYGFQNALAVP YTQKAPQVSTPILVEAARNLQPVSTKCOITLFEQQRLLPCVEDYLTAENKVCLLR EKLHVSERVTECCGGLVETVPOBALTVDSEFYVTECFKAMLETPHSDICTLS EKAQIKKQIALAALVKNLFEATARQLLTVMDFAQFLDTCKAAADKDCQFSTEG PNLNTFCBUDALA<u>GGGGSGGGSGGGGS</u>AS<b>DIQMTQSPSSLSASVGDRTTITCRA</b> <b>SQSYGGVAWYQQKPKAPKLLIYSASYLYSGVPSRFSGSRSGTDFTLTITSSLQP</b> <b>EDFATYYCQQPSHLITFGQGTEVEIKGTTAASGSSGGSSSGAEVQLVESGGGLV</b> <b>QPGGSLRLSCAASGSNPYYYGGTHWVRQAPGEELEWVASIGSYPGYTDYADSVK</b> <b>GRFTISADTSKNTAYLQMNSLRAEDTAVYYCARHYWYDATDYWGQGTTLTVSS</b> <u>GGGGS</u>SHHHHHH--</p>
<p>97</p> <p><i>LS-mouse</i> <i>SA-</i> <i>(Gly<sub>4</sub>Ser)<sub>3</sub>-</i> <i>scFv (V<sub>L</sub>-</i> <i>V<sub>H</sub>) CK129-</i> <i>(Gly<sub>4</sub>Ser)-</i> <i>His<sub>6</sub></i></p>		<p>MMGLVFAQLLGLLLEWLFQKCFARAKSETAHRVINDLSEQRFKGLVLEAFKQYLG KCSYGEHAALVQEVTDFAITTCVADESAENCKSLHTLFPDRALCAIPNLRENYS LADGCTKQEDPERNECFLQHFQONPILPFERPEAEAMCTSYKENGCTTFMCHYLE EVARRRPYFYAPPELLYYAEQTHEILITQCCAEADKESCLTFYKLDGVEEMALVSSV KQRNKCSSPAQKFGEPFKAWAVARLSQTEPHAFAMLELALATGLIEVHKEDCG DLLESCADPAELAKYMCENQATISKALQTCCKKFLKARGLSEVERHTMPADI PALAADFVEUQEVDCHYAEAADVFLGTFLEYGRRRPPYSYGLLRLAKKYEAT LEKCCABANPPFACTGTVLAEPQFVVEEPNLYKTNODLYEYLGQYGFQNALAVP YTQKAPQVSTPILVEAARNLQPVSTKCOITLFEQQRLLPCVEDYLTAENKVCLLR EKLHVSERVTECCGGLVETVPOBALTVDSEFYVTECFKAMLETPHSDICTLS EKAQIKKQIALAALVKNLFEATARQLLTVMDFAQFLDTCKAAADKDCQFSTEG PNLNTFCBUDALA<u>GGGGSGGGSGGGGS</u>AS<b>DIQMTQSPSPLSASVGDRTTITCRA</b> <b>SQYGGYVAWYQQKPKAPKLLIYGASLLYSGVPSRFSGGRSGTDFTLTITSSLQP</b> <b>EDFATYYCQRGHALITFGQGTKVEIEGTTAASGSSGGSSSGAEVQLVESGGGLV</b> <b>QPGGSLRLSCAASGFNIISSYGSMMHWVRQAPGKGLEWVASIYPYSSSTIYADSVK</b> <b>GRFTISADTSKNTAYLQMNSLRAEDTAVYYCARGYGPWYAYSYFALDYWGQGTI</b> <b>VTVSS</b><u>GGGGS</u>SHHHHHH--</p>
<p>98</p> <p><i>LS-mouse</i> <i>SA-</i> <i>(Gly<sub>4</sub>Ser)<sub>3</sub>-</i> <i>scFv (V<sub>L</sub>-</i> <i>V<sub>H</sub>) CK138-</i> <i>ds1</i> <i>(V<sub>L</sub>100<sup>Q&gt;C</sup> /</i> <i>V<sub>H</sub>44<sup>G&gt;C</sup>)-</i> <i>(Gly<sub>4</sub>Ser)-</i> <i>His<sub>6</sub></i></p>		<p>MMGLVFAQLLGLLLEWLFQKCFARAKSETAHRVINDLSEQRFKGLVLEAFKQYLG KCSYGEHAALVQEVTDFAITTCVADESAENCKSLHTLFPDRALCAIPNLRENYS LADGCTKQEDPERNECFLQHFQONPILPFERPEAEAMCTSYKENGCTTFMCHYLE EVARRRPYFYAPPELLYYAEQTHEILITQCCAEADKESCLTFYKLDGVEEMALVSSV KQRNKCSSPAQKFGEPFKAWAVARLSQTEPHAFAMLELALATGLIEVHKEDCG DLLESCADPAELAKYMCENQATISKALQTCCKKFLKARGLSEVERHTMPADI PALAADFVEUQEVDCHYAEAADVFLGTFLEYGRRRPPYSYGLLRLAKKYEAT LEKCCABANPPFACTGTVLAEPQFVVEEPNLYKTNODLYEYLGQYGFQNALAVP YTQKAPQVSTPILVEAARNLQPVSTKCOITLFEQQRLLPCVEDYLTAENKVCLLR EKLHVSERVTECCGGLVETVPOBALTVDSEFYVTECFKAMLETPHSDICTLS EKAQIKKQIALAALVKNLFEATARQLLTVMDFAQFLDTCKAAADKDCQFSTEG PNLNTFCBUDALA<u>GGGGSGGGSGGGGS</u>AS<b>AIQMTTRSPSSLSASVGDRTTITCRA</b></p>

		<p>SQYHDGSAAWYQQKPGKAPKLLIYGASYLYSGVPSRFSGSRSGTDFTLTISSLQ  PEDFATYYCQSSSYSLITFGQGTKVEIKGTTAASGSSGGSSSGAEVQLVESDGG  LVQPGGSLRLSCAASGFNLSYYGMHWVRQAPGKCLEWVAYIASYPGYTSYADSV  KGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARSYGYSYSPYYSWFSAGMNYWG  QGALVTVSS <u>GGGGSNNHHHH</u> --</p>
<p>99</p>	<p><i>LS-mouse</i>  SA-  <i>(Gly4Ser)</i><sub>3</sub>-  <i>scFv</i> (<i>V<sub>L</sub></i>-  <i>V<sub>H</sub></i>) <i>CK138-</i>  <i>ds2</i>  (<i>V<sub>L</sub></i>43<sup>A&gt;C</sup> /  <i>V<sub>H</sub></i>105<sup>Q&gt;C</sup>)-  <i>(Gly4Ser)</i>-  <i>His6</i></p>	<p><u>MDKRVPAQALLGLLLEWLEPCARDPARGSEIARRKYNDELSEQRKQGLVLEAFSRYEQ</u>  KCSDYDEHAKLVQEVLDVFAKTVADGSAANCDKSLHTLFGDALLCAIPNLPRNYGE  LADDCIEQEPERNECFLQHRDDNPQIPEPEEPFAEAMCISTYKENDCTFMGHYLA  EVARPHFYFYAPPELLYYAEQINELITQCCAEADKESCLIFNLDVREBALVSSV  KQRMKCSSEQKGLERAFKAWAVARLSQITFPNAUFAMELRLATDLIEVNRKDCAC  DLLECAEDDPAELAKYMCENQATLSSKLTQCCDQKPLAKARCLSEVEHDIMPADI  PALAADFVEUQEVCHYAEARDFVLCGTFLEYYSRRRDPYSVGLLRLAKKYNKAT  LEKCCALANDPACVGTVLAERQPLVNEPRLVKTNDLZEKLCRYGQFQAALLVR  YTQKAPQVDTFTLVEAARNLGRVTRCCTILPEDQPLPCVEDYLSALLNRVCLLN  ERTFVSEHVTDCSSGLVEEIRPQPPALTVDETVYVKEFKASTHCPHSDICTLES  KEEQIKKQFALASLVKKEKATAEQLITVMDFAQFLDTCCKAAKDCDCESTEC  PMLVTRCKDALLA <u>GGGGSGGGSGGGGS</u>ASAIQMTSPSSLSASVGDRTTITCRA  SQYHDGSAAWYQQKPGKAPKLLIYGASYLYSGVPSRFSGSRSGTDFTLTISSLQ  PEDFATYYCQSSSYSLITFGQGTKVEIKGTTAASGSSGGSSSGAEVQLVESDGG  LVQPGGSLRLSCAASGFNLSYYGMHWVRQAPGKCLEWVAYIASYPGYTSYADSV  KGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARSYGYSYSPYYSWFSAGMNYWG  QGALVTVSS <u>GGGGSNNHHHH</u> --</p>
<p>100</p>	<p><i>LS-mouse</i>  SA-  <i>(Gly4Ser)</i><sub>3</sub>-  <i>scFv</i> (<i>V<sub>L</sub></i>-  <i>V<sub>H</sub></i>) <i>CK157-</i>  <i>ds1</i>  (<i>V<sub>L</sub></i>100<sup>Q&gt;C</sup> /  <i>V<sub>H</sub></i>44<sup>E&gt;C</sup>)-  <i>(Gly4Ser)</i>-  <i>His6</i></p>	<p><u>MDKRVPAQALLGLLLEWLEPCARDPARGSEIARRKYNDELSEQRKQGLVLEAFSRYEQ</u>  KCSDYDEHAKLVQEVLDVFAKTVADGSAANCDKSLHTLFGDALLCAIPNLPRNYGE  LADDCIEQEPERNECFLQHRDDNPQIPEPEEPFAEAMCISTYKENDCTFMGHYLA  EVARPHFYFYAPPELLYYAEQINELITQCCAEADKESCLIFNLDVREBALVSSV  KQRMKCSSEQKGLERAFKAWAVARLSQITFPNAUFAMELRLATDLIEVNRKDCAC  DLLECAEDDPAELAKYMCENQATLSSKLTQCCDQKPLAKARCLSEVEHDIMPADI  PALAADFVEUQEVCHYAEARDFVLCGTFLEYYSRRRDPYSVGLLRLAKKYNKAT  LEKCCALANDPACVGTVLAERQPLVNEPRLVKTNDLZEKLCRYGQFQAALLVR  YTQKAPQVDTFTLVEAARNLGRVTRCCTILPEDQPLPCVEDYLSALLNRVCLLN  ERTFVSEHVTDCSSGLVEEIRPQPPALTVDETVYVKEFKASTHCPHSDICTLES  KEEQIKKQFALASLVKKEKATAEQLITVMDFAQFLDTCCKAAKDCDCESTEC  PMLVTRCKDALLA <u>GGGGSGGGSGGGGS</u>ASDIQMTQSPSSLSASVGDRTTITCRA  SQSYGGVAWYQQKPGKAPKLLIYSASYLYSGVPSRFSGSRSGTDFTLTISSLQ  EDFATYYCQQPSHLITFGQTEVEIKGTTAASGSSGGSSSGAEVQLVESGGGLV  QPGGSLRLSCAASGSNPYYYGGTHWVRQAPGKCLEWVASIGSYPGYTDYADSVK  GRFTISADTSKNTAYLQMNSLRAEDTAVYYCARHYWYDADTYWGQGTTLVTVSS  <u>GGGGSNNHHHH</u> --</p>
<p>101</p>	<p><i>LS-mouse</i>  SA-  <i>(Gly4Ser)</i><sub>3</sub>-  <i>scFv</i> (<i>V<sub>L</sub></i>-  <i>V<sub>H</sub></i>) <i>CK157-</i>  <i>ds2</i></p>	<p><u>MDKRVPAQALLGLLLEWLEPCARDPARGSEIARRKYNDELSEQRKQGLVLEAFSRYEQ</u>  KCSDYDEHAKLVQEVLDVFAKTVADGSAANCDKSLHTLFGDALLCAIPNLPRNYGE  LADDCIEQEPERNECFLQHRDDNPQIPEPEEPFAEAMCISTYKENDCTFMGHYLA  EVARPHFYFYAPPELLYYAEQINELITQCCAEADKESCLIFNLDVREBALVSSV  KQRMKCSSEQKGLERAFKAWAVARLSQITFPNAUFAMELRLATDLIEVNRKDCAC  DLLECAEDDPAELAKYMCENQATLSSKLTQCCDQKPLAKARCLSEVEHDIMPADI  PALAADFVEUQEVCHYAEARDFVLCGTFLEYYSRRRDPYSVGLLRLAKKYNKAT  LEKCCALANDPACVGTVLAERQPLVNEPRLVKTNDLZEKLCRYGQFQAALLVR  YTQKAPQVDTFTLVEAARNLGRVTRCCTILPEDQPLPCVEDYLSALLNRVCLLN  ERTFVSEHVTDCSSGLVEEIRPQPPALTVDETVYVKEFKASTHCPHSDICTLES  KEEQIKKQFALASLVKKEKATAEQLITVMDFAQFLDTCCKAAKDCDCESTEC  PMLVTRCKDALLA <u>GGGGSGGGSGGGGS</u>ASDIQMTQSPSSLSASVGDRTTITCRA</p>

	<p>(<i>V<sub>L</sub>43<sup>A&gt;C</sup> / V<sub>H</sub>105<sup>Q&gt;C</sup></i>)- (<i>Gly<sub>4</sub>Ser</i>)- <i>His<sub>6</sub></i></p>	<p>LEKCCAEAREFPACYGVVLABPQPLVVEEFPNVLVKTNGDLYEKLCBYCFQNALIVR          YIQKAPQVSTPTLVEAARNLORVUTKOOTLPEDQRLPCVVEQYLSALLIRVOLLER          ERTFVSEBVTKQCSGLVERPPCPFSALTVDETYVPKKFKASTFTEHSDICTLIRE          ERFQIKKQTAALAEVLVKAEPKATAEQLITVWLDFAQFLDTTCRAAKLCTPSTEG          FHLVTRCKDALAGGGGSGGGSGGGGSA<b>DIQMTQSPSSLSASVGDVRTITCRA</b>  <b>SQSYGGVAWYQQKPKGKPKLLIYSASYLYSGVPSRFSGSRSGTDFTLTITSSLOP</b>  <b>EDFATYYCQQPSHLITFGQGTEVEIKGTTAASGSSGGSSSGAEVQLVESGGGLV</b>  <b>QPGGSLRLSCAA</b>SGSNPYYYGGTHWVRQAPGEELEWVASIGSYPGYTDYADSVK  <b>GRFTISADTSKNTAYLQMN</b>SLRAEDTAVYYCARHYYWYDATDYWGQGTTLVTVSS  <u>GGGGSNNNNHHH</u></p>
<p>102</p>	<p><i>LS-mouse</i> <i>SA-</i> (<i>Gly<sub>4</sub>Ser</i>)-<i>V<sub>L</sub></i> <i>CK157-His<sub>6</sub></i></p>	<p><u>MMNRYFAQLIGLLLLDLFPCARCEPAUKSEIARRHYNDLGEQNTKGLVLLAFSQYLQ</u>          KCSYDEHAKLVQEVTLFAKINVAIENSAAMCDASLHILLCFSLCAIENLRENTCE          LADCTTKQDEEENECEFLQHRDDNPGIPEPEPEEAEMCTSPKENTCTFMGHYLR          EVARHPYFYAPMLLYXAEQITHEILITQCCAEADKKSCLLIPALDGVKEKALVGGV          RQRMKCSQKPKGEFAFKAVAVARLQCTFFNADFAEITKLAIDLTVKVKECOCG          ULLECAEDDPAELAKYMCENQATLSKLLQTCCKPPLLAARGLSEVEHDTMPADL          FALADPVEDQEVCKNYAEAKVDFLQCTFLYENSRNPDNYVRLILKAKKYEAT          LEKCCAEAREFPACYGVVLABPQPLVVEEFPNVLVKTNGDLYEKLCBYCFQNALIVR          YIQKAPQVSTPTLVEAARNLORVUTKOOTLPEDQRLPCVVEQYLSALLIRVOLLER          ERTFVSEBVTKQCSGLVERPPCPFSALTVDETYVPKKFKASTFTEHSDICTLIRE          ERFQIKKQTAALAEVLVKAEPKATAEQLITVWLDFAQFLDTTCRAAKLCTPSTEG          FHLVTRCKDALAGGGGSGGGSGGGGSA<b>DIQMTQSPSSLSASVGDVRTITCRA</b>  <b>SQSYGGVAWYQQKPKGKPKLLIYSASYLYSGVPSRFSGSRSGTDFTLTITSSLOP</b>  <b>EDFATYYCQQPSHLITFGQGTEVEIK</b><u>GGGGSRRNNHHH</u>--</p>
<p>103</p>	<p><i>LS-mouse</i> <i>SA-</i> (<i>Gly<sub>4</sub>Ser</i>)- <i>V<sub>H</sub> CK157-</i> <i>His<sub>6</sub></i></p>	<p><u>MMNRYFAQLIGLLLLDLFPCARCEPAUKSEIARRHYNDLGEQNTKGLVLLAFSQYLQ</u>          KCSYDEHAKLVQEVTLFAKINVAIENSAAMCDASLHILLCFSLCAIENLRENTCE          LADCTTKQDEEENECEFLQHRDDNPGIPEPEPEEAEMCTSPKENTCTFMGHYLR          EVARHPYFYAPMLLYXAEQITHEILITQCCAEADKKSCLLIPALDGVKEKALVGGV          RQRMKCSQKPKGEFAFKAVAVARLQCTFFNADFAEITKLAIDLTVKVKECOCG          ULLECAEDDPAELAKYMCENQATLSKLLQTCCKPPLLAARGLSEVEHDTMPADL          FALADPVEDQEVCKNYAEAKVDFLQCTFLYENSRNPDNYVRLILKAKKYEAT          LEKCCAEAREFPACYGVVLABPQPLVVEEFPNVLVKTNGDLYEKLCBYCFQNALIVR          YIQKAPQVSTPTLVEAARNLORVUTKOOTLPEDQRLPCVVEQYLSALLIRVOLLER          ERTFVSEBVTKQCSGLVERPPCPFSALTVDETYVPKKFKASTFTEHSDICTLIRE          ERFQIKKQTAALAEVLVKAEPKATAEQLITVWLDFAQFLDTTCRAAKLCTPSTEG          FHLVTRCKDALAGGGGSGGGSGGGGSA<b>AEVQLVESGGGLVQPGGSLRLSCAA</b>  <b>SGSNPYYYGGTHWVRQAPGEELEWVASIGSYPGYTDYADSVKGRFTISADTSKN</b>  <b>TAYLQMN</b>SLRAEDTAVYYCARHYYWYDATDYWGQGTTLVTVSS<u>CCCSNNNNHHH</u>--          --</p>
<p>104</p>	<p><i>LS-mouse</i> <i>SA-</i> (<i>Gly<sub>4</sub>Ser</i>)<sub>3</sub>- <i>scFv (V<sub>L</sub>-</i> <i>V<sub>H</sub>) CK129-</i> <i>ds1</i></p>	<p><u>MMNRYFAQLIGLLLLDLFPCARCEPAUKSEIARRHYNDLGEQNTKGLVLLAFSQYLQ</u>          KCSYDEHAKLVQEVTLFAKINVAIENSAAMCDASLHILLCFSLCAIENLRENTCE          LADCTTKQDEEENECEFLQHRDDNPGIPEPEPEEAEMCTSPKENTCTFMGHYLR          EVARHPYFYAPMLLYXAEQITHEILITQCCAEADKKSCLLIPALDGVKEKALVGGV          RQRMKCSQKPKGEFAFKAVAVARLQCTFFNADFAEITKLAIDLTVKVKECOCG          ULLECAEDDPAELAKYMCENQATLSKLLQTCCKPPLLAARGLSEVEHDTMPADL          FALADPVEDQEVCKNYAEAKVDFLQCTFLYENSRNPDNYVRLILKAKKYEAT          LEKCCAEAREFPACYGVVLABPQPLVVEEFPNVLVKTNGDLYEKLCBYCFQNALIVR          YIQKAPQVSTPTLVEAARNLORVUTKOOTLPEDQRLPCVVEQYLSALLIRVOLLER          ERTFVSEBVTKQCSGLVERPPCPFSALTVDETYVPKKFKASTFTEHSDICTLIRE          ERFQIKKQTAALAEVLVKAEPKATAEQLITVWLDFAQFLDTTCRAAKLCTPSTEG          FHLVTRCKDALAGGGGSGGGSGGGGSA<b>AEVQLVESGGGLVQPGGSLRLSCAA</b>  <b>SGSNPYYYGGTHWVRQAPGEELEWVASIGSYPGYTDYADSVKGRFTISADTSKN</b>  <b>TAYLQMN</b>SLRAEDTAVYYCARHYYWYDATDYWGQGTTLVTVSS<u>CCCSNNNNHHH</u>--          --</p>





	<p><i>hCXCL1</i><sup>38-</sup> <i>107-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>	<p><u>AAGAGG</u> GCCACCGAGCTGAGATGCCAGTGCCTGCAGACCTGCAGGGCATCCAC          CCCAAGAACATCCAGAGCGTGAACGTGAAGTCCCCTGGCCCCACTGCGCCCAG          ACCGAAGTGATCGCCACCCTGAAGAACGGCCGGAAGGCCTGCCTGAACCCCGCC          AGCCCCATCGTGAAGAAAATCATCGAGAAGATGCTGAACAGCGACAAGAGCAAC  <u>GGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTG</u> ACCCAAC GACAAT          ATATGCGAGCAATCCCTTCAACACTTTAGATCAACAGCCGTAACCTTTCTCA          ACCACTACTACTTTGGCCAAAGCCAAAGCCAAATGCAAGGASTTTCTGAAATATAC          AAATFACGTAACCTTTCTCACTAATTCCTCTCTCACTCC TCAAGAACCAAC AAA          GCGAGCTTCA AAAACACACACTATATGTTTTT <b>TAA</b></p>
<p>108</p>	<p><i>pCHA-LS-</i> <i>hCXCL2</i><sup>38-</sup> <i>107-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>	<p><b>ATG</b> <u>AAGGTTT</u> GAACTGCTGATGCTGCTGCAGACCTGCAGGGCATCCAC          GCTCAAGCGCTTATCTCACTAAGCTCCGCTGGCCGAAAGAGCCCTCCAGC  <u>AAGAGG</u> GCCACAGAGCTGAGATGCCAGTGCCTCCAGACACTCCAGGGCATCCAC          CTGAAGAACATCCAGAGCGTGAAGTGAAGTCCCCTGGCCCCACTGCGCCCAG          ACAGAAGTGATCGCCACCCTGAAGAAATGGCCAGAAGGCCTGCCTGAACCCCGCC          AGCCCTATGGTCAAGAAAATCATCGAGAAGATGCTGAAGAACGGCAAGAGCAAC  <u>GGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTG</u> ACCCAAC GACAAT          ATATGCGAGCAATCCCTTCAACACTTTAGATCAACAGCCGTAACCTTTCTCA          ACCACTACTACTTTGGCCAAAGCCAAAGCCAAATGCAAGGASTTTCTGAAATATAC          AAATFACGTAACCTTTCTCACTAATTCCTCTCTCACTCC TCAAGAACCAAC AAA          GCGAGCTTCA AAAACACACACTATATGTTTTT <b>TAA</b></p>
<p>109</p>	<p><i>pCHA-LS-</i> <i>hCXCL3</i><sup>38-</sup> <i>107-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>	<p><b>ATG</b> <u>AAGGTTT</u> GAACTGCTGATGCTGCTGCAGACCTGCAGGGCATCCAC          GCTCAAGCGCTTATCTCACTAAGCTCCGCTGGCCGAAAGAGCCCTCCAGC  <u>AAGAGG</u> GTGACCGAGCTGAGATGCCAGTGCCTCCAGACACTCCAGGGCATCCAC          CTGAAGAACATCCAGAGCGTGAACGTGCGGAGCCCTGGCCCTCATTGTGCCCAG          ACAGAAGTGATCGCCACCCTGAAGAAATGGCAAGAAGGCCTGCCTGAACCCCGCC          AGCCCTATGGTGCAGAAGATCATCGAGAAGATCCTGAACAAGGGCAGCACCAAC  <u>GGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTG</u> ACCCAAC GACAAT          ATATGCGAGCAATCCCTTCAACACTTTAGATCAACAGCCGTAACCTTTCTCA          ACCACTACTACTTTGGCCAAAGCCAAAGCCAAATGCAAGGASTTTCTGAAATATAC          AAATFACGTAACCTTTCTCACTAATTCCTCTCTCACTCC TCAAGAACCAAC AAA          GCGAGCTTCA AAAACACACACTATATGTTTTT <b>TAA</b></p>
<p>110</p>	<p><i>pCHA-LS-</i> <i>hCXCL4</i><sup>32-</sup> <i>101-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>	<p><b>ATG</b> <u>AAGGTTT</u> GAACTGCTGATGCTGCTGCAGACCTGCAGGGCATCCAC          GCTCAAGCGCTTATCTCACTAAGCTCCGCTGGCCGAAAGAGCCCTCCAGC  <u>AAGAGG</u> GAGGCTGAAGAGGACGGCGATCTCCAGTGCCTGTGCGTGAAAACCACC          AGCCAAGTGGGGCCAGACACATCACCAGCCTGGAAGTGATCAAGGCCGGACCC          CACTGTCTACCGCCCAGCTGATTGCCACCCTGAAGAACGGCCGGAAGATCTGC          CTGGACCTCCAGGCCCCCTGTACAAGAAGATCATCAAGAAGCTGCTGGAAAGC  <u>GGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTG</u> ACCCAAC GACAAT          ATATGCGAGCAATCCCTTCAACACTTTAGATCAACAGCCGTAACCTTTCTCA          ACCACTACTACTTTGGCCAAAGCCAAAGCCAAATGCAAGGASTTTCTGAAATATAC          AAATFACGTAACCTTTCTCACTAATTCCTCTCTCACTCC TCAAGAACCAAC AAA          GCGAGCTTCA AAAACACACACTATATGTTTTT <b>TAA</b></p>
<p>111</p>	<p><i>pCHA-LS-</i> <i>hCXCL5</i><sup>44-</sup> <i>114-G<sub>3</sub>-c-</i></p>	<p><b>ATG</b> <u>AAGGTTT</u> GAACTGCTGATGCTGCTGCAGACCTGCAGGGCATCCAC          GCTCAAGCGCTTATCTCACTAAGCTCCGCTGGCCGAAAGAGCCCTCCAGC  <u>AAGAGG</u> CTGCGGAGCTGAGATGCGTGTGCCTGCAGACCACCCAGGGCGTGCAC</p>

	<i>myc-Aga2</i>	<p>CCCAAGATGATCAGCAACCTCCAGGTGTTCCGCCATCGGCCCCAGTGCAGCAAG                  GTGGAAGTGGTGGCCAGCCTGAAGAACGGCAAAGAGATCTGCCTGGACCCCGAG                  GCCCATTCTCTGAAGAAAGTGATCCAGAAGATCCTGGACGGCGGCAACAAGAG                  AACGGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTGAGGAACTGACA                  ACATATACGGAGGAAAACGATGACCAATLTAGAATGAGAGGCUAATGCTTG                  TCACCACTACTATCTTTGGGCAACGGGAAAGGCAATGCAAGGAGCTCTGATAT                  TACAAATCAGTAAAGCTTTGTCATTAATTCGGCTTCTGCACTCTCAACACACAGC                  AAAGGAGGCGCATTAACACACACTATCTTTTAA</p>
112	<i>pCHA-LS-hCXCL6<sup>44</sup>- 114-G<sub>3</sub>-c- myc-Aga2</i>	<p>ATGAGGCTTTCAGLSTEDLIGLGGALATCTGAGGAGCTGGCA...GGGCTTAA                  GDLKAAAGGDLTALSTUTACIACGUTGCGLGGDDTCCAGAAATGCGCTTGGAC                  AACACACTGACCGAGCTGCGGTGCACCTGTCTGAGAGTGACCCTGCGCGTGAAC                  CCCAAGACCATCGGCAAGCTCCAGGTGTTCCCTGCGGGCCCTCAGTGCAGCAAG                  GTGGAAGTGGTGGCCAGCCTGAAAAACGGAAAAACAAGTGTGCCTGGACCCCGAG                  GCCCATTCTCTGAAGAAAGTGATCCAGAAGATCCTGGACAGCGGCAACAAGAAG                  AACGGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTGAGGAACTGACA                  ACCTATACGGAGGAAAACGATGACCAATLTAGAATGAGAGGCUAATGCTTG                  TCACCACTACTATCTTTGGGCAACGGGAAAGGCAATGCAAGGAGCTCTGATAT                  TACAAATCAGTAAAGCTTTGTCATTAATTCGGCTTCTGCACTCTCAACACACAGC                  AAAGGAGGCGCATTAACACACACTATCTTTTAA</p>
113	<i>pCHA-LS-hCXCL7<sup>59</sup>- 121-G<sub>3</sub>-c- myc-Aga2</i>	<p>ATGAGGCTTTCAGLSTEDLIGLGGALATCTGAGGAGCTGGCA...GGGCTTAA                  GDLKAAAGGDLTALSTUTACIACGUTGCGLGGDDTCCAGAAATGCGCTTGGAC                  AACACACTGACCGAGCTGCGGTGCATGTGCATCAAGACCACCAGCGGAATCCACCCC                  AAGAATATCCAGTCCCTGGAAGTGATTTGGCAAGGGCACCCACTGCAACCAGGTG                  GAAGTGATTTGCCACACTGAAAGACGGCCGGAAGATCTGCCTGGACCCCTGACGCC                  CCCAGAATCAAGAAAATCGTGCAGAAAAAGCTG                  GGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTGAGGAACTGACA                  ACCTATACGGAGGAAAACGATGACCAATLTAGAATGAGAGGCUAATGCTTG                  TCACCACTACTATCTTTGGGCAACGGGAAAGGCAATGCAAGGAGCTCTGATAT                  TACAAATCAGTAAAGCTTTGTCATTAATTCGGCTTCTGCACTCTCAACACACAGC                  AAAGGAGGCGCATTAACACACACTATCTTTTAA</p>
114	<i>pCHA-LS-hCXCL8<sup>29</sup>- 99-G<sub>3</sub>-c- myc-Aga2</i>	<p>ATGAGGCTTTCAGLSTEDLIGLGGALATCTGAGGAGCTGGCA...GGGCTTAA                  GDLKAAAGGDLTALSTUTACIACGUTGCGLGGDDTCCAGAAATGCGCTTGGAC                  AACACACTGCCAAGAAGTGGGTGCCAGTGCATCAAGACCTACAGCAAGCCCTTC                  CACCCCAAGTTCATCAAAGAAGTGCAGAGTGATCGAGAGCGGCCCTCACTGCGCC                  AACACCGAGATCATCGTGAAGCTGAGCGACGGCAGAGAGCTGTGCCTGGACCCC                  AAAGAAAAGTGGGTGCAGCGGTGTTGAAAAAGTTCCTGAAGCGGGCCGAGAAC                  AGCGGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTGAGGAACTGACA                  ACCTATACGGAGGAAAACGATGACCAATLTAGAATGAGAGGCUAATGCTTG                  TCACCACTACTATCTTTGGGCAACGGGAAAGGCAATGCAAGGAGCTCTGATAT                  TACAAATCAGTAAAGCTTTGTCATTAATTCGGCTTCTGCACTCTCAACACACAGC                  AAAGGAGGCGCATTAACACACACTATCTTTTAA</p>
115	<i>pCHA-LS-hCXCL9<sup>23</sup>- 115-G<sub>3</sub>-c-</i>	<p>ATGAGGCTTTCAGLSTEDLIGLGGALATCTGAGGAGCTGGCA...GGGCTTAA                  GDLKAAAGGDLTALSTUTACIACGUTGCGLGGDDTCCAGAAATGCGCTTGGAC                  AACACACTACCCCGTTCGTGCGGAAGGGCAGATGCAGCTGTATCAGCACCAACCAG                  GGCACCATCCATCTCCAGTCTCTGAAGGACCTGAAGCAGTTCGCCCCCAGCCCC</p>



	<i>myc-Aga2</i>	<p>GCCCCCTGGTGCAGAAGATCATCCAGAAGATCCTGAACAAGGGCAAGGCCAAC  <u>GGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTGLAGGAACAGAAAT</u>          ATATGCAGDAAATCCDDTACCAACTTACAAATDACCDDCTACTCTTFFA          AOSRCTACTATTTTGGCCACCGGAAAGSAAATGCARSSAATTTTGAATATTAC          AAATUAGAAACUTTLGICATAAATGGUUTLPICAUDDICAAUAAALAGUAAA          GGGAGGCGCATAAACACACAGTATGTTTTT <b>TAA</b></p>
120	<i>pCHA-LS- mCXCL3<sup>31-</sup> 100-G<sub>3</sub>-c- myc-Aga2</i>	<p><b>ATG</b><u>AAAGGTTTGCATTTCTCTCTTCCCAATCTTCGCTDDETTGCCAATGGCCTTA</u>  <u>GCCTAAGCGGCTTATCTTACTACCGTCCGTTCCCGCTDCAAAAGCTTCTTGGAC</u>  <u>AAAGAG</u> GCCTCTGAGCTGAGATGCCAGTGCCTGAACACCCTGCCCGGGTGGAC          TTCGAGACAATCCAGAGCCTGACCGTGACCCCCCTGGCCCTCACTGTACCCAG          ACAGAAGTGATCGCCACCCTGAAGGACGGCCAGGAAGTGTGCCTGAATCCCAG          GGCCCCAGACTCCAGATCATCATCAAGAAGATCCTGAAGTCCGGCAAGAGCAGC  <u>GGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTGLAGGAACAGAAAT</u>          ATATGCAGGCGAAALCCUULDCCCAACTTAAAGAAATCCCGUULACGLTUTDICA          AOSRCTACTACTTTTGGCCACCGGAAAGSAAATGCARSSAATTTTGAATATTAC          AAATUAGTAAGCTTTDTCATAAATTCGGGTDTTCACUULTCAAACAACDAGGAAA          GGGAGGCGCATAAACACACAGTATGTTTTT <b>TAA</b></p>
121	<i>pCHA-LS- mCXCL4<sup>30-</sup> 105-G<sub>3</sub>-c- myc-Aga2</i>	<p><b>ATG</b><u>AAAGGTTTGCATTTCTCTCTTCCCAATCTTCGCTDDETTGCCAATGGCCTTA</u>  <u>GCCTAAGCGGCTTATCTTACTACCGTCCGTTCCCGCTDCAAAAGCTTCTTGGAC</u>  <u>AAAGAG</u> GTGACATCTGCCGGCCCTGAGGAAAGCGACGGCGATCTGTCTTGGCGTG          TGCGTGAAAACCATCAGCAGCGGCATCCACCTGAAGCACATCACCAGCCTGGAA          GTGATCAAGGCCCGGCAGGCACCTGTGCCGTGCCTCAGCTGATTGCCACCCTGAAG          AACGGCCGGAAGATCTGCCTGGACAGACAGGCCCCCCCTGTACAAGAAAGTGATT          AAGAAGATCCTGGAAAGC <u>GGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGAC</u>          TTGTAAGGAALGACAAATAAATGGGAGCAAAATUUDTCASUAAATLJASAAITGG          ADDDCJAUFDITCTUAASACTAALATLTDCCAAACDCAAGCGCAALDKAA          GGASTTTTGAATACACAAATCAGTAACCTTTCAGTAAATLGGGCTTCCAC          CCTCAAGTAAGTACCAACCCAAUCCATAAACACACACTATCTCTT <b>TAA</b></p>
122	<i>pCHA-LS- mCXCL5<sup>48-</sup> 118-G<sub>3</sub>-c- myc-Aga2</i>	<p><b>ATG</b><u>AAAGGTTTGCATTTCTCTCTTCCCAATCTTCGCTDDETTGCCAATGGCCTTA</u>  <u>GCCTAAGCGGCTTATCTTACTACCGTCCGTTCCCGCTDCAAAAGCTTCTTGGAC</u>  <u>AAAGAG</u> GCCACCGAGCTGAGATGCGTGTGCCTGACCGTGACCCCCAAGATCAAC          CCCAAGCTGATCGCCAACCTGGAAGTGATCCCTGCCGGCCCTCAGTGCCCCACC          GTGGAAGTGATTGCCAAGCTGAAGAACCAGAAAGAAGTGTGCCTGGACCCCGAG          GCCCCCCTGATCAAGAAGATCATCCAGAAGATCCTGGGCAGGACAAGAAGAAA  <u>GCCGGCGGAGGCGAACAAAAGCTTATCTCCGAAGAAGACTTGLAGGAACAGAAAT</u>          ACTATTTGGAGCGAATTCDDTCCGCAACTTAAATGAAATGCGCCGACTCTTTG          TAAAGGACTAALATTTTGGCCACCGGAAAGGUAALGCAAGGAAALJASAAITGL          TACAAATCAGTACGTTTTSTURGTAATTCGGTTTSTURMCCCTCAGCACTAAC          AAACCCDACC CATAAACACACACTATCTCTT <b>TAA</b></p>
123	<i>pCHA-LS- mCXCL7<sup>48-</sup> 113-G<sub>3</sub>-c- myc-Aga2</i>	<p><b>ATG</b><u>AAAGGTTTGCATTTCTCTCTTCCCAATCTTCGCTDDETTGCCAATGGCCTTA</u>  <u>GCCTAAGCGGCTTATCTTACTACCGTCCGTTCCCGCTDCAAAAGCTTCTTGGAC</u>  <u>AAAGAG</u> ATCGAGCTGCGGTGCCGGTGCACCAACACCATCAGCGGCATCCCTTTC          AACAGCATCAGCCTCGTGAACGTGTACAGACCCGGCGTGCCTGCGCCGACGTG          GAAGTGATTGCTACACTGAAGATGGGCAGAAAACCTGCCTGGACCCCCAACGCC          CCTGCCGTGAAGCGGATCGTGTGAAGATTCTGGAAGGCTAC <u>GGCGGAGGCGRA</u></p>

		<p>CAAAAGCTTATCTCCGAAGAAGACTTGGAGGACTGGACAACTACATGCGAGCAA          ATCCGCTCAGCAAGCTTTACAAATCCAGCCGCGTCTCTTTTTCAGAGCACTACATAT          TTGATCAGGCTTAACCCCAATTCAGGCAATTTTTCATATATACAAATCAGCTAAG          TTCTCAGTAATTCGCTCTCTCAGCCCTCAACTACTAGTAAAGGCGAGCCCAATA          AACAAACAGATATTTTAA <b>TAA</b></p>
124	<i>pCHA-LS- mCXCL9<sup>22</sup>- 126-G<sub>3</sub>-c- myc-Aga2</i>	<p><b>ATG</b>AAAGCTTTCGATCTGCTCTTGGCCATCTTCGCTGCTTTGCCAATGGCCTTA          GCAGAACTGGTAAATTCAGAACTGTCGATTCGGCTGGGATGAGGCTTCTTGGAC          AAGGAT <b>ACCCTCGTGATCCGGAACGCCCGGTGCAGCTGTATCAGCACCAGCAGA</b>  <b>GGCACCATCCACTACAAGAGCCTGAAGGATCTGAAGCAGTTCCGCCCCAGCCCC</b>  <b>AACTGCAACAAGACCGAGATTATCGCCACACTGAAAAACGGGGACCAGACCTGT</b>  <b>CTGGACCCCGACAGCGCAACGTGAAGAAACTGATGAAGGAATGGGAGAAGAAG</b>  <b>ATCAGCCAGAAGAAGAAGCAGAAGCGGGGCAAGAAACACCAGAAAAACATGAAG</b>  <b>AACCGGAAGCCCCAAGACCCCCCAGAGCCGGCGGAGATCCAGAAAAGACCACA</b> <i>GGC</i>  <i>GGAGGGCAACAAAAGCTTATCTCCGAAGAAGACTTGGACCAACTCACAACCTATA</i>  <i>TGCSAGCAAAACCCCTCAGCAACTTASAAATCGAGCGCTTACTCTCTCAGAG</i>  <i>ACTACTATTTCTGGCAAGCGGAAAGGCAATTCAGAGGATTTCTGACACTACAAA</i>  <i>TCAGTAACTTCTCAGTAATTCGCTCTCTCAGCCCTCAACTACTAGCAAAACCC</i>  <i>AAGCCCAAAAACAGAAATATGTTT <b>TAA</b></i></p>
125	<i>pCHA-LS- mCXCL10<sup>22</sup>- 98-G<sub>3</sub>-c- myc-Aga2</i>	<p><b>ATG</b>AAAGCTTTCGATCTGCTCTTGGCCATCTTCGCTGCTTTGCCAATGGCCTTA          GCTGAACTGGTAAATTCAGAACTGTCGATTCGGCTGGGATGAGGCTTCTTGGAC          AAGGAT <b>ATCCCACTGGCCAGAACCCTGCGGTGCAACTGCATCCACATCGACGAT</b>  <b>GGCCCCGTGCGGATGAGAGCCATCGGCAAGCTGGAAATCATCCCCGCCAGCCTG</b>  <b>AGCTGCCCCAGAGTGGAAATTTATCGCCACCATGAAGAAGAACGACGAGCAGCGG</b>  <b>TGCCTGAACCCCGAGAGCAAGACCATCAAGAACCTGATGAAGGCCTTTAGCCAG</b>  <b>AAGCGGAGCAAGAGGGCCCCA</b> <i>GGCGGAGGGCAACAAAAGCTTATCTCCGAAGAA</i>  <i>GACTTGCAGCAACTGACAACTTATCCGAGCAAACTGCTTCAACCACTCAGAA</i>  <i>TCGAGCCGCTACTCTTTCTCAACTGACTCTATTTCTGGCAAGCGGAAAGGCAATG</i>  <i>CAAGGATTTCTGAAATATCAAAAACAGTAAGCTTCTCAGTAATTCGCTCTCT</i>  <i>CAGCCCTCAAACTGCAAGGCTGAGCCCAATAAATACAGGATATGTTTT <b>TAA</b></i></p>
126	<i>pCHA-LS- mCXCL11<sup>22</sup>- 100-G<sub>3</sub>-c- myc-Aga2</i>	<p><b>ATG</b>AAAGCTTTCGATCTGCTCTTGGCCATCTTCGCTGCTTTGCCAATGGCCTTA          CCTGAACTGGTAAATTCAGAACTGTCGATTCGGCTGGGATGAGGCTTCTTGGAC          AAGGAT <b>TTCTTGATGTTCAAGCAGGGCCCGGTGCCTGTGCTATCGGCCCTGGAATG</b>  <b>AAGGCCGTGAAGATGGCCGAGATCGAGAAGGCCAGCGTGATCTACCCCAGCAAC</b>  <b>GGCTGCGACAAGGTGGAAGTGCCTGACCATGAAGGCCACAAGCGGCAGAGA</b>  <b>TGCCCTGACCCAGATCCAAGCAGGCCCGGCTGATCATGCAGGCTATCGAGAAG</b>  <b>AAGAATTTCTGCGGCGGCAGAACATG</b> <i>GGCGGAGGGCAACAAAAGCTTATCTCC</i>  <i>GAAGAAGACTTGCAGCAACTGACAACTTATCCGAGCAAACTGCTTCAACCACTCAGAA</i>  <i>TTAGAACTGAGCCGCTACTCTTTCTCAACTGACTCTATTTCTGGCAAGCGGAAAG</i>  <i>GCATGCAAGGATTTCTGAAATATACAACTGAGCAAGCTTCTGAGCAATTCG</i>  <i>CGCTCTACCCCTCAACCAACTGCAAGGCTGAGCCCAATAAATACAGGATATGTTTT <b>TAA</b></i></p>
127	<i>LS- hCXCL1<sup>38</sup>- 107-G<sub>3</sub>-c- myc-Aga2</i>	<p>MKVLIIVLEAIFPAALPEALAGTCTSTIVCSAAAGCSLIRATELRCCLOTLQGIH          PKNIQSVNVKSPGPHCAQTEVIATLKNRKAACLNPAASP IVKKIIEKMLNSDKSN          GGGEQKLISEEDLQELTTLTQQLFQPLLESLLYSLSLIHLIANGKAMQGVKFTL          KSVTFVSNDCSHPSTEEKSPENTQVVF-</p>

<p>128</p> <p><i>LS-</i> <i>hCXCL2</i><sup>38-</sup> <i>107-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>ATELRCCQCLQTLOGIH                  LKNIQSVKVKSPGPHCAQTEVIATLKNQKAKLNPASPMVKKIIEKMLKNGKSN  <u>GGGEQKLI SEEDLQ</u>ELTTIDQEQIFSPDLESSTPYSLSTTTILANGKAMQGVFYY                  KSVTFVSNCGSRPSTTSKQSPINTQYVF-</p>
<p>129</p> <p><i>LS-</i> <i>hCXCL3</i><sup>38-</sup> <i>107-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>VTELRCCQCLQTLOGIH                  LKNIQSVNVRSPGPHCAQTEVIATLKNQKAKLNPASPMVQKIIEKILNKGSTN  <u>GGGEQKLI SEEDLQ</u>ELTTIDQEQIFSPDLESSTPYSLSTTTILANGKAMQGVFYY                  KSVTFVSNCGSRPSTTSKQSPINTQYVF</p>
<p>130</p> <p><i>LS-</i> <i>hCXCL4</i><sup>32-</sup> <i>101-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>EAEDGDLCVCKTT                  SQVPRRHITSLEVIKAGPHCPTAQLIATLKNGRKICLDLQAPLYKKIIEKLLS  <u>GGGEQKLI SEEDLQ</u>ELTTIDQEQIFSPDLESSTPYSLSTTTILANGKAMQGVFYY                  KSVTFVSNCGSRPSTTSKQSPINTQYVF-</p>
<p>131</p> <p><i>LS-</i> <i>hCXCL5</i><sup>44-</sup> <i>114-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>LRELRVCVLOTTOGVH                  PKMISNLQVFAIGPQCSKVEVVASLKNQKICLDPEAPFLKKVIQKILDGGNKE  <u>NGGGEQKLI SEEDLQ</u>ELTTIDQEQIFSPDLESSTPYSLSTTTILANGKAMQGVFYY                  YKSVTFVSNCGSRPSTTSKQSPINTQYVF-</p>
<p>132</p> <p><i>LS-</i> <i>hCXCL6</i><sup>44-</sup> <i>114-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>LTELRCTCLRVTLRVN                  PKTIGKLQVFPAGPQCSKVEVVASLKNQKQVCLDPEAPFLKKVIQKILDGSGNKK  <u>NGGGEQKLI SEEDLQ</u>ELTTIDQEQIFSPDLESSTPYSLSTTTILANGKAMQGVFYY                  YKSVTFVSNCGSRPSTTSKQSPINTQYVF-</p>
<p>133</p> <p><i>LS-</i> <i>hCXCL7</i><sup>59-</sup> <i>121-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>AELRCMCIKTTSGIHP                  KNIQSLEVIKGTGHCNQVEVIATLKDGRKICLDPDAPRIKKIVQKKL  <u>GGGEQKLI SEEDLQ</u>ELTTIDQEQIFSPDLESSTPYSLSTTTILANGKAMQGVFYY                  KSVTFVSNCGSRPSTTSKQSPINTQYVF-</p>
<p>134</p> <p><i>LS-</i> <i>hCXCL8</i><sup>29-</sup> <i>99-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>AKELRCQCIKTYSKPF                  HPKFIKELRVIESGPHCANTEIIVKLSDGRELCLDPKENWVQRVVEKFLKRAEN  <u>SGGGEQKLI SEEDLQ</u>ELTTIDQEQIFSPDLESSTPYSLSTTTILANGKAMQGVFYY                  YKSVTFVSNCGSRPSTTSKQSPINTQYVF-</p>
<p>135</p> <p><i>LS-</i> <i>hCXCL9</i><sup>23-</sup> <i>115-G<sub>3</sub>-c-</i> <i>myc-Aga2</i></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>TPVVRKGRCSICISTNQ                  GTIHLQSLKDLKQFAPSPSCEKIEIIATLKNQVQTCNLNPDADVKELIKKEKQ                  VSQKKKQKNGKKHQKKVLRKRSQRSRQKKT<u>GGGEQKLI SEEDLQ</u>ELTTIDQEQIFSPDLESSTPYSLSTTTILANGKAMQGVFYY                  YKSVTFVSNCGSRPSTTSKQSPINTQYVF-</p>
<p>136</p> <p><i>LS-</i> <i>hCXCL10</i><sup>22-</sup></p>		<p><u>MKVLIYVLAIFPAALFLALAQPVLSSTVGSAAEGSLDNR</u>VPLSRTVTRCTCISISN                  QPVNPRSLEKLEIIPASQFCPRVEIATMKKKGKRCCLNPESKAIKNLLKAVSK</p>

	<sup>98</sup> -G <sub>3</sub> -c- <i>myc-Aga2</i>	<u>ERSKRSPGGGEQKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-
137	<i>LS-</i> <i>hCXCL11</i> <sup>22</sup> - <sup>94</sup> -G <sub>3</sub> -c- <i>myc-Aga2</i>	<u>MKVLIVDLSAIFPAALPLALAQVYLSSTTVGSAANEGLDQKAFPMFKRGRCLCIGPGV</u> <u>KAVKVADIEKASIMYP SNNCDKIEVIITLKENKGRCLNPKSKQARLI IKKVER</u> <u>KNFGGGEQKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-
138	<i>LS-</i> <i>mCXCL1</i> <sup>28</sup> - <sup>96</sup> -G <sub>3</sub> -c- <i>myc-Aga2</i>	<u>MEVLEVDLSAIFPAALPLALAQVYLSSTTVGSAANEGLDQKAFANELRCQCLQTMAGIH</u> <u>LKNIQSLKVLPSGPHCTQTEVIATLKNGREACLDPEAPLVQKIVQKMLKGVPKG</u> <u>GGGEQKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-
139	<i>LS-</i> <i>mCXCL2</i> <sup>31</sup> - <sup>100</sup> -G <sub>3</sub> -c- <i>myc-Aga2</i>	<u>MKVLIVDLSAIFPAALPLALAQVYLSSTTVGSAANEGLDQKAFASELRCQCLKTLPRVD</u> <u>FKNIQSLSVTPPPGPHCAQTEVIATLKGQKVCVDPEAPLVQKIIQKILNKGKAN</u> <u>GGGEQKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-
140	<i>LS-</i> <i>mCXCL3</i> <sup>31</sup> - <sup>100</sup> -G <sub>3</sub> -c- <i>myc-Aga2</i>	<u>MEVLEVDLSAIFPAALPLALAQVYLSSTTVGSAANEGLDQKAFASELRCQCLNTLPRVD</u> <u>FETIQSLTVTPPPGPHCTQTEVIATLKDGGQEVCLNPQGPRLQII IKKILKSGKSS</u> <u>GGGEQKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-
141	<i>LS-</i> <i>mCXCL4</i> <sup>30</sup> - <sup>105</sup> -G <sub>3</sub> -c- <i>myc-Aga2</i>	<u>MKVLIVDLSAIFPAALPLALAQVYLSSTTVGSAANEGLDQKAFVTSAGPEESDGDLSCV</u> <u>CVKTISSGIHLKHITSLEVIKAGRHCAPQLIATLKNRKCICLDRQAPLYKKVI</u> <u>KKILES GGGEQKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-
142	<i>LS-</i> <i>mCXCL5</i> <sup>48</sup> - <sup>118</sup> -G <sub>3</sub> -c- <i>myc-Aga2</i>	<u>MEVLEVDLSAIFPAALPLALAQVYLSSTTVGSAANEGLDQKAFATELRCVCLTVTPKIN</u> <u>PKLIANLEVIPAGPOCPTVEVI AKLNQKEVCLDPEAPVIKKIIQKILGSDKKK</u> <u>AGGGEQKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-
143	<i>LS-</i> <i>mCXCL7</i> <sup>48</sup> - <sup>113</sup> -G <sub>3</sub> -c- <i>myc-Aga2</i>	<u>MKVLIVDLSAIFPAALPLALAQVYLSSTTVGSAANEGLDQKAFIELRCRCTNTISGIPF</u> <u>NSISLVNVYRPGVHCADVEVIATLKNQKTCCLDPNAPGVKRIVMKILEGYGGGE</u> <u>QKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-
144	<i>LS-</i> <i>mCXCL9</i> <sup>22</sup> - <sup>126</sup> -G <sub>3</sub> -c-	<u>MEVLEVDLSAIFPAALPLALAQVYLSSTTVGSAANEGLDQKFTLVIRNARCSCISTSR</u> <u>GTIHYKSLKDLKQFAPSPNCNKTETIATLKNGDQTCCLDPDSANVKKMLKEWEKK</u> <u>ISQKKRQKRGKKHQKNMKNRKPPTPQSRRRSRKTT GGGEQKLI SEEDLQ</u> ELTTTICGQIPSPTELESTPYSLSTTTILANGKAMQGVFEYKSVTFVSNCGSHFSTTSKQSPINTQYVF-



	<i>myc-Aga2</i>	CEQIPSEPTLESTFYSLSTTTLLANGKAMQGVFEYNE SVL FVSNCGSHPSLERSG SPINTQYVF-
145	<i>LS- mCXCL10<sup>22</sup> -98-G<sub>3</sub>-c- myc-Aga2</i>	MKVLIIVLLAIFPAALPLALAQPVISTTVGSAAEGLD <sup>98</sup> RIPLARTVRCNCIHIDD GPVRMRAIGKLEIIPASLSCPVEIIATMKKNDEQRCLNPESKTIKNLMKAFSQ KRSKRAPGGGEQKLISEEDLQELTTICEQIPSEPTLESTFYSLSTTTLLAN KAMQGVFEYKSVTFVSNCGSHPSLERSGSPINTQYVF-
146	<i>LS- mCXCL11<sup>22</sup> -100-G<sub>3</sub>-c- myc-Aga2</i>	MKVLIIVLLAIFPAALPLALAQPVISTTVGSAAEGLD <sup>100</sup> FLMFKQGRCLCIGPGM KAVKMAEIEKASVIYPSNGCDKVEIVTMKAHKRQRCLDPRSKQARLIMQAIK KNFLRRQNMGGGEQKLISEEDLQELTTICEQIPSEPTLESTFYSLSTTTLLANCR AMQGVFEYKSVTFVSNCGSHPSLERSGSPINTQYVF-
147	<i>pCHA-LS- hCXCL1- G<sub>3</sub>-c-myc- Aga2</i>	<b>ATG</b> AAGCCTTTTCATTTCTCTGTTGGCTACTCTTCGGTGGCTTTGGGA TTGGCCTTAGCTCAACCGGTATTTTCTACTACCGTCTGCTTCCGCT GCAGAAAGGCCTCTTGGACAAGAGAGCCACCGAGCTGAGATGCCAG TGCCTGCAGACCCTGCAGGGCATCCACCCCAAGAACATCCAGAGC GTGAACGTGAAGTCCCCTGGCCCCACTGCGCCAGACCGAAGTG ATCGCCACCCTGAAGAACGGCCGGAAGGCCTGCCTGAACCCCGCC AGCCCCATCGTGAAGAAAATCATCGAGAAGATGCTGAACAGCGAC AAGAGCAACGGCGGAGGCCAACAAAAGCTTATCTCCGAAGAAGAC <b>TTG</b> CTGGAACTGCAACTATATGGGAGCAATCCCTCACCBACT TTAGAAATCGACGGCGTACTCTTTGTCAACGAC TACTAFTTTGGCC AACCGGAAAGCCAAATGCAAGGCASTTTTTGAATATTACAAATCGATA ACGTTTGTTCAGTAATTTGGCTTCTCACCCCTCAACAAGTACGAAA GGCAGCCCTATAAACAACACAGTATGTTTT <b>TAA</b>
148	<i>LS- hCXCL1- G<sub>3</sub>-c-myc- Aga2</i>	MKVLIIVLLAIFPAALPLALAQPVISTTVGSAAEGLD <sup>98</sup> SPATELRQC CLQTLQGIHPKNIQSVNVKSPGPHCAQTEVIATLKNRKAQLNPA SPIVKKIIEKMLNSDKSNGGGEQKLISEEDLQELTTICEQIPSEPT LESTFYSLSTTTLLANGKAMQGVFEYKSVTFVSNCGSHPSLERSG SPINTQYVF-
149	<i>mouse SA- (Gly<sub>4</sub>Ser)<sub>3</sub>- scFv (V<sub>L</sub>- V<sub>H</sub>) CK138</i>	<b>ATG</b> CAAGCAGCAAGAGTGGGATGGCCCTCGGTATAAATGATTCGGGAGAACAA CGTTTCRAAGGCGTATGTCCTGATTTGGCTTTTCCGAGTATCTCCGAAATGCTCA TACCATATCCATATCCAAATTAATTCACCCAAATTAACACACTTTTCRAAGACCTCT GTTTCGCGATGATTCGCGGCAACCTGTCACAAATCTGTCACACTCTCTTLLGAA CALAAGTCTCTGCGATTCGCAAAAGCTCCGTCGAAATTAAGTCAAGTCCGCGAC TCTTSTACAAAGCAAGTCCGCAAGGACCAATGTTTTCTCCGACACCAAGT GACAACTCCGAGCTTACCAATTTGAAAGTCCAGAGGCTTCCGCTAATGTCGAC TCCTTTACGAAATTCGCAAGCACTTTCATCTACACTATTTGCATCAAGTCCG AGAAAGCACTCTTACTTCTATGCGCAAGAACTTCTTTACTAAGCTGACACAGTAC AATCAGATTCCTGACCCACTCTTCTCTCAAGCCCTCAAAACCAAGCTCCCTTACC







		<pre>ATCAACTCCTTCCACTATCCAGCAATTTCGAATAGACAGCCCTTTTAAAGCATGCCCCA CTAGCTCCTTCTGAGCCACACACTTTCGCATCTTCTTCACTTTCGACAAATCCACCGAAA TTGAAAGCAADANTTCACTAAAGTCAATACACCACTATTCCCATATGAGCCTTTTGC GATATCCGATATGACAGGCGGCAACTTCCCATAGTACATATATGAAAACCAAGGG AGLAEVLCAGUAAATIGUAAATIGUTUAGATAAAGUATIGLUAGAAAGUU CACTCTTTAGTAACTTGGAGGATGACACCATATGCTTCTTCACTTTCCTTCTCTT GUTGCTGATTTTGTGAGGACCAAGAGTGTGACAGAAATATGCTGAGGUCAG CATATTCCTGCTTCCGACCTTTTCTTCTGAAATATTACAAAGACATCCCTCATATC TCTTAAATCCCTTTGCTGACACTTTCCTGAGAAATATGAAAGCCTCTTGGAAAAG TGCTTDTGAACTATCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCT CAGCTCTTGTGAAAGACCTTAATCACTTCTTCAAAAGCACTTCTGCTTCTTAC GAGAACCTTGGAGAAATAGAAAGGAAAATIGUAAATIGUAAATIGUAAATIGUAAAT AAAGGCTTCACTTCTCACTTCTCACTTCTCACTTCTCACTTCTCACTTCTCACTTCT AGATGCTGACCAAGAGTATGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCT CAACTCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCT ACAGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCT TCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCT CTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCTGCTTCT GGTGGAGGAGGCTCTGGTGGAGGCGGT AGCGGAGGCGGAGGGTCTGGCTATCCAGATGACCCGGTCCCAGCTCCCTGTCC GCCTCTGTGGGGGATAGGGTCAACATCACCTGCCGTGCCAGTCACTACCACGAC GGTCTGCAGCCTGGTATCAACAGAAACCAGGAAAAGCTCCGAAGCTTCTGATT TACGGTGCATCCTACCTCTACTCTGGAGTCCCTTCCCCTTCTCTGGTAGCCGT TCCGGGACGGATTTCACTCTGACCATCAGCAGTCTGCAGCCGGAAGACTTCGCA ACTTATTACTGTGAGCAATCTTCTTATTCTCTGATCAGTFCGGATGCGGTAC AAGGTGGAGATCAAAGGTACTACTGCGCCTAGTGGTAGTAGTGGTGGCAGTAGC AGTGGTGGCGAGGTTCACTGCTGGTGGAGTCTGACGGTGGCTGGTGCAGCCAGGG GGCTCACTCCGTTTGTCTGTCAGCTTCTGGCTTCAACCTCTCTTACTACGGT ATGCACFGGGTGGCTCAGGCCCCGGGTAAGTGCCTGGAATGGGTGTCATACAT GCTTCTTACCCTGGCTACACTTCTTATGCCGATAGCGTCAAGGGCCGTTTCACT ATAAGCGCAGACACATCCAAAACACAGCCTACCTACAAATGAACAGCTTAAGA GCTGAGGACACTGCCGCTACTATTGTGCTCGCTCTGGTTACAGTTACTCTCCG TATTATTCTTGGTTCTCTGCTGGTATGAACTACTGGGGTCAAGGAGCCCTGGTC ACCGTCTCCTCGTGATAG</pre>
<p>153</p>	<p><i>mouse SA-</i> <i>(Gly<sub>4</sub>Ser)<sub>3</sub>-</i> <i>scFv (V<sub>L</sub>-</i> <i>V<sub>H</sub>) CK138-</i> <i>ds2</i> <i>(V<sub>L</sub>43<sup>A&gt;C</sup> /</i> <i>V<sub>H</sub>105<sup>Q&gt;C</sup>)</i></p>	<pre>ATGTAAGCAACAAGAGTGTGATTCCTCCCATCCGTATAAATGATCCTGGGACAAACA GATTENAAAGGGTATAGTGTUAAATGCTTTTCCGAGATLCTGLAGAAATGUELA TACCCTTAGCATATCCAAATCACTCTGACCAATTAACACACTTTCGAAAGACCTCT GTTCCGCAATGATCTCCTCCGCACTCTGACAAATCCCTTACAGCTCTCTTTCGAA GALAAATGCTGAGGCAATCTCCAAACTCTTGAAAAATGCTTCCAGACTCTCTTTCGAA TGTGCTTACAAATCAAGAGGCTGAAAGAAACCAATGTTTCTCTGACACAAAGAA GAGAACTCCAGCTTACCACTTTCGAAAGCTCAGAGATLTCGCTTATGAGATGCTTCCG TCTTTATGAAAGAGCCAGCACTCTTATGCACTACTTTCATATGAACTCTTCCG AGAAGGCTGCTTACTTCTTATGCTTCAAGACTTCTTTATGATGCTGAGGATGAT ATTGAGATTCCTACCACTTTCTGCTGAGCCTCATAACCAAGCTTCCCTTACC CGAGAGCTTCACTTCTGCTGAGAAAGCAATGCTTCTTCTTCTTCTGCTTCTGAA</pre>













		<p>GCCTCAGACTTTGAGTTTCAGCTTTGATATCTTTGACACTTTCACAGAAAGGACAAAC  CACATTTAGCAAAACAAAGCCCTGTTGCTGAGCTTCTTAAACAGAAAGCCCAAGCTT  ACATCCGAGGAACTCAACATTTGATATCACTTTGACAGACTTCCGCAACTTCCGCAATACA  TCTTTCAGAGCTTCTTACAGAGGAACTTCTGCTTCTGCACTTTCAGGTTCCAAAGCTTT  GTCAATNGAIGCAAAGAGGAAATLAAACGGTGGAGGAGGCTCTGGTGGAGGCGGT  <u>AGCCGACCCGACCGCTCCGATATCCAGATGACCCAGTCCCGAGCCCCCTGTCC</u>  GCCTCTGTGGGGATAGGGTCACCATCACCTGCCGTGCCAGTCAGTACGGTGGT  TACGTAGCCTGGTATCAACAGAAACCAGGAAAAGCTCCGAAGCTTCTGATTTAC  GGTGCATCCCTTCTCTACTCTGGAGTCCCTTCTCGCTTCTCTGGTGGCCGTTCC  GGGACGGATTTCACTCTGACCATCAGCAGTCTGCAGCCGGAAGACTTCGCAACT  TATTACTGTCAGCGAGGTCAATGCTCTGATCACGTTCCGGAATCCGGTACCAAGGTG  GAGATCGAAGGTACTACTGCCGCTAGTGGTAGTAGTGGTGGCAGTAGCAGTGGT  GCCGAGGTTCACTGGTGGAGTCTGGCCGTGGCCTGGTGCAGCCAGGGGGCTCA  CTCCGTTTATCCTGTGCAGCTTCTGGCTTCAACATCTCTTCTTACGGTTCTATG  CACTGGGTGCGTCAGGCCCGGGTAAGATGCCTGGAATGGGTTGCATCTATTTAC  CCTTACTCTAGCTCTACTTACTATGCCGATAGCGTCAAGGGCCGTTTCACTATA  AGCGCAGACACATCAAAAACACAGCCTACCTACAAATGAACAGCTTAAGAGCT  GAGGACACTGCCGTCTATTATTGTGCTCGTGGTTACGGTCCGTGGTACGCTTAC  TCTTACTTCGCTTTGGACTACTGGGGTCAAGGAACCCTGGTCACCGTCTCCTCG  TGATAG</p>
159	<p><i>mouse SA-  (Gly<sub>4</sub>Ser)<sub>3</sub>-  scFv (V<sub>L</sub>-  V<sub>H</sub>) CK129-  ds2  (V<sub>L</sub>43<sup>A&gt;C</sup> /  V<sub>H</sub>105<sup>Q&gt;C</sup>)</i></p>	<p><b>ATG</b>CAAACACAGAAACAGACAAACAGCAATCCGCTATCCGATAAALGALGAGGAGAA  CAATTCAGAGGAGGCTAGCTCTGATTTGCTTTTCCGAGTATCTCCAGAAATGCTCA  TACATTCAGGATGCGCAATTTATTCAGGAAATGACAGACTTTTCAGAGAGCTTCT  CTTATTCAGATCTTCCGATCAACTTCCGCAACTTCCGCAACTTCCGCAACTTCCGCA  GATCACTTCTGCTGCTTCCAAAGCTTCCGTCAGAAACTATGCTGCACTTCCGCACT  TCCTCTAAGAAACAGAGCCGCAAGCAAAATGATCTTTCTGCAAGCAAAACAT  GAGAAACCCAGGCTACCTCCATTTGAAAGGCTCAGAGGCTGAGGCTATCTGCACT  TCTTAAAGGAAACCAAGGAGCTTAAAGGAAACCAAGGAGCTTAAAGGAAACCAAGG  ACAGGAGATCTTATTTCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACT  ATGAAATTCAGGCTTCTGCTTCTGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCA  CCCAACTTTCAGTCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCG  ATGAAATTCAGGCTTCTGCTTCTGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCA  CTAATTCAGTCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCA  TTTAAAGGAAACCAAGGAGCTTAAAGGAAACCAAGGAGCTTAAAGGAAACCAAGG  GAATGCTCAGATGAGAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACT  ACTATTCAGGCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCA  CACTCTTCTAGTCTGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  CTTCTTCACTTCTGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  GATTTCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  TKCTTCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  TRCTGCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  CAGCTTCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  GATTTCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  AAAGGAACTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  AGACTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  GATTTCTTCCGCAAGGCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  CAATTCAGTCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCGCAACTTCCG  CAATTCAGTCTTCCGCAAGGCTTCCGCAACTTCCGCAACTTCCGCAACTTCCGCAACTTCCG</p>

		<p>GCCTCAGACTTTGAGTTTCAGCTCTGATATCTTCACACTTCTACACAAAGGACAAAC  CACATTTAGCAAAACAAAGCCGCTCTTCTGCTGAGCTGCTGAAACAGAAAGCCCAAGGCT  AGAAACGAGGAACTCAACAACTGCTCATATATCACTTTCACACACTTCCGCAACTTCCGCAATACA  TCTTTCACAGGCTGCTGACAGGAAACGCTGCTTCTGCACTTTCAGGCTGCAAAAGCTT  GTCAATNGATGAAAGAGGAAATLAAAGCGGTGGAGGAGGCTCTGGTGGAGGCGGT  <u>AGCCGACGCCGAGCGCTCCGATATCCAGATGACCCAGTCCCGAGCCCCCTGTCC</u>  GCCTCTGTGGGGATAGGGTCACCATCACCTGCCGTGCCAGTCACTACGGTGGT  TACGTAGCCTGGTATCAACAGAAACCAGGAAAAAGCCGAAGCTTCTGATTTAC  GGTGCATCCCTTCTCTACTCTGGAGTCCCTTCTCGCTTCTCTGGTGGCCGTTCC  GGGACGGATTTCACTCTGACCATCAGCAGTCTGCAGCCGGAAGACTTCGCAACT  TATTACTGTCAGCGAGGTCACTGCTCTGATCACGTTCCGGACAGGGTACCAAGGTG  GAGATCGAAGGTACTACTGCCGCTAGTGGTAGTAGTGGTGGCAGTAGCAGTGGT  GCCGAGGTTCACTGGTGGAGTCTGGCGGTGGCCTGGTGCAGCCAGGGGGCTCA  CTCCGTTTATCCTGTGCAGCTTCTGGCTTCAACATCTCTTCTTACGGTTCTATG  CACTGGGTGCGTCAGGCCCGGGTAAGGGCCTGGAATGGGTTGCATCTATTTAC  CCTTACTCTAGCTCTACTTACTATGCCGATAGCGTCAAGGGCCGTTTCACTATA  AGCGCAGACACATCAAAAACACAGCCTACCTACAAATGAACAGCTTAAGAGCT  GAGGACACTGCCGTCTATTATTGTGCTCGTGGTTACGGTCCGTGGTACGCTTAC  TCTTACTTCGCTTTGGACTACTGGGGTTCGCGAACCTGGTCAACCGTCTCCTCG  TGATAG</p>
160	<i>mouse SA-(Gly<sub>4</sub>Ser)<sub>3</sub>-scFv (V<sub>L</sub>-V<sub>H</sub>) CK138</i>	<p>RANFSELAHPENHLGKQHFSGIVLLAFPSQYLQKCSYDHAALVQGVLDKAEIIV  ADEFAARCDKSLATLFGKLCALPHIENYSELALCCTEKQEPERNECFLQHAGD  NPSLPPFEPPEAAMCTSPKSHFTTFNGHILMEVARRRPYTYABELLYAAEQYR  EILTPQCASADKESCLTPKLDGVSERALVSSVSRQMKCSQKQKQERAFKAWAV  ARLSQTFPRADFAEITLALATDIKRVNHEGCHQDLDECAEDDPAELAKYNQENQAT  EGSSLOTCDDKFLKKAHOLSEVHMDDFADLEPLAAGDFVHDQEVOKHYREASG  VFLATPLVENSRRRPFDYGVFLLEPLAKKVEATLEKQCAERAPPACTYTHIARFQ  FLYEMFANLVKIHCDLYEKLAGSYGFQNALLVKXTQKAPQVDTPLVBAANKLQK  VCTKCTLPEDQRIPOVEDYLSAFLNEVCLLREKTPVSEKRVTECCSDFLVREFF  CFSAITVDETIVKKEFAETPTFRSDLOTIPEKAEQIKKQYALSLVKAERFVAT  AEQLSTVMDDEFAQFLDTCCSAADKDTICFSTECENLVTRIKDALA <u>GGGGSGGGGS</u>  <u>GGGGSAGAIQMTRSPSSLSASVGDRTITCRASQYHDGSAAWYQKPKGKPKLL</u>  IYGASYLYSGVPSRFRSGRSRGTDFTLTISSLQPEDFATYYCQQSSSYSLITFGQG  TKVEIKGTTAASGSSGGSSSGAEVQLVESDGLVQPGGSLRLSCAASGFNLSYY  GMHWVRQAPGKGLEWVAYIASYPGYTSYADSVKGRFTIISADTSKNTAYLQMNLSL  RAEDTAVYYCARSGYSYSPYYSNFSAAGMNYWGQALVTVSS--</p>
161	<i>mouse SA-(Gly<sub>4</sub>Ser)<sub>3</sub>-scFv (V<sub>L</sub>-V<sub>H</sub>) CK157</i>	<p>RANFSELAHPENHLGKQHFSGIVLLAFPSQYLQKCSYDHAALVQGVLDKAEIIV  ADEFAARCDKSLATLFGKLCALPHIENYSELALCCTEKQEPERNECFLQHAGD  NPSLPPFEPPEAAMCTSPKSHFTTFNGHILMEVARRRPYTYABELLYAAEQYR  EILTPQCASADKESCLTPKLDGVSERALVSSVSRQMKCSQKQKQERAFKAWAV  ARLSQTFPRADFAEITLALATDIKRVNHEGCHQDLDECAEDDPAELAKYNQENQAT  EGSSLOTCDDKFLKKAHOLSEVHMDDFADLEPLAAGDFVHDQEVOKHYREASG  VFLATPLVENSRRRPFDYGVFLLEPLAKKVEATLEKQCAERAPPACTYTHIARFQ  FLYEMFANLVKIHCDLYEKLAGSYGFQNALLVKXTQKAPQVDTPLVBAANKLQK  VCTKCTLPEDQRIPOVEDYLSAFLNEVCLLREKTPVSEKRVTECCSDFLVREFF  CFSAITVDETIVKKEFAETPTFRSDLOTIPEKAEQIKKQYALSLVKAERFVAT  AEQLSTVMDDEFAQFLDTCCSAADKDTICFSTECENLVTRIKDALA <u>GGGGSGGGGS</u></p>

		<p><u>GGGGS</u><b>ASDIQMTQSPSSLSASVGD</b>RVTITCRASQSYGGVAVYQKPKGKAPKLLI  <b>YSASYLYSGVPSRFSGSRSGTD</b>FTLTISSLQPEDFATYYCQQP<b>SHLITFGQGTE</b>  <b>VEIKGTTAASGSSGGSSSGAEVQ</b>LVESSGGGLVQPGGSLRLSCAASGSNPFYYGG  <b>THWVRQAPGEELEWVASIGSYP</b>GYTDYADSVKGRFTTISADTSKNTAYLQ<b>MNSLR</b>  <b>AEDTAVYYCARHYWYDATDYWG</b>QGT<b>LVTVSS</b>--</p>
<p>162</p>	<p><i>mouse SA- (Gly<sub>4</sub>Ser)<sub>3</sub>- scFv (V<sub>L</sub>- V<sub>H</sub>) CK129</i></p>	<p>EAHYSEIARRZSDI<b>GEORF</b>KSTVLI<b>AF</b>SQYLQKCSYD<b>ERANL</b>VQEV<b>DF</b>FA<b>HTCV</b>          ADESAANQDESL<b>ET</b>LF<b>GR</b>AL<b>GA</b>LPHLPENY<b>GR</b>LA<b>Q</b>UT<b>KQ</b>MP<b>EN</b>NE<b>CF</b>LQ<b>HN</b>U          NPSL<b>PF</b>EP<b>PE</b>AA<b>AM</b>CT<b>S</b>FR<b>EN</b>FT<b>TF</b>MG<b>RY</b>L<b>HE</b>VA<b>RR</b>NP<b>Y</b>Y<b>AP</b>EL<b>LY</b>AE<b>Q</b>YN          EIL<b>TC</b>CR<b>EA</b>DK<b>ES</b>CL<b>TP</b>K<b>LP</b>G<b>V</b>NE<b>K</b>AL<b>V</b>SV<b>R</b>Q<b>R</b>NR<b>CS</b>SA<b>Q</b>K<b>F</b>GE<b>PA</b>FK<b>AW</b>Y          AKLSQ<b>I</b>PF<b>N</b>AD<b>Y</b>AL<b>L</b>TK<b>L</b>A<b>IDL</b>LV<b>N</b>K<b>EC</b>CH<b>CH</b>L<b>EC</b>AL<b>L</b>SA<b>L</b>DA<b>Y</b>MC<b>EN</b>Q<b>L</b>          L<b>SS</b>VL<b>Q</b>TC<b>OD</b>NE<b>L</b>L<b>K</b>K<b>AR</b>CL<b>SE</b>VE<b>RD</b>TE<b>MP</b>AD<b>LP</b>AL<b>LA</b>DE<b>F</b>VE<b>D</b>Q<b>E</b>PK<b>NY</b>AE<b>AK</b>U          VE<b>L</b>ST<b>F</b>LY<b>EN</b>Y<b>SR</b>NP<b>D</b>Y<b>S</b>VS<b>LI</b>L<b>R</b>L<b>AR</b>Y<b>EA</b>L<b>LE</b>Q<b>LA</b>AN<b>MP</b>PA<b>UY</b>Q<b>L</b>YL<b>AE</b>F<b>Q</b>          PV<b>VE</b>EP<b>EN</b>LV<b>K</b>T<b>NC</b>D<b>LY</b>E<b>K</b>L<b>GE</b>Y<b>GF</b>Q<b>N</b>AIL<b>VE</b>Y<b>T</b>Q<b>RA</b>F<b>Q</b>V<b>ST</b>P<b>LV</b>EA<b>AR</b>N<b>L</b>GE          W<b>L</b>K<b>CC</b>IL<b>U</b>ED<b>Q</b>RL<b>F</b>CV<b>ED</b>Y<b>L</b>SA<b>L</b>LN<b>R</b>V<b>CL</b>LE<b>KL</b>PV<b>S</b>ER<b>VT</b>K<b>CS</b>S<b>GL</b>VE<b>PP</b>F          CP<b>ER</b>L<b>IV</b>DE<b>T</b>Z<b>V</b>PE<b>KA</b>ET<b>TF</b>PR<b>AD</b>L<b>CT</b>L<b>PE</b>KE<b>Q</b>Y<b>K</b>Q<b>T</b>AL<b>EL</b>V<b>K</b>AE<b>F</b>Y<b>AT</b>          AE<b>Q</b>LY<b>VM</b>DD<b>F</b>Z<b>Q</b>FL<b>D</b>TC<b>KA</b>AD<b>R</b>DT<b>CF</b>ST<b>EP</b>HL<b>V</b>TR<b>F</b>RD<b>AL</b>L<b>GGGGS</b><b>GGGGS</b>  <u>GGGGS</u><b>ASDIQMTQSPSPLSASVGD</b>RVTITCRASQYGGYVAVYQKPKGKAPKLLI  <b>YGASLLYSGVPSRFSGSRSGTD</b>FTLTISSLQPEDFATYYC<b>QR</b>GHALIT<b>FGQGTK</b>  <b>VEIEGTTAASGSSGGSSSGAEVQ</b>LVESSGGGLVQPGGSLRLSCAASGFNISSYGS  <b>MHWVRQAPGKGLEWVASI</b>YPYSSSTYYADSVKGRFTTISADTSKNTAYLQ<b>MNSLR</b>  <b>AEDTAVYYCARGYGPWYAYS</b>YFALDYWGQGT<b>LVTVSS</b>--</p>
<p>163</p>	<p><i>mouse SA- (Gly<sub>4</sub>Ser)<sub>3</sub>- scFv (V<sub>L</sub>- V<sub>H</sub>) CK138- ds1 (V<sub>L</sub>100<sup>Q&gt;C</sup> / V<sub>H</sub>44<sup>G&gt;C</sup>)</i></p>	<p>EAHYSEIARRZSDI<b>GEORF</b>KSTVLI<b>AF</b>SQYLQKCSYD<b>ERANL</b>VQEV<b>DF</b>FA<b>HTCV</b>          ADESAANQDESL<b>ET</b>LF<b>GR</b>AL<b>GA</b>LPHLPENY<b>GR</b>LA<b>Q</b>UT<b>KQ</b>MP<b>EN</b>NE<b>CF</b>LQ<b>HN</b>U          NPSL<b>PF</b>EP<b>PE</b>AA<b>AM</b>CT<b>S</b>FR<b>EN</b>FT<b>TF</b>MG<b>RY</b>L<b>HE</b>VA<b>RR</b>NP<b>Y</b>Y<b>AP</b>EL<b>LY</b>AE<b>Q</b>YN          EIL<b>TC</b>CR<b>EA</b>DK<b>ES</b>CL<b>TP</b>K<b>LP</b>G<b>V</b>NE<b>K</b>AL<b>V</b>SV<b>R</b>Q<b>R</b>NR<b>CS</b>SA<b>Q</b>K<b>F</b>GE<b>PA</b>FK<b>AW</b>Y          AKLSQ<b>I</b>PF<b>N</b>AD<b>Y</b>AL<b>L</b>TK<b>L</b>A<b>IDL</b>LV<b>N</b>K<b>EC</b>CH<b>CH</b>L<b>EC</b>AL<b>L</b>SA<b>L</b>DA<b>Y</b>MC<b>EN</b>Q<b>L</b>          L<b>SS</b>VL<b>Q</b>TC<b>OD</b>NE<b>L</b>L<b>K</b>K<b>AR</b>CL<b>SE</b>VE<b>RD</b>TE<b>MP</b>AD<b>LP</b>AL<b>LA</b>DE<b>F</b>VE<b>D</b>Q<b>E</b>PK<b>NY</b>AE<b>AK</b>U          VE<b>L</b>ST<b>F</b>LY<b>EN</b>Y<b>SR</b>NP<b>D</b>Y<b>S</b>VS<b>LI</b>L<b>R</b>L<b>AR</b>Y<b>EA</b>L<b>LE</b>Q<b>LA</b>AN<b>MP</b>PA<b>UY</b>Q<b>L</b>YL<b>AE</b>F<b>Q</b>          PV<b>VE</b>EP<b>EN</b>LV<b>K</b>T<b>NC</b>D<b>LY</b>E<b>K</b>L<b>GE</b>Y<b>GF</b>Q<b>N</b>AIL<b>VE</b>Y<b>T</b>Q<b>RA</b>F<b>Q</b>V<b>ST</b>P<b>LV</b>EA<b>AR</b>N<b>L</b>GE          W<b>L</b>K<b>CC</b>IL<b>U</b>ED<b>Q</b>RL<b>F</b>CV<b>ED</b>Y<b>L</b>SA<b>L</b>LN<b>R</b>V<b>CL</b>LE<b>KL</b>PV<b>S</b>ER<b>VT</b>K<b>CS</b>S<b>GL</b>VE<b>PP</b>F          CP<b>ER</b>L<b>IV</b>DE<b>T</b>Z<b>V</b>PE<b>KA</b>ET<b>TF</b>PR<b>AD</b>L<b>CT</b>L<b>PE</b>KE<b>Q</b>Y<b>K</b>Q<b>T</b>AL<b>EL</b>V<b>K</b>AE<b>F</b>Y<b>AT</b>          AE<b>Q</b>LY<b>VM</b>DD<b>F</b>Z<b>Q</b>FL<b>D</b>TC<b>KA</b>AD<b>R</b>DT<b>CF</b>ST<b>EP</b>HL<b>V</b>TR<b>F</b>RD<b>AL</b>L<b>GGGGS</b><b>GGGGS</b>  <u>GGGGS</u><b>SAIQMTRSPSSLSASVGD</b>RVTITCRASQYHDGSAAWYQKPKGKAPKLLI  <b>IYGASYLYSGVPSRFSGSRSGTD</b>FTLTISSLQPEDFATYYCQ<b>QSS</b>YSLIT<b>FGCG</b>  <b>TKVEIKGTTAASGSSGGSSSGAEVQ</b>LVESSD<b>G</b>GLVQPGGSLRLSCAASGFNLSYY  <b>GMHWVRQAPGKCLEWVAYIAS</b>YPGYTSYADSVKGRFTTISADTSKNTAYLQ<b>MNSL</b>  <b>RAEDTAVYYCARSYSYSPYYS</b>WF<b>SAGMNYWGQ</b>AL<b>VTVSS</b>--</p>
<p>164</p>	<p><i>mouse SA- (Gly<sub>4</sub>Ser)<sub>3</sub>- scFv (V<sub>L</sub>- V<sub>H</sub>) CK138- ds2 (V<sub>L</sub>43<sup>A&gt;C</sup> / V<sub>H</sub>105<sup>Q&gt;C</sup>)</i></p>	<p>EAHYSEIARRZSDI<b>GEORF</b>KSTVLI<b>AF</b>SQYLQKCSYD<b>ERANL</b>VQEV<b>DF</b>FA<b>HTCV</b>          ADESAANQDESL<b>ET</b>LF<b>GR</b>AL<b>GA</b>LPHLPENY<b>GR</b>LA<b>Q</b>UT<b>KQ</b>MP<b>EN</b>NE<b>CF</b>LQ<b>HN</b>U          NPSL<b>PF</b>EP<b>PE</b>AA<b>AM</b>CT<b>S</b>FR<b>EN</b>FT<b>TF</b>MG<b>RY</b>L<b>HE</b>VA<b>RR</b>NP<b>Y</b>Y<b>AP</b>EL<b>LY</b>AE<b>Q</b>YN          EIL<b>TC</b>CR<b>EA</b>DK<b>ES</b>CL<b>TP</b>K<b>LP</b>G<b>V</b>NE<b>K</b>AL<b>V</b>SV<b>R</b>Q<b>R</b>NR<b>CS</b>SA<b>Q</b>K<b>F</b>GE<b>PA</b>FK<b>AW</b>Y          AKLSQ<b>I</b>PF<b>N</b>AD<b>Y</b>AL<b>L</b>TK<b>L</b>A<b>IDL</b>LV<b>N</b>K<b>EC</b>CH<b>CH</b>L<b>EC</b>AL<b>L</b>SA<b>L</b>DA<b>Y</b>MC<b>EN</b>Q<b>L</b>          L<b>SS</b>VL<b>Q</b>TC<b>OD</b>NE<b>L</b>L<b>K</b>K<b>AR</b>CL<b>SE</b>VE<b>RD</b>TE<b>MP</b>AD<b>LP</b>AL<b>LA</b>DE<b>F</b>VE<b>D</b>Q<b>E</b>PK<b>NY</b>AE<b>AK</b>U          VE<b>L</b>ST<b>F</b>LY<b>EN</b>Y<b>SR</b>NP<b>D</b>Y<b>S</b>VS<b>LI</b>L<b>R</b>L<b>AR</b>Y<b>EA</b>L<b>LE</b>Q<b>LA</b>AN<b>MP</b>PA<b>UY</b>Q<b>L</b>YL<b>AE</b>F<b>Q</b>          PV<b>VE</b>EP<b>EN</b>LV<b>K</b>T<b>NC</b>D<b>LY</b>E<b>K</b>L<b>GE</b>Y<b>GF</b>Q<b>N</b>AIL<b>VE</b>Y<b>T</b>Q<b>RA</b>F<b>Q</b>V<b>ST</b>P<b>LV</b>EA<b>AR</b>N<b>L</b>GE          W<b>L</b>K<b>CC</b>IL<b>U</b>ED<b>Q</b>RL<b>F</b>CV<b>ED</b>Y<b>L</b>SA<b>L</b>LN<b>R</b>V<b>CL</b>LE<b>KL</b>PV<b>S</b>ER<b>VT</b>K<b>CS</b>S<b>GL</b>VE<b>PP</b>F</p>

		<p>CFGALTVDEHYVFKREFKAETFTFHSDICTLPEKKEKQIKKQFALASLVKHKPRGAT          ASQLRTVMDDFPAQFLDTCKKADNVTCESTECFNLVTRKMDALAGGGGSGGGGS  <u>GGGGSAGAIQMTSPSSLSASVGDVRTITCRASQYHDGSSAAWYQQKPGKCPKLL</u>  <b>IYGASYLYSGVPSRFSGSRSGTDFTLTITSSLPEDFATYYCQQSSYSLITFGQG</b>  <b>TKVEIKGTTAASGSSGGSSSGAEVQLVESDGGLVQPGGSLRLSCAASGFNLSYY</b>  <b>GMHWVRQAPGKGLEWVAYIASYPGYTSYADSVKGRFTISADTSKNTAYLQMNLSL</b>  <b>RAEDTAVYYCARSGYSYSPYYSWFSAGMNYWGCGALVTVSS--</b></p>
<p>165</p> <p><i>mouse SA- (Gly<sub>4</sub>Ser)<sub>3</sub>- scFv (V<sub>L</sub>- V<sub>H</sub>) CK157- ds1 (V<sub>L</sub>100<sup>Q&gt;C</sup> / V<sub>H</sub>44<sup>E&gt;C</sup>)</i></p>		<p>EAKHSELRKYNDLGEQHFRGLVLIAPFQYLQKCSYDEHAKLVQEVDFARTQV          ADESAAHCUKSLATLDFGDKLCALENIENITGELADDOCTEQEPERNECFLOHADD          NPSLPPFBKPYEALAMCTSEKAMPFTYMDKLLREVARPHFYFYAPELLLYXAKQTH          ELLTQQCAADNFEESCLTFLDGVKRELAIVSVPQPMKCSMQLTFERAEKAWAV          APLSQTFPHADFAELTKLATDILKVNHEECHDILLECADDPAELAKYMCENQAT          IGSRLQTCCKEPLLEKAKHCLSEVEMDTMFAADLPATAADFEVUQEVCHYAEARD          VFLGTFLYEYXSRPHFFYSVSLLELAKKTEATLEKTCALANUPAOTGLVLAENQ          ELVDEPKNLVETNCLLYEKLSEYQFQKELVRYTQKAPQVTFPTLVEAARNLGR          VYTKGCTLPEEQALPOVEDYLSALINPVCLLREKTFVSEHVTLCGSGFLYERSP          CFGALTVDEHYVFKREFKAETFTFHSDICTLPEKKEKQIKKQFALASLVKHKPRGAT          ASQLRTVMDDFPAQFLDTCKKADNVTCESTECFNLVTRKMDALAGGGGSGGGGS  <u>GGGGSAGDIQMTQSPSSLSASVGDVRTITCRASQSYGGVAWYQQKPGKAPKLLI</u>  <b>YSASYLYSGVPSRFSGSRSGTDFTLTITSSLPEDFATYYCQQPSHLITFGQGT</b>  <b>VEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGSNPPYYGG</b>  <b>THWVRQAPGEELEWVASIGSYPGYTDYADSVKGRFTISADTSKNTAYLQMNLSL</b>  <b>AEDTAVYYCARHYWYDATDYWGQGTLVTVSS--</b></p>
<p>166</p> <p><i>mouse SA- (Gly<sub>4</sub>Ser)<sub>3</sub>- scFv (V<sub>L</sub>- V<sub>H</sub>) CK157- ds2 (V<sub>L</sub>43<sup>A&gt;C</sup> / V<sub>H</sub>105<sup>Q&gt;C</sup>)</i></p>		<p>EAKHSELRKYNDLGEQHFRGLVLIAPFQYLQKCSYDEHAKLVQEVDFARTQV          ADESAAHCUKSLATLDFGDKLCALENIENITGELADDOCTEQEPERNECFLOHADD          NPSLPPFBKPYEALAMCTSEKAMPFTYMDKLLREVARPHFYFYAPELLLYXAKQTH          ELLTQQCAADNFEESCLTFLDGVKRELAIVSVPQPMKCSMQLTFERAEKAWAV          APLSQTFPHADFAELTKLATDILKVNHEECHDILLECADDPAELAKYMCENQAT          IGSRLQTCCKEPLLEKAKHCLSEVEMDTMFAADLPATAADFEVUQEVCHYAEARD          VFLGTFLYEYXSRPHFFYSVSLLELAKKTEATLEKTCALANUPAOTGLVLAENQ          ELVDEPKNLVETNCLLYEKLSEYQFQKELVRYTQKAPQVTFPTLVEAARNLGR          VYTKGCTLPEEQALPOVEDYLSALINPVCLLREKTFVSEHVTLCGSGFLYERSP          CFGALTVDEHYVFKREFKAETFTFHSDICTLPEKKEKQIKKQFALASLVKHKPRGAT          ASQLRTVMDDFPAQFLDTCKKADNVTCESTECFNLVTRKMDALAGGGGSGGGGS  <u>GGGGSAGDIQMTQSPSSLSASVGDVRTITCRASQSYGGVAWYQQKPGKCPKLLI</u>  <b>YSASYLYSGVPSRFSGSRSGTDFTLTITSSLPEDFATYYCQQPSHLITFGQGT</b>  <b>VEIKGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGSNPPYYGG</b>  <b>THWVRQAPGEELEWVASIGSYPGYTDYADSVKGRFTISADTSKNTAYLQMNLSL</b>  <b>AEDTAVYYCARHYWYDATDYWGQGTLVTVSS--</b></p>
<p>167</p> <p><i>mouse SA- (Gly<sub>4</sub>Ser)-V<sub>L</sub> CK157</i></p>		<p>EAKHSELRKYNDLGEQHFRGLVLIAPFQYLQKCSYDEHAKLVQEVDFARTQV          ADESAAHCUKSLATLDFGDKLCALENIENITGELADDOCTEQEPERNECFLOHADD          NPSLPPFBKPYEALAMCTSEKAMPFTYMDKLLREVARPHFYFYAPELLLYXAKQTH          ELLTQQCAADNFEESCLTFLDGVKRELAIVSVPQPMKCSMQLTFERAEKAWAV          APLSQTFPHADFAELTKLATDILKVNHEECHDILLECADDPAELAKYMCENQAT          IGSRLQTCCKEPLLEKAKHCLSEVEMDTMFAADLPATAADFEVUQEVCHYAEARD          VFLGTFLYEYXSRPHFFYSVSLLELAKKTEATLEKTCALANUPAOTGLVLAENQ</p>

		<p>PLVGGPKHIVFTNCDLYEKLGCEYGFQNAILLVRYTQKAPQVSTPCLVEAARNLGR  WVTKGCTEAVEDQRLFCVEDYLSAIIENRYVCLLEKTEPVBREVTKQSSSLVERRF  QPSALIVY-ETVYVKEPKAETFTTPHSDLOTILPEREKQIKKQTAIAELVGRPKYAT  AEQLKTVMDDFRQFLDTCCKAARDPTCFSTEGPFLVTRFKDALL <u>GGGSGGGGS</u>  <u>GGGSA</u> <b>DIQMTQSPSSLSASVGDRTITCRASQSYGGVAVYQQKPKAPKLLI</b>  <b>YSASYLSGVPSRFRSGSRSGTDFTLTISLQPEDFATYYCQQPSHLITFGQGT</b>  <b>VEIK</b>---</p>
<p>168</p>	<p><i>mouse SA- (Gly<sub>4</sub>Ser)- V<sub>II</sub> CK157</i></p>	<p>EAHNSETARRZSDIAGEORFYSIVLITAFSQYLQKCSYDEHAKLVQEVDFPACTV  ADESAANQDPSLWTLKGGKALAIENRYVCLLEKTEPVBREVTKQSSSLVERRF  NPSLPPFEPPEAAMCTSPFRENFTTFMGRYLHEVARNRPYFYAPELLYYAEQYN  EILTQCCREADKESCLTPKLPGVNEKALVSVVRQRNACSSIAQKFGEPAPKAWAY  APLSQTFPHADFAELTKLATAIDLIVNKECCHCHLLECAADPAELAKYMCENQAT  ISSFLQTCODNEFLKKAHCLSEVERDTPADLPAALAADEVEDQEVCKNYAEAKD  VELSTYLYEYSSNRPDYSVSDILRLAKRYEALILEQALANRPFAUYQVLAAPQ  PLVEEPEHIVKTNCDLYEKLGCEYGFQNAILLVRYTQKAPQVSTPCLVEAARNLGR  VWTKGCTEAVEDQRLFCVEDYLSAIIENRYVCLLEKTEPVBREVTKQSSSLVERRF  CFSAITVDEETVYVKEPKAETFTTPHSDLOTILPEREKQIKKQTAIAELVGRPKYAT  AEQLKTVMDDFRQFLDTCCKAARDPTCFSTEGPFLVTRFKDALL <u>GGGSGGGGS</u>  <u>GGGSA</u> <b>AEVQLVESGGGLVQPGGSLRLSCAASGSNPYYGGTHWVRQAPGEEL</b>  <b>EWVASIGSYPGYTDYADSVKGRFTISADTSKNTAYLQMNLSRAEDTAVYYCARH</b>  <b>YYWDATDYWGQGTTLVTVSS</b>---</p>
<p>169</p>	<p><i>mouse SA- (Gly<sub>4</sub>Ser)<sub>3</sub>- scFv (V<sub>L</sub>- V<sub>H</sub>) CK129- ds1 (V<sub>L</sub>100<sup>Q&gt;C</sup> / V<sub>H</sub>44<sup>G&gt;C</sup>)</i></p>	<p>EAHNSETARRZSDIAGEORFYSIVLITAFSQYLQKCSYDEHAKLVQEVDFPACTV  ADESAANQDPSLWTLKGGKALAIENRYVCLLEKTEPVBREVTKQSSSLVERRF  NPSLPPFEPPEAAMCTSPFRENFTTFMGRYLHEVARNRPYFYAPELLYYAEQYN  EILTQCCREADKESCLTPKLPGVNEKALVSVVRQRNACSSIAQKFGEPAPKAWAY  AKLSQTFPHADFAELTKLATAIDLIVNKECCHCHLLECAADPAELAKYMCENQAT  ISSFLQTCODNEFLKKAHCLSEVERDTPADLPAALAADEVEDQEVCKNYAEAKD  VELSTYLYEYSSNRPDYSVSDILRLAKRYEALILEQALANRPFAUYQVLAAPQ  PLVEEPEHIVKTNCDLYEKLGCEYGFQNAILLVRYTQKAPQVSTPCLVEAARNLGR  WVTKGCTEAVEDQRLFCVEDYLSAIIENRYVCLLEKTEPVBREVTKQSSSLVERRF  CFSELTVDDETIVYVKEPKAETFTTPHSDLOTILPEREKQIKKQTAIAELVGRPKYAT  AEQLKTVMDDFRQFLDTCCKAARDPTCFSTEGPFLVTRFKDALL <u>GGGSGGGGS</u>  <u>GGGSA</u> <b>DIQMTQSPSPLSASVGDRTITCRASQYGGYVAVYQQKPKAPKLLI</b>  <b>YGASLLYSGVPSRFRSGGRSGTDFTLTISLQPEDFATYYCQRGHALITFGCGTK</b>  <b>VEIEGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGFNISSYGS</b>  <b>MHWVRQAPGKCLEWVASIYPYSSSTYYADSVKGRFTISADTSKNTAYLQMNLSR</b>  <b>AEDTAVYYCARGYPWYAYSYFALDYWGQGTTLVTVSS</b>---</p>
<p>170</p>	<p><i>mouse SA- (Gly<sub>4</sub>Ser)<sub>3</sub>- scFv (V<sub>L</sub>- V<sub>H</sub>) CK129- ds2 (V<sub>L</sub>43<sup>A&gt;C</sup> / V<sub>H</sub>105<sup>Q&gt;C</sup>)</i></p>	<p>EAHNSETARRZSDIAGEORFYSIVLITAFSQYLQKCSYDEHAKLVQEVDFPACTV  ADESAANQDPSLWTLKGGKALAIENRYVCLLEKTEPVBREVTKQSSSLVERRF  NPSLPPFEPPEAAMCTSPFRENFTTFMGRYLHEVARNRPYFYAPELLYYAEQYN  EILTQCCREADKESCLTPKLPGVNEKALVSVVRQRNACSSIAQKFGEPAPKAWAY  AKLSQTFPHADFAELTKLATAIDLIVNKECCHCHLLECAADPAELAKYMCENQAT  ISSFLQTCODNEFLKKAHCLSEVERDTPADLPAALAADEVEDQEVCKNYAEAKD  VELSTYLYEYSSNRPDYSVSDILRLAKRYEALILEQALANRPFAUYQVLAAPQ  PLVEEPEHIVKTNCDLYEKLGCEYGFQNAILLVRYTQKAPQVSTPCLVEAARNLGR  WVTKGCTEAVEDQRLFCVEDYLSAIIENRYVCLLEKTEPVBREVTKQSSSLVERRF</p>

		<p>CFGSAITVDEHYVFKKFAETFTFHSDICTLPEKEKQIKKQITALAGLVKHPKAT                  AEQLRTVMDDFAQFLDTCCKAADKDTCFSTEGPNLVTRCKDALA <u>GGGSGCGGGS</u>  <u>GGGSAADIQMTQSPSPLSASVGDVVTITCRASQYGGYVAVYQKPKGPKLLI</u>                  YGASLLYSGVPSRFRSGGRSGTDFTLTISLQPEDFATYYCQRGHALITFGQGTK                  VEIEGTTAASGSSGGSSSGAEVQLVESGGGLVQPGGSLRLSCAASGFNISSYGS                  MHWVRQAPGKGLEWVASIYPYSSSTYYADSVKGRFTISADTSKNTAYLQMNLSL                  AEDTAVYYCARGYGPWYAYSYFALDYWGQGLVTVSS--</p>
171	Human serum albumin (mature) (HSA)	<p>DAHKSEVAHRFKDLGEENFKALVLI AFAQYLQCCPFEDHVKLVNEVTEFAKTCV                  ADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDD                  NPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIAARRHPYFYAPELLFFAKRYK                  AAFTECCQAADKAACLLPKLDELDRDEGKASSAKQRLKCASLQKFGERAFKAWAV                  ARLSQRFPAEFAEVSKLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDS                  ISSKLEKCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKD                  VFLGMFLYEYARRHPDYSVLLRLAKTYETTLEKCCAAADPHECYAKVDFEFK                  PLVEEPQNLIKONCELFEQLGEYKFNALLVRYTKKVPQVSTPTLVEVSRNLGK                  VGSKCKHPKAEKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRP                  CFSALVDETYVPKEFNAETFTFHADICTLSEKERQIKKQITALVELVKHKPKAT                  KEQLKAVMDDFAAFVEKCKKADDKETCFAEEGKKLVAASQAALGL</p>
172	Human IgG1 constant region (amino acid sequence)	<p>ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW                  NSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYIC                  NVNHKPSNTKVDKKEPKSCDKTHTCPPCPAPELLGGPSVF                  LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG                  EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC                  KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQV                  SLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSF                  FLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSP                  GK</p>
173	Mouse serum albumin	<p>EAHKSEIAHRYNDLGEQHFKGLVLI AFSQYLQKCSYDEHAKLVQEVTDFAKTCV                  ADESAANCDKSLHTLFGDKLCAIPNLRNYGELADCCTKQEPERNECFLQHKDD                  NPSLPPFERPEAEAMCTSFKENPTTFMGHYLHEVARRHPYFYAPELLLYAEQYN                  EILTQCCAADKESCLTPKLDGVKEKALVSVRQRMKCSSMQKFGERAFKAWAV                  ARLSQTFPNADFAEITKLATDLTKVNKECCHGDLLECADDRADLAKYMCENQAT                  ISSKLQTCCKDPLLKKAHCLSEVEHDTMPADLPAIAADFVEDQEVCKNYAEAKD                  VFLGTFLYEYSRRHPDYSVSLRLAKKYEATLEKCCAEANPPACYGTVLAEFQ                  PLVEEPKNLVKTNCDLYEKLGEYGFQNAILVRYTQKAPQVSTPTLVEAARNLGR                  VGTKCCTLPEDQRLPCVEDYLSAILNRVCLLHEKTPVSEHVTKCCSGSLVERRP                  CFSALVDETYVPKEFNAETFTFHSDICTLPEKEKQIKKQITALAELVKHKPKAT                  AEQLKTVMDDFAQFLDTCCKAADKDTCFSTEGPNLVTRCKDALA</p>
174	Human IgG1 Fc domain (amino acid sequence)	<p>EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE                  VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN                  STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK                  AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE                  WESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQG                  NVFCSSVMHEALHNHYTQKSLSLSPGK</p>
175	HSA domain I	<p>DAHKSEVAHRFKDLGEENFKALVLI AFAQYLQCCPFEDHVKLVNEVTEFAKTCV                  ADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDD                  NPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIAARRHPYFYAPELLFFAKRYK                  AAFTECCQAADKAACLLPKLDELDRDEGKASSAKQR</p>
176	HSA domain II	<p>GKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPAEFAEVSKLVTDLTKVH                  TECCHGDLLECADDRADLAKYICENQDSISSKLEKCEKPLLEKSHCIAEVEND                  EMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVLLRLA</p>



		KTYETTLEKCCAAADPHECYAKVFDEFKPLVEEPQ
177	HSA domain III	NLIKQNCLELFEQLGEYKFNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCCK HPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEV DETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAV MDDFAAFVEKCKADDKETCFAEEGKKLVAASQAALGL
178	(Gly <sub>4</sub> Ser) <sub>3</sub> linker domain	GGGGSGGGSGGGGS
179	Secretory leader sequence	MDMRVPAQLLGLLLWLPGARC
180	FLAG tag	DYKDDDDK
181	Polyhistidine (6-His)	HHHHHH
182	Hemagglutinin	YPYDVPDYA

## SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 209

<210> SEQ ID NO 1  
 <211> LENGTH: 127  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK138 VH amino acid sequence

<400> SEQUENCE: 1

Glu Val Gln Leu Val Glu Ser Asp Gly Gly Leu Val Gln Pro Gly Gly  
 1 5 10 15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Leu Ser Tyr Tyr  
 20 25 30  
 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
 35 40 45  
 Ala Tyr Ile Ala Ser Tyr Pro Gly Tyr Thr Ser Tyr Ala Asp Ser Val  
 50 55 60  
 Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr  
 65 70 75 80  
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys  
 85 90 95  
 Ala Arg Ser Gly Tyr Ser Tyr Ser Pro Tyr Tyr Ser Trp Phe Ser Ala  
 100 105 110  
 Gly Met Asn Tyr Trp Gly Gln Gly Ala Leu Val Thr Val Ser Ser  
 115 120 125

<210> SEQ ID NO 2  
 <211> LENGTH: 107  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK138 VL amino acid sequence

<400> SEQUENCE: 2

Ala Ile Gln Met Thr Arg Ser Pro Ser Ser Leu Ser Ala Ser Val Gly  
 1 5 10 15  
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr His Asp Gly Ser  
 20 25 30  
 Ala Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile  
 35 40 45  
 Tyr Gly Ala Ser Tyr Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly  
 50 55 60  
 Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro  
 65 70 75 80  
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ser Tyr Ser Leu Ile  
 85 90 95  
 Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
 100 105

<210> SEQ ID NO 3  
 <211> LENGTH: 381  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK138 VH nucleic acid sequence

<400> SEQUENCE: 3

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gaggttcagc tggtaggagtc tgacgggtgc ctggtgcagc cagggggctc actccgtttg      60
tcctgtgcag cttctggcct caacctctct tactacggta tgcactgggt gcgtcaggcc      120
ccgggtaagg gcctggaatg ggttgcatatc attgcttctt accctggcta cacttcttat      180
gccgatagcg tcaagggcgc tttcactata agcgcagaca catccaaaaa cacagcctac      240
ctacaaatga acagcttaag agctgaggac actgcctctt actattgtgc tcgctctggt      300
tacagttact ctccgtatta ttcttggttc tctgctgcta tgaactactg gggccaagga      360
gccctggtea ccgtctcttc g                                     381

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<210> SEQ ID NO 4
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: CK138 VL nucleic acid sequence

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<400> SEQUENCE: 4

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gctatccaga tgaccgggtc ccgagctcc ctgtccgcct ctgtgggaga tagggtcacc      60
atcacctgcc gtgccagtca gtaccacgac ggttctgcag cctggatca acagaaacca      120
ggaaaagctc cgaagcttct gatttacggt gcactctacc tctactctgg agtcccttcc      180
cgcttctctg gtacgcgttc cgggacggat ttcactctga ccatcagcag tetgcagccg      240
gaagacttgc caacttatta ctgtcagcaa tcttcttatt ctctgatcac gttcggacag      300
ggtaccaagg tggagatcaa a                                     321

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<210> SEQ ID NO 5
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: CK138 VH CDR1

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<400> SEQUENCE: 5

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Asn Leu Ser Tyr Tyr Gly Met His
1           5

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<210> SEQ ID NO 6
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: CK138 VH CDR2

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<400> SEQUENCE: 6

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Ala Tyr Ile Ala Ser Tyr Pro Gly Tyr Thr Ser Tyr
1           5           10

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<210> SEQ ID NO 7
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: CK138 VH CDR3

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<400> SEQUENCE: 7

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Arg Ser Gly Tyr Ser Tyr Ser Pro Tyr Tyr Ser Trp Phe Ser Ala Gly
1           5           10           15

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Met Asn

<210> SEQ ID NO 8  
 <211> LENGTH: 7  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK138 VL CDR1

&lt;400&gt; SEQUENCE: 8

Gln Tyr His Asp Gly Ser Ala  
 1 5

<210> SEQ ID NO 9  
 <211> LENGTH: 6  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK138 VL CDR2

&lt;400&gt; SEQUENCE: 9

Tyr Gly Ala Ser Tyr Leu  
 1 5

<210> SEQ ID NO 10  
 <211> LENGTH: 8  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK138 VL CDR3

&lt;400&gt; SEQUENCE: 10

Gln Ser Ser Tyr Ser Leu Ile Thr  
 1 5

<210> SEQ ID NO 11  
 <211> LENGTH: 120  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK157 VH amino acid sequence

&lt;400&gt; SEQUENCE: 11

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Asn Pro Tyr Tyr Tyr  
 20 25 30

Gly Gly Thr His Trp Val Arg Gln Ala Pro Gly Glu Glu Leu Glu Trp  
 35 40 45

Val Ala Ser Ile Gly Ser Tyr Pro Gly Tyr Thr Asp Tyr Ala Asp Ser  
 50 55 60

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala  
 65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr  
 85 90 95

Cys Ala Arg His Tyr Tyr Trp Tyr Asp Ala Thr Asp Tyr Trp Gly Gln  
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser  
 115 120

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<210> SEQ ID NO 12  
 <211> LENGTH: 105  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK157 VL amino acid sequence

<400> SEQUENCE: 12

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly  
 1 5 10 15  
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Tyr Gly Gly Val  
 20 25 30  
 Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr  
 35 40 45  
 Ser Ala Ser Tyr Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser  
 50 55 60  
 Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu  
 65 70 75 80  
 Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Pro Ser His Leu Ile Thr Phe  
 85 90 95  
 Gly Gln Gly Thr Glu Val Glu Ile Lys  
 100 105

<210> SEQ ID NO 13  
 <211> LENGTH: 360  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK157 VH nucleic acid sequence

<400> SEQUENCE: 13

gaggttcagc tgggtgagtc tggcgggtgc ctggtgcagc cagggggctc actccgtttg 60  
 tcctgtgcag cttctggctc caaccctac tactacgggtg gtacgcactg ggtgcgtcag 120  
 gccccgggtg aggagctgga atgggttgca tctattggtt cttaccctgg ctacactgac 180  
 tatgccgata gcgtcaaggg ccgtttcact ataagcgcag acacatccaa aaacacagcc 240  
 tacctacaaa tgaacagctt aagagctgag gacactgccg tctattattg tgctcgccat 300  
 tactactggt acgatgctac tgactactgg ggtcaaggaa ccctgggtcac cgtctctctc 360

<210> SEQ ID NO 14  
 <211> LENGTH: 315  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK157 VL nucleic acid sequence

<400> SEQUENCE: 14

gatatccaga tgaccagtc cccgagctcc ctgtccgcct ctgtgggcga tagggtcacc 60  
 atcacctgcc gtgccagtc gtcttacgggt ggtgtagcct ggtatcaaca gaaaccagga 120  
 aaagccccga agcttctgat ttactctgca tcttaacctct actctggagt cccttctctc 180  
 ttctctggta gccgttcogg gacggatttc actctgacca tcagcagtct gcagccggaa 240  
 gacttcgcaa cttattactg tcagcaacca tctcatctga tcacgttcgg acaggggtacc 300  
 gaggtggaga tcaaa 315

<210> SEQ ID NO 15

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<211> LENGTH: 9  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: CK157 VH CDR1

<400> SEQUENCE: 15

Asn Pro Tyr Tyr Tyr Gly Gly Thr His  
1 5

<210> SEQ ID NO 16  
<211> LENGTH: 12  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: CK157 VH CDR2

<400> SEQUENCE: 16

Ala Ser Ile Gly Ser Tyr Pro Gly Tyr Thr Asp Tyr  
1 5 10

<210> SEQ ID NO 17  
<211> LENGTH: 10  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: CK157 VH CDR3

<400> SEQUENCE: 17

Arg His Tyr Tyr Trp Tyr Asp Ala Thr Asp  
1 5 10

<210> SEQ ID NO 18  
<211> LENGTH: 6  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: CK157 VL CDR1

<400> SEQUENCE: 18

Gln Ser Tyr Gly Gly Val  
1 5

<210> SEQ ID NO 19  
<211> LENGTH: 6  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: CK157 VL CDR2

<400> SEQUENCE: 19

Tyr Ser Ala Ser Tyr Leu  
1 5

<210> SEQ ID NO 20  
<211> LENGTH: 7  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: CK157 VL CDR3

<400> SEQUENCE: 20

Gln Pro Ser His Leu Ile Thr  
1 5

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<210> SEQ ID NO 21  
 <211> LENGTH: 125  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK129 VH amino acid sequence

<400> SEQUENCE: 21

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
 1 5 10 15  
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser Ser Tyr  
 20 25 30  
 Gly Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp  
 35 40 45  
 Val Ala Ser Ile Tyr Pro Tyr Ser Ser Ser Thr Tyr Tyr Ala Asp Ser  
 50 55 60  
 Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala  
 65 70 75 80  
 Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr  
 85 90 95  
 Cys Ala Arg Gly Tyr Gly Pro Trp Tyr Ala Tyr Ser Tyr Phe Ala Leu  
 100 105 110  
 Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
 115 120 125

<210> SEQ ID NO 22  
 <211> LENGTH: 105  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK129 VL amino acid sequence

<400> SEQUENCE: 22

Asp Ile Gln Met Thr Gln Ser Pro Ser Pro Leu Ser Ala Ser Val Gly  
 1 5 10 15  
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Gly Gly Tyr Val  
 20 25 30  
 Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr  
 35 40 45  
 Gly Ala Ser Leu Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Gly  
 50 55 60  
 Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu  
 65 70 75 80  
 Asp Phe Ala Thr Tyr Tyr Cys Gln Arg Gly His Ala Leu Ile Thr Phe  
 85 90 95  
 Gly Gln Gly Thr Lys Val Glu Ile Glu  
 100 105

<210> SEQ ID NO 23  
 <211> LENGTH: 375  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK129 VH nucleic acid sequence

<400> SEQUENCE: 23

gaggttcagc tgggtgagtc tggcgggtggc ctggtgcagc cagggggctc actccgttta 60

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tctctgtcag cttctggcct caacatctct tcttacggtt ctatgcactg ggtgcgtcag   120
gccccgggta agggcctgga atgggttgca tctatttacc cttactctag ctctacttac   180
tatgccgata gcgtcaaggg ccgtttcact ataagcgag acacatccaa aaacacagcc   240
tacctacaaa tgaacagcct aagagctgag gacactgccg tctattattg tgctcgtggt   300
tacggtcctg ggtacgctta ctcttacttc gctttggact actgggggtca aggaacctg   360
gtcaccgtct cctcg   375

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<210> SEQ ID NO 24
<211> LENGTH: 315
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: CK129 VL nucleic acid sequence

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<400> SEQUENCE: 24

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gatatccaga tgaccagtc cccgagcccc ctgtccgcct ctgtgggcca tagggtcacc   60
atcacctgcc gtgccagtea gtacgggtgt tacgtagcct ggtatcaaca gaaaccagga   120
aaagctccga agcttctgat ttacgggtgca tcccttctct actctggagt cccttctcgc   180
ttctctggtg gccgttccgg gacggatttc actctgacca tcagcagtct gcagccggaa   240
gacttcgcaa cttattactg tcagcgaggt catgctctga tcacgttcgg acaggggtacc   300
aaggtggaga tcgaa   315

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<210> SEQ ID NO 25
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: CK129 VH CDR1

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<400> SEQUENCE: 25

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Asn Ile Ser Ser Tyr Gly Ser Met His
1           5

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<210> SEQ ID NO 26
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: CK129 VH CDR2

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<400> SEQUENCE: 26

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Ala Ser Ile Tyr Pro Tyr Ser Ser Ser Thr Tyr Tyr
1           5           10

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<210> SEQ ID NO 27
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: CK129 VH CDR3

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<400> SEQUENCE: 27

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Arg Gly Tyr Gly Pro Trp Tyr Ala Tyr Ser Tyr Phe Ala Leu Asp
1           5           10           15

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<210> SEQ ID NO 28

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<211> LENGTH: 6  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK129 VL CDR1

<400> SEQUENCE: 28

Gln Tyr Gly Gly Tyr Val  
 1 5

<210> SEQ ID NO 29  
 <211> LENGTH: 7  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK129 VL CDR2

<400> SEQUENCE: 29

Tyr Gly Ala Ser Leu Leu Tyr  
 1 5

<210> SEQ ID NO 30  
 <211> LENGTH: 7  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: CK129 VL CDR3

<400> SEQUENCE: 30

Arg Gly His Ala Leu Ile Thr  
 1 5

<210> SEQ ID NO 31  
 <211> LENGTH: 1104  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic:  
 gWiz-LS-Fc (mIgG2)-His6-linker-TEV-hCXCL138-107-G2-AviTag

<400> SEQUENCE: 31

atgaggggtcc cgcctcagct cctgggggtc ctgctgctct ggctcccagg tgcacgatgt	60
gagcccagag tgcccataac acagaacccc tgtcctccac tcaaagagtg tccccatgc	120
gcagctccag acctcttggg tggaccatcc gtcttcatct tccctccaaa gatcaaggat	180
gtactcatga tctccctgag ccccatggtc acatgtgtgg tgggtgatgt gagcgaggat	240
gaccagacg tccagatcag ctgggtttgtg aacaacgtgg aagtacacac agctcagaca	300
caaacccata gagaggatta caacagtact ctccgggttg tcaagtgcct ccccatccag	360
caccaggact ggatgagtgg caaggagttc aaatgcaagg tcaacaacag agccctccca	420
tccccatcg agaaaacat ctcaaaaccc agagggccag taagagctcc acaggtatat	480
gtcttgctc caccagcaga agagatgact aagaaagagt tcagttctgac ctgcatgatc	540
acaggcttct tacctgcca aattgctgtg gactggacca gcaatgggag tacagagcaa	600
aactacaaga acaccgcaac agtccctggac tctgatggtt cttacttcat gtacagcaag	660
ctcagagtac aaaagagcac ttgggaaaga ggaagtcttt tcgcctgctc agtgggtccac	720
gagggctctgc acaatcacct tacgactaag accatctccc ggtctctggg taaacacat	780
caccatcatc actcttctgg cgtggatctg ggtaccgaga acctgtactt ccaagccacc	840

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gagctgagat gccagtgcct gcagaccctg cagggcatcc accccaagaa catccagagc 900
gtgaacctga agtcccctgg cccccactgc gccagaccg aagtgatcgc caccctgaag 960
aacggccgga aggctgcct gaaccccgcc agccccatcg tgaagaaaa catcgagaag 1020
atgctgaaca gcgacaagag caacggcgga gccctgaacg acatcttcga ggcccagaaa 1080
atcgagtggc acgagtgatg ataa 1104

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<210> SEQ ID NO 32
<211> LENGTH: 1110
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic:
      gWiz-LS-Fc (mIgG2) -His6-linker-TEV-hCXCL543-114-G2-AviTag

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<400> SEQUENCE: 32
atgaggggtcc cgcctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60
gagcccagag tgcccataac acagaacccc tgtcctccac tcaaagagtg tccccatgc 120
gcagctccag acctcttggg tggaccatcc gtcttcatct tccctccaaa gatcaaggat 180
gtactcatga tctccctgag ccccatggtc acatgtgtgg tgggtgatgt gagcgaggat 240
gaccagacg tccagatcag ctggtttgtg aacaacgtgg aagtacacac agctcagaca 300
caaacccata gagaggatta caacagtact ctccgggtgg tcagtgcctt ccccatccag 360
caccaggact ggatgagtgg caaggagttc aaatgcaagg tcaacaacag agccctccca 420
tccccatcg agaaaacccat ctcaaacccc agagggccag taagagctcc acaggtatat 480
gtcttgcttc caccagcaga agagatgact aagaaagagt tcagtctgac ctgcatgatc 540
acaggcttct tacctgccga aattgctgtg gactggacca gcaatgggcg tacagagcaa 600
aactacaaga acaccgcaac agtccctggac tctgatggtt cttacttcat gtacagcaag 660
ctcagagtac aaaagagcac ttgggaaaga ggaagtcttt tcgctgctc agtgggtccac 720
gaggtcttgc acaatcacct tacgactaag accatctccc ggtctctggg taaacacccat 780
caccatcatc actcttctgg cgtggatctg ggtaccgaga acctgtactt ccaagtgtctg 840
cgcgagctga gatgcgtgtg cctgcagacc acccagggcg tgcaccccaa gatgatcagc 900
aacctccagg tgttcccoat cgccccccag tgcagcaagg tggaaagtgg ggccagcctg 960
aagaacggca aagagatctg cctggacccc gagggcccat tcctgaagaa agtgateccag 1020
aagatcctgg acggcggcaa caaagagaac ggccggaggcc tgaacgacat cttcgaggcc 1080
cagaaaaatcg agtggcacga gtgatgataa 1110

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<210> SEQ ID NO 33
<211> LENGTH: 1107
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic:
      gWiz-LS-Fc (mIgG2) -His6-linker-TEV-hCXCL829-99-G2-AviTag

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<400> SEQUENCE: 33
atgaggggtcc cgcctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60
gagcccagag tgcccataac acagaacccc tgtcctccac tcaaagagtg tccccatgc 120
gcagctccag acctcttggg tggaccatcc gtcttcatct tccctccaaa gatcaaggat 180

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gtactcatga tctccctgag ccccatggtc acatgtgtgg tggaggatgt gagcgaggat 240
gaccagagcg tccagatcag ctggtttggg aacaacgtgg aagtacacac agctcagaca 300
caaaccata gagaggatta caacagtact ctccgggtgg tcagtgcctt ccccatccag 360
caccaggact ggatgagtgg caaggagttc aaatgcaagg tcaacaacag agcctccca 420
tccccatcg agaaaacat ctcaaaacc agagggccag taagagctcc acaggtatat 480
gtcttgcttc caccagcaga agagatgact aagaagagt tcagtctgac ctgcatgatc 540
acaggcttct tacctgcoga aattgctgtg gactggacca gcaatgggag tacagagcaa 600
aactacaaga acaccgcaac agtccctggac tctgatggtt cttacttcat gtacagcaag 660
ctcagagtac aaaagagcac ttgggaaaga ggaagtcttt tcgcctgctc agtggctccac 720
gaggtctctg acaatcacct tacgactaag accatctccc ggtctctggg taaacacat 780
caccatcatc actcttctgg cgtggatctg ggtaccgaga acctgtactt ccaagccaaa 840
gaactgcggt gccagtgcct caagacctac agcaagcctt tccaccccaa gttcatcaaa 900
gaactgagag tgatcgagag cggccctcac tgcgccaaca ccgagatcat cgtgaagctg 960
agcgacggca gagagctgtg cctggacccc aaagaaaact ggggtgcagcg ggtggaggaa 1020
aagttcttga agcgggcccga gaacagcggc ggaggcctga acgacatctt cgaggcccag 1080
aaaatcgagt ggcacgagtg atgataa 1107

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&lt;210&gt; SEQ ID NO 34

&lt;211&gt; LENGTH: 1101

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic:

gWiz-LS-Fc(mIgG2)-His6-linker-TEV-mCXCL128-96-G2-AviTag

&lt;400&gt; SEQUENCE: 34

```

atgaggggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60
gagcccagag tgcccataac acagaacccc tgcctccac tcaagagtg tccccatgc 120
gcagctccag acctcttggg tggaccatcc gtcttcatct tccctccaaa gatcaaggat 180
gtactcatga tctccctgag ccccatggtc acatgtgtgg tggaggatgt gagcgaggat 240
gaccagagcg tccagatcag ctggtttggg aacaacgtgg aagtacacac agctcagaca 300
caaaccata gagaggatta caacagtact ctccgggtgg tcagtgcctt ccccatccag 360
caccaggact ggatgagtgg caaggagttc aaatgcaagg tcaacaacag agcctccca 420
tccccatcg agaaaacat ctcaaaacc agagggccag taagagctcc acaggtatat 480
gtcttgcttc caccagcaga agagatgact aagaagagt tcagtctgac ctgcatgatc 540
acaggcttct tacctgcoga aattgctgtg gactggacca gcaatgggag tacagagcaa 600
aactacaaga acaccgcaac agtccctggac tctgatggtt cttacttcat gtacagcaag 660
ctcagagtac aaaagagcac ttgggaaaga ggaagtcttt tcgcctgctc agtggctccac 720
gaggtctctg acaatcacct tacgactaag accatctccc ggtctctggg taaacacat 780
caccatcatc actcttctgg cgtggatctg ggtaccgaga acctgtactt ccaagccaac 840
gagctgcggt gccagtgcct gcagacctg gccggcatcc acctgaagaa catccagagc 900
ctgaaggtgc tgcccagcgg cctcactgc acccagaccg aagtgatcgc caccctgaag 960
aacggcagag aggcctgctt ggatcccag gccccctgg tgcagaaaa cgtgcagaaa 1020

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 atgctgaagg gcgtgcccaa gggcggaggc ctgaacgaca tcttcgaggc ccagaaaatc 1080

gagtggcaag agtgatgata a 1101

&lt;210&gt; SEQ ID NO 35

&lt;211&gt; LENGTH: 1104

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic:

gWiz-LS-Fc(mIgG2)-His6-linker-TEV-mCXCL231-100-G2-AviTag

&lt;400&gt; SEQUENCE: 35

atgaggggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60

gagcccagag tgcccataac acagaacccc tgtcctccac tcaaagagtg tccccatgc 120

gcagctccag acctcttggg tggaccatcc gtcttcatct tccctccaaa gatcaaggat 180

gtactcatga tctccctgag ccccatggtc acatgtgtgg tgggtgatgt gagcgaggat 240

gaccagaag tccagatcag ctggtttgtg aacaacgtgg aagtacacac agctcagaca 300

caaaccata gagaggatta caacagtact ctccgggtgg tcagtgcctt ccccatccag 360

caccaggact ggatgagtg caaggagtcc aatgcaagg tcaacaacag agccctccca 420

tccccatcg agaaaacccat ctcaaaaccc agagggccag taagagctcc acaggtatat 480

gtcttgctc caccagcaga agagatgact aagaaagagt tcagtctgac ctgcatgatc 540

acaggctctt tacctgcca aattgctgtg gactggacca gcaatgggag tacagagcaa 600

aactacaaga acaccgcaac agtccctggac tctgatggtt cttacttcat gtacagcaag 660

ctcagagtac aaaagagcac ttgggaaaga ggaagtcttt tcgctgctc agtgggccac 720

gagggctctg acaatcaact tacgactaag acctctccc ggtctctggg taaacaccat 780

caccatcatc actcttctgg cgtggatctg ggtaccgaga acctgtactt ccaagccagc 840

gagctgcggt gccagtgctt gaaaaccctg ccccggtggg acttcaagaa catccagagc 900

ctgagcgtga cccccctgg cctcactgt gccagaccg aagtgatcgc caccctgaag 960

ggcggccaga aagtgtgctt ggaccccgag gccccctgg tgcagaagat catccagaag 1020

atcctgaaca agggcaaggc caacggcgga ggcctgaacg acatcttcca ggcccagaaa 1080

atcgagtggc acgagtgatg ataa 1104

&lt;210&gt; SEQ ID NO 36

&lt;211&gt; LENGTH: 1107

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic:

gWiz-LS-Fc(mIgG2)-His6-linker-TEV-mCXCL548-118-G2-AviTag

&lt;400&gt; SEQUENCE: 36

atgaggggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60

gagcccagag tgcccataac acagaacccc tgtcctccac tcaaagagtg tccccatgc 120

gcagctccag acctcttggg tggaccatcc gtcttcatct tccctccaaa gatcaaggat 180

gtactcatga tctccctgag ccccatggtc acatgtgtgg tgggtgatgt gagcgaggat 240

gaccagaag tccagatcag ctggtttgtg aacaacgtgg aagtacacac agctcagaca 300

caaaccata gagaggatta caacagtact ctccgggtgg tcagtgcctt ccccatccag 360

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caccaggact ggatgagtgg caaggagttc aaatgcaagg tcaacaacag agcctcccca 420
tcccccatcg agaaaacccat ctcaaaacc agagggccag taagagctcc acaggtatat 480
gtcttgccctc caccagcaga agagatgact aagaagagt tcagtctgac ctgcatgatc 540
acaggcttct tacctgccga aattgtgtg gactggacca gcaatgggcg tacagagcaa 600
aactacaaga acaccgcaac agtccctggac tctgatggtt cttacttcat gtacagcaag 660
ctcagagtac aaaagagcac ttgggaaaga ggaagtcttt tcgcctgctc agtgggccac 720
gagggctctgc acaatcaoct tacgactaag accatctccc ggtctctggg taaacacccat 780
caccatcatc actcttctgg cgtggatctg ggtaccgaga acctgtactt ccaagccacc 840
gagctgagat gcgtgtgcct gaccgtgacc cccaagatca accccaagct gatcgccaac 900
ctggaagtga tccttgccgg cctcagtgc cccaccgtgg aagtgattgc caagctgaag 960
aaccagaaag aagtgtgcct ggaccccgag gccccctga tcaagaagat catccagaag 1020
atcctgggca gcgacaagaa gaaagccggc ggaggcctga acgacatctt cgaggcccgag 1080
aaaatcgagt ggcacgagtg atgataa 1107

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&lt;210&gt; SEQ ID NO 37

&lt;211&gt; LENGTH: 365

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-Fc-His6-linker-TEV-hCXCL138-107-G2-AviTag

&lt;400&gt; SEQUENCE: 37

```

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro
1           5           10           15
Gly Ala Arg Cys Glu Pro Arg Val Pro Ile Thr Gln Asn Pro Cys Pro
20          25          30
Pro Leu Lys Glu Cys Pro Pro Cys Ala Ala Pro Asp Leu Leu Gly Gly
35          40          45
Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile
50          55          60
Ser Leu Ser Pro Met Val Thr Cys Val Val Val Asp Val Ser Glu Asp
65          70          75          80
Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His
85          90          95
Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg
100         105         110
Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys
115         120         125
Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ser Pro Ile Glu
130         135         140
Lys Thr Ile Ser Lys Pro Arg Gly Pro Val Arg Ala Pro Gln Val Tyr
145         150         155         160
Val Leu Pro Pro Pro Ala Glu Glu Met Thr Lys Lys Glu Phe Ser Leu
165         170         175
Thr Cys Met Ile Thr Gly Phe Leu Pro Ala Glu Ile Ala Val Asp Trp
180         185         190
Thr Ser Asn Gly Arg Thr Glu Gln Asn Tyr Lys Asn Thr Ala Thr Val
195         200         205

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Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Gln  
 210 215 220  
 Lys Ser Thr Trp Glu Arg Gly Ser Leu Phe Ala Cys Ser Val Val His  
 225 230 235 240  
 Glu Gly Leu His Asn His Leu Thr Thr Lys Thr Ile Ser Arg Ser Leu  
 245 250 255  
 Gly Lys His His His His His Ser Ser Gly Val Asp Leu Gly Thr  
 260 265 270  
 Glu Asn Leu Tyr Phe Gln Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln  
 275 280 285  
 Thr Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys  
 290 295 300  
 Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys  
 305 310 315 320  
 Asn Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys  
 325 330 335  
 Ile Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn Gly Gly Gly Leu  
 340 345 350  
 Asn Asp Ile Phe Glu Ala Gln Lys Ile Glu Trp His Glu  
 355 360 365

&lt;210&gt; SEQ ID NO 38

&lt;211&gt; LENGTH: 367

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-Fc-His6-linker-TEV-hCXCL543-114-G2-AviTag

&lt;400&gt; SEQUENCE: 38

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro  
 1 5 10 15  
 Gly Ala Arg Cys Glu Pro Arg Val Pro Ile Thr Gln Asn Pro Cys Pro  
 20 25 30  
 Pro Leu Lys Glu Cys Pro Pro Cys Ala Ala Pro Asp Leu Leu Gly Gly  
 35 40 45  
 Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile  
 50 55 60  
 Ser Leu Ser Pro Met Val Thr Cys Val Val Val Asp Val Ser Glu Asp  
 65 70 75 80  
 Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His  
 85 90 95  
 Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg  
 100 105 110  
 Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys  
 115 120 125  
 Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ser Pro Ile Glu  
 130 135 140  
 Lys Thr Ile Ser Lys Pro Arg Gly Pro Val Arg Ala Pro Gln Val Tyr  
 145 150 155 160  
 Val Leu Pro Pro Pro Ala Glu Glu Met Thr Lys Lys Glu Phe Ser Leu  
 165 170 175  
 Thr Cys Met Ile Thr Gly Phe Leu Pro Ala Glu Ile Ala Val Asp Trp

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180					185					190					
Thr	Ser	Asn	Gly	Arg	Thr	Glu	Gln	Asn	Tyr	Lys	Asn	Thr	Ala	Thr	Val
		195					200					205			
Leu	Asp	Ser	Asp	Gly	Ser	Tyr	Phe	Met	Tyr	Ser	Lys	Leu	Arg	Val	Gln
	210					215					220				
Lys	Ser	Thr	Trp	Glu	Arg	Gly	Ser	Leu	Phe	Ala	Cys	Ser	Val	Val	His
	225					230					235				240
Glu	Gly	Leu	His	Asn	His	Leu	Thr	Thr	Lys	Thr	Ile	Ser	Arg	Ser	Leu
				245					250					255	
Gly	Lys	His	His	His	His	His	Ser	Ser	Gly	Val	Asp	Leu	Gly	Thr	
		260					265					270			
Glu	Asn	Leu	Tyr	Phe	Gln	Val	Leu	Arg	Glu	Leu	Arg	Cys	Val	Cys	Leu
		275					280					285			
Gln	Thr	Thr	Gln	Gly	Val	His	Pro	Lys	Met	Ile	Ser	Asn	Leu	Gln	Val
	290					295					300				
Phe	Ala	Ile	Gly	Pro	Gln	Cys	Ser	Lys	Val	Glu	Val	Val	Ala	Ser	Leu
	305					310					315				320
Lys	Asn	Gly	Lys	Glu	Ile	Cys	Leu	Asp	Pro	Glu	Ala	Pro	Phe	Leu	Lys
				325					330					335	
Lys	Val	Ile	Gln	Lys	Ile	Leu	Asp	Gly	Gly	Asn	Lys	Glu	Asn	Gly	Gly
			340					345					350		
Gly	Leu	Asn	Asp	Ile	Phe	Glu	Ala	Gln	Lys	Ile	Glu	Trp	His	Glu	
		355					360					365			

&lt;210&gt; SEQ ID NO 39

&lt;211&gt; LENGTH: 366

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-Fc-His6-linker-TEV-hCXCL829-99-G2-AviTag

&lt;400&gt; SEQUENCE: 39

Met	Arg	Val	Pro	Ala	Gln	Leu	Leu	Gly	Leu	Leu	Leu	Leu	Leu	Trp	Leu	Pro
1				5					10						15	
Gly	Ala	Arg	Cys	Glu	Pro	Arg	Val	Pro	Ile	Thr	Gln	Asn	Pro	Cys	Pro	
			20					25					30			
Pro	Leu	Lys	Glu	Cys	Pro	Pro	Cys	Ala	Ala	Pro	Asp	Leu	Leu	Gly	Gly	
		35					40					45				
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Lys	Ile	Lys	Asp	Val	Leu	Met	Ile	
	50					55					60					
Ser	Leu	Ser	Pro	Met	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Glu	Asp	
	65					70					75			80		
Asp	Pro	Asp	Val	Gln	Ile	Ser	Trp	Phe	Val	Asn	Asn	Val	Glu	Val	His	
				85					90					95		
Thr	Ala	Gln	Thr	Gln	Thr	His	Arg	Glu	Asp	Tyr	Asn	Ser	Thr	Leu	Arg	
		100						105					110			
Val	Val	Ser	Ala	Leu	Pro	Ile	Gln	His	Gln	Asp	Trp	Met	Ser	Gly	Lys	
			115				120					125				
Glu	Phe	Lys	Cys	Lys	Val	Asn	Asn	Arg	Ala	Leu	Pro	Ser	Pro	Ile	Glu	
	130					135					140					
Lys	Thr	Ile	Ser	Lys	Pro	Arg	Gly	Pro	Val	Arg	Ala	Pro	Gln	Val	Tyr	
	145					150					155				160	

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Val Leu Pro Pro Pro Ala Glu Glu Met Thr Lys Lys Glu Phe Ser Leu  
 165 170 175

Thr Cys Met Ile Thr Gly Phe Leu Pro Ala Glu Ile Ala Val Asp Trp  
 180 185 190

Thr Ser Asn Gly Arg Thr Glu Gln Asn Tyr Lys Asn Thr Ala Thr Val  
 195 200 205

Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Gln  
 210 215 220

Lys Ser Thr Trp Glu Arg Gly Ser Leu Phe Ala Cys Ser Val Val His  
 225 230 235 240

Glu Gly Leu His Asn His Leu Thr Thr Lys Thr Ile Ser Arg Ser Leu  
 245 250 255

Gly Lys His His His His His Ser Ser Gly Val Asp Leu Gly Thr  
 260 265 270

Glu Asn Leu Tyr Phe Gln Ala Lys Glu Leu Arg Cys Gln Cys Ile Lys  
 275 280 285

Thr Tyr Ser Lys Pro Phe His Pro Lys Phe Ile Lys Glu Leu Arg Val  
 290 295 300

Ile Glu Ser Gly Pro His Cys Ala Asn Thr Glu Ile Ile Val Lys Leu  
 305 310 315 320

Ser Asp Gly Arg Glu Leu Cys Leu Asp Pro Lys Glu Asn Trp Val Gln  
 325 330 335

Arg Val Val Glu Lys Phe Leu Lys Arg Ala Glu Asn Ser Gly Gly Gly  
 340 345 350

Leu Asn Asp Ile Phe Glu Ala Gln Lys Ile Glu Trp His Glu  
 355 360 365

<210> SEQ ID NO 40  
 <211> LENGTH: 364  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-Fc-His6-linker-TEV-mCXCL128-96-G2-AviTag

<400> SEQUENCE: 40

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro  
 1 5 10 15

Gly Ala Arg Cys Glu Pro Arg Val Pro Ile Thr Gln Asn Pro Cys Pro  
 20 25 30

Pro Leu Lys Glu Cys Pro Pro Cys Ala Ala Pro Asp Leu Leu Gly Gly  
 35 40 45

Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile  
 50 55 60

Ser Leu Ser Pro Met Val Thr Cys Val Val Val Asp Val Ser Glu Asp  
 65 70 75 80

Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His  
 85 90 95

Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg  
 100 105 110

Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys  
 115 120 125

Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ser Pro Ile Glu  
 130 135 140



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Lys Thr Ile Ser Lys Pro Arg Gly Pro Val Arg Ala Pro Gln Val Tyr  
 145 150 155 160  
 Val Leu Pro Pro Pro Ala Glu Glu Met Thr Lys Lys Glu Phe Ser Leu  
 165 170 175  
 Thr Cys Met Ile Thr Gly Phe Leu Pro Ala Glu Ile Ala Val Asp Trp  
 180 185 190  
 Thr Ser Asn Gly Arg Thr Glu Gln Asn Tyr Lys Asn Thr Ala Thr Val  
 195 200 205  
 Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Gln  
 210 215 220  
 Lys Ser Thr Trp Glu Arg Gly Ser Leu Phe Ala Cys Ser Val Val His  
 225 230 235 240  
 Glu Gly Leu His Asn His Leu Thr Thr Lys Thr Ile Ser Arg Ser Leu  
 245 250 255  
 Gly Lys His His His His His His Ser Ser Gly Val Asp Leu Gly Thr  
 260 265 270  
 Glu Asn Leu Tyr Phe Gln Ala Asn Glu Leu Arg Cys Gln Cys Leu Gln  
 275 280 285  
 Thr Met Ala Gly Ile His Leu Lys Asn Ile Gln Ser Leu Lys Val Leu  
 290 295 300  
 Pro Ser Gly Pro His Cys Thr Gln Thr Glu Val Ile Ala Thr Leu Lys  
 305 310 315 320  
 Asn Gly Arg Glu Ala Cys Leu Asp Pro Glu Ala Pro Leu Val Gln Lys  
 325 330 335  
 Ile Val Gln Lys Met Leu Lys Gly Val Pro Lys Gly Gly Gly Leu Asn  
 340 345 350  
 Asp Ile Phe Glu Ala Gln Lys Ile Glu Trp His Glu  
 355 360

&lt;210&gt; SEQ ID NO 41

&lt;211&gt; LENGTH: 365

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-Fc-His6-linker-TEV-mCXCL231-100-G2-AviTag

&lt;400&gt; SEQUENCE: 41

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro  
 1 5 10 15  
 Gly Ala Arg Cys Glu Pro Arg Val Pro Ile Thr Gln Asn Pro Cys Pro  
 20 25 30  
 Pro Leu Lys Glu Cys Pro Pro Cys Ala Ala Pro Asp Leu Leu Gly Gly  
 35 40 45  
 Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile  
 50 55 60  
 Ser Leu Ser Pro Met Val Thr Cys Val Val Val Asp Val Ser Glu Asp  
 65 70 75 80  
 Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His  
 85 90 95  
 Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg  
 100 105 110  
 Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys

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115			120			125									
Glu	Phe	Lys	Cys	Lys	Val	Asn	Asn	Arg	Ala	Leu	Pro	Ser	Pro	Ile	Glu
130						135					140				
Lys	Thr	Ile	Ser	Lys	Pro	Arg	Gly	Pro	Val	Arg	Ala	Pro	Gln	Val	Tyr
145				150						155					160
Val	Leu	Pro	Pro	Pro	Ala	Glu	Glu	Met	Thr	Lys	Lys	Glu	Phe	Ser	Leu
				165						170				175	
Thr	Cys	Met	Ile	Thr	Gly	Phe	Leu	Pro	Ala	Glu	Ile	Ala	Val	Asp	Trp
			180					185						190	
Thr	Ser	Asn	Gly	Arg	Thr	Glu	Gln	Asn	Tyr	Lys	Asn	Thr	Ala	Thr	Val
		195					200						205		
Leu	Asp	Ser	Asp	Gly	Ser	Tyr	Phe	Met	Tyr	Ser	Lys	Leu	Arg	Val	Gln
210						215					220				
Lys	Ser	Thr	Trp	Glu	Arg	Gly	Ser	Leu	Phe	Ala	Cys	Ser	Val	Val	His
225				230						235					240
Glu	Gly	Leu	His	Asn	His	Leu	Thr	Thr	Lys	Thr	Ile	Ser	Arg	Ser	Leu
			245						250					255	
Gly	Lys	His	His	His	His	His	His	Ser	Ser	Gly	Val	Asp	Leu	Gly	Thr
		260						265						270	
Glu	Asn	Leu	Tyr	Phe	Gln	Ala	Ser	Glu	Leu	Arg	Cys	Gln	Cys	Leu	Lys
		275					280					285			
Thr	Leu	Pro	Arg	Val	Asp	Phe	Lys	Asn	Ile	Gln	Ser	Leu	Ser	Val	Thr
	290					295					300				
Pro	Pro	Gly	Pro	His	Cys	Ala	Gln	Thr	Glu	Val	Ile	Ala	Thr	Leu	Lys
305				310						315					320
Gly	Gly	Gln	Lys	Val	Cys	Leu	Asp	Pro	Glu	Ala	Pro	Leu	Val	Gln	Lys
			325						330					335	
Ile	Ile	Gln	Lys	Ile	Leu	Asn	Lys	Gly	Lys	Ala	Asn	Gly	Gly	Gly	Leu
		340						345						350	
Asn	Asp	Ile	Phe	Glu	Ala	Gln	Lys	Ile	Glu	Trp	His	Glu			
		355					360					365			

&lt;210&gt; SEQ ID NO 42

&lt;211&gt; LENGTH: 366

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-Fc-His6-linker-TEV-mCXCL548-118-G2-AviTag

&lt;400&gt; SEQUENCE: 42

Met	Arg	Val	Pro	Ala	Gln	Leu	Leu	Gly	Leu	Leu	Leu	Leu	Trp	Leu	Pro
1				5					10					15	
Gly	Ala	Arg	Cys	Glu	Pro	Arg	Val	Pro	Ile	Thr	Gln	Asn	Pro	Cys	Pro
			20						25					30	
Pro	Leu	Lys	Glu	Cys	Pro	Pro	Cys	Ala	Ala	Pro	Asp	Leu	Leu	Gly	Gly
		35					40						45		
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Lys	Ile	Lys	Asp	Val	Leu	Met	Ile
	50					55					60				
Ser	Leu	Ser	Pro	Met	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	Glu	Asp
65					70					75					80
Asp	Pro	Asp	Val	Gln	Ile	Ser	Trp	Phe	Val	Asn	Asn	Val	Glu	Val	His
				85					90						95

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Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg  
 100 105 110

Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys  
 115 120 125

Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ser Pro Ile Glu  
 130 135 140

Lys Thr Ile Ser Lys Pro Arg Gly Pro Val Arg Ala Pro Gln Val Tyr  
 145 150 155 160

Val Leu Pro Pro Pro Ala Glu Glu Met Thr Lys Lys Glu Phe Ser Leu  
 165 170 175

Thr Cys Met Ile Thr Gly Phe Leu Pro Ala Glu Ile Ala Val Asp Trp  
 180 185 190

Thr Ser Asn Gly Arg Thr Glu Gln Asn Tyr Lys Asn Thr Ala Thr Val  
 195 200 205

Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Gln  
 210 215 220

Lys Ser Thr Trp Glu Arg Gly Ser Leu Phe Ala Cys Ser Val Val His  
 225 230 235 240

Glu Gly Leu His Asn His Leu Thr Thr Lys Thr Ile Ser Arg Ser Leu  
 245 250 255

Gly Lys His His His His His Ser Ser Gly Val Asp Leu Gly Thr  
 260 265 270

Glu Asn Leu Tyr Phe Gln Ala Thr Glu Leu Arg Cys Val Cys Leu Thr  
 275 280 285

Val Thr Pro Lys Ile Asn Pro Lys Leu Ile Ala Asn Leu Glu Val Ile  
 290 295 300

Pro Ala Gly Pro Gln Cys Pro Thr Val Glu Val Ile Ala Lys Leu Lys  
 305 310 315 320

Asn Gln Lys Glu Val Cys Leu Asp Pro Glu Ala Pro Val Ile Lys Lys  
 325 330 335

Ile Ile Gln Lys Ile Leu Gly Ser Asp Lys Lys Lys Ala Gly Gly Gly  
 340 345 350

Leu Asn Asp Ile Phe Glu Ala Gln Lys Ile Glu Trp His Glu  
 355 360 365

<210> SEQ ID NO 43  
 <211> LENGTH: 2100  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL135-107-(Gly4Ser)2-  
 mouse SA-(Gly4Ser)-His6

<400> SEQUENCE: 43

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atgagggtcc cgcctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt    60
gcctctgtcg ccaccgagct gagatgccag tgctgcaga ccctgcaggg catccacccc    120
aagaacatcc agagcgtgaa cgtgaagtcc cctggcccc actgcgccc gaccgaagtg    180
atcgccaccc tgaagaacgg ccggaaggcc tgctgaacc ccgcccagccc catcgtgaag    240
aaaatcatcg agaagatgct gaacagcgac aagagcaacg gtggaggcgg tagcggaggg    300
ggagggtcgg aagcacacaa gactgagatc gcccatcggt ataatgattt gggagaacaa    360
catttcaaag gcctagtoct gattgccttt tcccagatc tccagaaatg ctcatacgat    420
    
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gagcatgcc aattagtca ggaagtaaca gactttgcaa agacgtgtgt tgccgatgag 480
tctgcccga actgtgacaa atcccttcac actctttttg gagataagtt gtgtgccatt 540
ccaaacctcc gtgaaaacta tggtaactg gctgactgct gtacaaaaca agagcccga 600
agaaacgaat gtttctgca acacaaagat gacaacccca gcctgccacc atttgaaggg 660
ccagaggctg aggccatgtg cacctccttt aaggaaaacc caaccacctt tatgggacac 720
tatttgcag aagttgccag aagacatcct tatttctatg ccccagaact tctttactat 780
gctgagcagt acaatgagat tctgaccag tgttgtgagc aggctgacaa ggaaagctgc 840
ctgacccca agcttgatgg tgtgaaggag aaagcattgg tctcatctgt ccgtcagaga 900
atgaagtgt ccagatgca gaagtttga gagagagctt ttaaagcatg ggcagtagct 960
cgtctgagcc agacattccc caatgctgac tttgcagaaa tcaccaaatt ggcaacagac 1020
ctgaccaaag tcaacaagga gtgctgccat ggtgacctgc tggaatgccc agatgacagg 1080
gcggaacttg ccaagtacat gtgtgaaaac caggcgacta tctccagcaa actgcagact 1140
tgctgcgata aacctgtgt gaagaaagcc cactgtctta gtgaggtgga gcatgacacc 1200
atgcctgctg atctgcctgc cattgtgctt gattttgttg aggaccagga agtgtgcaag 1260
aactatgctg aggccaagga tgtcttctg ggcacgttct tgtatgaata ttcaagaaga 1320
caccctgatt actctgtatc cctgttctg agacttgcta agaaatga agccactctg 1380
gaaaagtgt gcgctgaagc caatcctccc gcatgctacg gcacagtgtc tgctgaattt 1440
cagcctcttg tagaagagcc taagaacttg gtcaaaaacca actgtgatct ttacgagaag 1500
cttgagaaat atggattcca aaatgccatt ctagtctgct acaccagaa agcacctcag 1560
gtgtcaaccc caactctcgt ggaggctgca agaaacctag gaagagtggg caccaagtgt 1620
tgtacacttc ctgaagatca gagactgcct tgtgtggaag actatctgtc tgcaatcctg 1680
aaccgtgtgt gtctgctgca tgagaagacc ccagtgagtg agcatgttac caagtgtgt 1740
agtggatccc tgggtgaaag gcggccatgc ttctctgctc tgacagtga tgaacatat 1800
gtccccaaag agtttaaagc tgagacctc accttccact ctgatatctg cacacttcca 1860
gagaaggaga agcagattaa gaacaaacg gctcttgctg agctggtgaa gcacaagccc 1920
aaggctacag cggagcaact gaagactgtc atggatgact ttgcacagtt cctggataca 1980
tgttgcaagg ctgctgacaa ggacacctgc ttctcgactg aggggtccaaa ccttgtcact 2040
agatgcaaag acgccttagc cggagggggc ggttcccacc atcaccacca tcaactgataa 2100

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&lt;210&gt; SEQ ID NO 44

&lt;211&gt; LENGTH: 2100

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL235-107- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 44

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atgaggggcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60
gctcctctgg ccacagagct gagatgccag tgcctccaga cactccaggg catccacctg 120
aagaacatcc agagcgtgaa agtgaagtcc cctggccccc actgcccaca gacagaagtg 180
atgccacccc tgaagaatgg ccagaaggcc tgctgaacc ccgccagccc tatggtcaag 240
aaaatcatcg agaagatgct gaagaacggc aagagcaacg gtggaggcgg tagcggaggc 300

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ggagggtcgg aagcacacaa gagtgagatc gcccatcggg ataatgattt gggagaacaa 360
catttcaaag gcctagtoct gattgccttt tcccagatc tccagaaatg ctcatacgat 420
gagcatgcc aattagtgc ggaagtaaca gactttgcaa agacgtgtgt tgccgatgag 480
tctgccgcca actgtgacaa atcccttcac actctttttg gagataagtt gtgtgccatt 540
ccaaacctcc gtgaaaacta tggatgaactg gctgactgct gtacaaaaca agagcccga 600
agaaacgaat gtttcctgca acacaagat gacaacccca gcctgccacc atttgaag 660
ccagaggctg aggccatgtg cacctccttt aaggaaaacc caaccacctt tatgggacac 720
tatttgcatg aagttgccag aagacatcct tatttctatg ccccagaact tctttactat 780
gctgagcagt acaatgagat tctgaccag tgttgtgagc aggctgacaa ggaagctgc 840
ctgaccccg agettgatgg tgtgaaggag aaagcattgg tctcatctgt ccgtcagaga 900
atgaagtgct ccagtatgca gaagtttga gagagagctt ttaaagcatg ggcagtagct 960
cgtctgagcc agacattccc caatgctgac tttgcagaaa tcaccaaatt ggcaacagac 1020
ctgaccaaag tcaacaagga gtgctgccat ggtgacctgc tggaatgccc agatgacagg 1080
gcggaacttg ccaagtaacat gtgtgaaaac caggcgacta tctccagcaa actgcagact 1140
tgctgagata aacctctgtt gaagaaagcc cactgtctta gtgaggtgga gcatgacacc 1200
atgctgctg atctgctgct cattgtgctt gattttgttg aggaccagga agtgtgcaag 1260
aactatgctg aggccaaagga tgtcttctg ggcacgttct tgtatgaata ttcaagaaga 1320
cacctgatt actctgtatc cctgttctg agacttgcta agaaatatga agccactctg 1380
gaaaagtgct gcgctgaagc caatcctccc gcatgctacg gcacagtgtg tgetgaattt 1440
cagcctcttg tagaagagcc taagaacttg gtcaaaacca actgtgatct ttacgagaag 1500
cttgagaat atggattcca aaatgccatt ctagtctgct acaccagaa agcacctcag 1560
gtgtcaaccc caactctgtg ggaggtgca agaaacctag gaagagtggg caccaagtgt 1620
tgtacacttc ctgaagatca gagactgcct tgtgtggaag actatctgct tgcaatcctg 1680
aacctgtgtg gtctgctgca tgagaagacc ccagtgagtg agcatgttac caagtgtgt 1740
agtggatccc tgggtgaaag gcggccatgc ttctctgctc tgacagtga tgaacatat 1800
gtcccaaag agtttaaagc tgagacctc accttccact ctgatctctg cacactcca 1860
gagaaggaga agcagattaa gaaacaaacg gctcttgctg agctggtgaa gcacaagccc 1920
aaggctacag cggagcaact gaagactgct atggatgact ttgcacagtt cctggatata 1980
tgttgcaagg ctgctgacaa ggacacctgc ttctcgactg agggtcocaa ccttgctact 2040
agatgcaaa acgcttagc cggagggggc ggttcccacc atcaccacca tcaactgataa 2100

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&lt;210&gt; SEQ ID NO 45

&lt;211&gt; LENGTH: 2100

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL335-107- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 45

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atgagggctcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60
gcctctgtcg tgaccgagct gagatgccag tgcctccaga cactccaggg catccacctg 120

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aagaacatcc agagcgtgaa cgtgcggagc cctggccctc attgtgccca gacagaagtg 180
atcgccaccc tgaagaatgg caagaaggcc tgcctgaacc ccgccagccc tatggtgcag 240
aagatcatcg agaagatcct gaacaagggc agcaccacag gtggaggcgg tagcggaggc 300
ggagggtcgg aagcacacaa gactgagatc gcccatcggg ataatgattt gggagaacaa 360
catttcaaag gcctagtctt gattgccttt tcccagatc tccagaaatg ctcatatgat 420
gagcatgcc aattagtgca ggaagtaaca gactttgcaa agacgtgtgt tgccgatgag 480
tctgccgcca actgtgacaa atccctcac actctttttg gagataagtt gtgtgccatt 540
ccaaacctcc gtgaaaacta tggatgaactg gctgactgct gtacaaaaca agagcccgaa 600
agaaacgaat gtttcctgca acacaagat gacaacccca gcctgccacc atttgaaggg 660
ccagaggctg aggccatgtg cacctccttt aaggaaaacc caaccacctt tatgggacac 720
tatttgcatt aagtgtccag aagacatcct tatttctatg cccagaaact tctttactat 780
gctgagcagt acaatgagat tctgaccagc tgttgtgcag aggctgacaa ggaagctgc 840
ctgaccccca agcttgatgg tgtgaaggag aaagcattgg tctcatctgt ccgtcagaga 900
atgaagtgtc ccagtatgca gaagtttga gagagagctt ttaaagcatg ggcagtagct 960
cgtctgagcc agacattccc caatgtgac tttgcagaaa tcaccaaatt ggcaacagac 1020
ctgaccaaag tcaacaagga gtgctgccat ggtgacctgc tggaaatgag agatgacagg 1080
gcggaacttg ccaagtacat gtgtgaaaac caggcgacta tctccagcaa actgcagact 1140
tgctgcgata aacctgtgtt gaagaagacc cactgtctta gtgaggtgga gcatgacacc 1200
atgcctgctg atctgcctgc cattgtgctt gattttgttg aggaccagga agtgtgcaag 1260
aactatgctg aggccaaagga tgtcttctct ggcacgttct tgatgaata ttcaagaaga 1320
cacctgatt actctgtatc cctgttctgt agacttgcta agaaatatga agccactctg 1380
gaaaagtgtc gcgctgaagc caatcctccc gcatgctacg gcacagtgtc tgctgaattt 1440
cagcctcttg tagaagagcc taagaacttg gtcaaaaaca actgtgatct ttacgagaag 1500
cttgagaaat atggattcca aaatgccatt ctagtctgct acaccagaa agcacctcag 1560
gtgtcaaccc caactctctg ggaggctgca agaaacctag gaagagtggg caccaagtgt 1620
tgtacacttc ctgaagatca gagactgcct tgtgtggaag actatctgtc tgcaatcctg 1680
aacctgtgtg gtctgctgca tgagaagacc ccagtgtgtg agcatgttac caagtgtgtg 1740
agtggatccc tgggtgaaag gcggccatgc ttctctgctc tgacagtga tgaacatat 1800
gtccccaaag agtttaaagc tgagaccttc acctccact ctgatctctg cacacttcca 1860
gagaaggaga agcagattaa gaaacaaacg gctcttctgt agctgggtgaa gcacaagccc 1920
aaggctacag cggagcaact gaagactgtc atggatgact ttgcacagtt cctggatata 1980
tgttgcaagg ctgctgacaa ggacacctgc ttctcagctg aggggtccaaa ccttctcact 2040
agatgcaaa acgcttagc cggagggggc ggttcccacc atcaccacca tcaactgataa 2100

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&lt;210&gt; SEQ ID NO 46

&lt;211&gt; LENGTH: 2091

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL432-101- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 46

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atgaggggtcc	ccgctcagct	cctgggggtcc	ctgctgctct	ggctcccagg	tgcacgatgt	60
gaggctgaag	aggacggcga	tctccagtgc	ctgtgcgtga	aaaccaccag	ccaagtgcgg	120
cccagacaca	tcaccagcct	ggaagtgatc	aaggccggac	cccactgtcc	taccgccag	180
ctgattgcc	ccctgaagaa	cgcccggaag	atctgcctgg	acctccaggc	ccccctgtac	240
aagaagatca	tcaagaagct	gctggaaagc	ggtggaggcg	gtagcggagg	cggagggtcg	300
gaagcacaca	agagtgaat	cgcccatcgg	tataatgatt	tgggagaaca	acatttcaaa	360
ggcctagtcc	tgattgcctt	ttcccagtat	ctccagaaat	gctcatacga	tgagcatgcc	420
aaattagtgc	aggaagtaac	agactttgca	aagacgtgtg	ttgccgatga	gtctgccgcc	480
aactgtgaca	aatcccttca	cactcttttt	ggagataagt	tgtgtgcat	tccaaacctc	540
cgtgaaaact	atggtgaact	ggctgactgc	tgtacaaaac	aagagcccca	aagaaacgaa	600
tgtttcctgc	aacacaaaaga	tgacaacccc	agcctgccac	catttgaaag	gccagaggct	660
gaggccatgt	gcacctcctt	taaggaaaac	ccaaccacct	ttatgggaca	ctatttgcac	720
gaagttgcc	gaagacatcc	ttatttctat	gccccagaac	ttctttacta	tgctgagcag	780
tacaatgaga	ttctgaccca	gtgtttgtca	gaggctgaca	aggaaagctg	cctgaccccg	840
aagcttgatg	gtgtgaagga	gaaagcattg	gtctcatctg	tccgtcagag	aatgaagtgc	900
tccagtatgc	agaagtttgg	agagagagct	tttaagcat	gggcagtagc	tcgtctgagc	960
cagacattcc	ccaatgctga	ctttgcagaa	atcaccaaat	tggcaacaga	cctgacccaaa	1020
gtcaacaagg	agtgtctcca	tggtgacctg	ctggaatgcg	cagatgacag	ggcggaaactt	1080
gccaagtaca	tgtgtgaaaa	ccaggcgact	atctccagca	aactgcagac	ttgtctggat	1140
aaaccactgt	tgaagaaagc	ccactgtcct	agtgaggtgg	agcatgacac	catgcctgct	1200
gatctgcctg	ccattgtctg	tgattttgtt	gaggaccagg	aagtgtgcaa	gaactatgct	1260
gaggccaagg	atgtcttctc	gggcacgttc	ttgtatgaat	attcaagaag	acaccctgat	1320
tactctgtat	ccctgttctg	gagacttgct	aagaaatag	aagccactct	ggaaaagtgc	1380
tgcgctgaag	ccaatcctcc	cgcagtctac	ggcacagtgc	ttgtgaatt	tcagcctcct	1440
gtagaagagc	ctaagaactt	ggtcaaaacc	aactgtgatc	tttacgagaa	gcttgagaaa	1500
tatggattcc	aaaatgcoat	tctagttcgc	tacaccaga	aagcacctca	ggtgtcaacc	1560
ccaactctcg	tggaggctgc	aagaaacctt	ggaagagtgg	gcaccaagtg	ttgtacactt	1620
cctgaagatc	agagactgcc	ttgtgtggaa	gactatctgt	ctgcaatcct	gaaccgtgtg	1680
tgtctgctgc	atgagaagac	cccagtgagt	gagcatgtta	ccaagtctct	tagtggatcc	1740
ctggtgaaaa	ggcggccatg	cttctctgct	ctgacagttg	atgaaacata	tgtcccacaa	1800
gagtttaaa	ctgagacctt	caccttcac	tctgatctct	gcacacttcc	agagaaggag	1860
aagcagatta	agaacaaaac	ggctcttgct	gagctggtga	agcacaagcc	caaggctaca	1920
gcgagacaac	tgaagactgt	catggatgac	tttgacagct	tcctggatac	atggttcaag	1980
gctgctgaca	aggacacctg	cttctcgact	gagggtccaa	accttctcac	tagatgcaaa	2040
gacgccttag	ccggaggggg	cggttcccac	catcaccacc	atcactgata	a	2091

&lt;210&gt; SEQ ID NO 47

&lt;211&gt; LENGTH: 2094

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

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&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL544-114-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 47

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atgaggggtcc cgcctcagct cctgggggtc ctgctgctct ggctcccagg tgcacgatgt    60
ctgcgcgagc tgagatgogt gtgcctgcag accaccagg gcgtgcaccc caagatgatc    120
agcaacctcc aggtgttcgc catcgcccc cagtgcagca aggtggaagt ggtggccagc    180
ctgaagaacg gcaaagagat ctgcctggac cccgagggcc cattcctgaa gaaagtgatc    240
cagaagatcc tggacggcgg caacaagag aacgggtggag gcggtagcgg aggcggaggg    300
tcggaagcac acaagagtga gatcgcccat cgggtataatg atttgggaga acaacatttc    360
aaaggcctag tcctgattgc cttttcccag tatctccaga aatgctcata cgatgagcat    420
gccaaattag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc    480
gccaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac    540
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gaatgtttcc tgcaacacaa agatgacaac cccagcctgc caccatttga aaggccagag    660
gctgaggcca tgtgcacctc ctttaaggaa aaccaacca cctttatggg aactatttg    720
catgaagttg ccagaagaca tccttatttc tatgcccag aacttcttta ctatgctgag    780
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gctgatctgc ctgccattgc tgetgatttt gttgaggacc aggaagtgtg caagaactat   1260
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gattactctg tatccctggt gctgagactt gctaagaaat atgaagccac tctggaaaag   1380
tgctgcgctg aagccaatcc tcccgcacgc tacggcacag tgettgctga atttcagcct   1440
cttgtagaag agcctaagaa cttggtcaaa accaactgtg atctttacga gaagcttggg   1500
gaatatggat tccaaaatgc cattctagtt cgctacaccc agaaagcacc tcaggtgtca   1560
acccaactc tcgtggaggg tgcaagaaac cttaggaagag tgggcaccaa gtgtgtgaca   1620
cttctgaag atcagagact gccttggtg gaagactatc tgtctgcaat cctgaaccgt   1680
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tccctggtgg aaaggcggcc atgctctctt gctctgacag ttgatgaaac atatgtcccc   1800
aaagagttta aagctgagac cttcaccttc cactctgata tctgcacact tccagagaag   1860
gagaagcaga ttaagaaaca aacggctctt gctgagctgg tgaagcacia gcccaggctc   1920
acagcggagc aactgaagac tgcattggat gactttgcac agttcctgga tacatgttgc   1980
aaggctgctg acaaggacac ctgctctctg actgagggtc caaacctgtg cactagatgc   2040
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<210> SEQ ID NO 48
<211> LENGTH: 2097
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL643-114-(Gly4Ser)2-
mouse SA-(Gly4Ser)-His6

<400> SEQUENCE: 48
atgaggggtcc cgcctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt    60
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atcggcaagc tccagggtgt cctgcccggc cctcagtgca gcaagggtga agtgggtggc    180
agcctgaaaa acgaaaaaca agtgtgcctg gaccccaggg cccattcct gaagaaagtg    240
atccagaaga tcctggacag cggcaacaag aagaacgggtg gaggcggtag cggaggcggg    300
gggtcgggaag cacacaagag tgagatcgcc catcgggata atgatttggg agaacaacat    360
ttcaaaggcc tagtcctgat tgccttttcc cagtatctcc agaaatgctc atacgatgag    420
catgccaaat tagtgcagga agtaacagac tttgcaaaga cgtgtgttgc cgatgagtct    480
gccgccaact gtgacaaaac ccttcacact ctttttgag ataagttgtg tgccattcca    540
aacctccgtg aaaactatgg tgaactggct gactgctgta caaaacaaga gcccgaaaga    600
aacgaatggt tcctgcaaca caaagatgac aaccccagcc tgccaccatt tgaaggcca    660
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tatgtctgagg ccaaggatgt ctctctgggc acgttcttgt atgaatatc aagaagacac    1320
cctgattact ctgtatccct gttgctgaga cttgctaaga aatatgaagc cactctggaa    1380
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aaggagaagc agattaagaa acaaacggct cttgctgagc tgggtgaagca caagcccaag    1920
gctacagcgg agcaactgaa gactgtcatg gatgactttg cacagttcct ggatacatgt    1980

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tgcaaggctg ctgacaagga cacctgcttc tggactgagg gtccaaaacct tgtcactaga 2040  
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<210> SEQ ID NO 49  
 <211> LENGTH: 2070  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL759-121- (Gly4Ser)2-  
 mouse SA-(Gly4Ser)-His6

<400> SEQUENCE: 49

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 gccgagctgc ggtgcatgtg catcaagacc accagcggaa tccaccccaa gaatatccag 120  
 tccctggaag tgattggcaa gggcaccac tgcaaccagg tggaagtgat tgccacactg 180  
 aaagacggcc ggaagatctg cctggaccct gacgccccca gaatcaagaa aatcgtgcag 240  
 aaaaagctgg gtggaggcgg tagcggaggc ggagggtcgg aagcacacaa gactgagatc 300  
 gcccatcggg ataatgattt gggagaacaa catttcaaag gcctagtcct gattgccttt 360  
 tcccagatc tccagaaatg ctcatagat gagcatgcca aattagtga ggaagtaaca 420  
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 gacaacccca gcctgccacc atttgaagc ccagaggctg aggccatgtg cacctccttt 660  
 aaggaaaacc caaccacctt tatgggacac tatttgcag aagttgccag aagacatcct 720  
 tatttctatg cccagaact tctttactat gctgagcagt acaatgagat tctgaccag 780  
 tgttgtgcag aggctgacaa gaaaagctgc ctgaccccga agcttgatgg tgtgaaggag 840  
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 gagagagctt ttaaagcatg ggcagtagct cgtctgagcc agacattccc caatgctgac 960  
 tttgcagaaa tcaccaaatt ggcaacagac ctgaccaaag tcaacaagga gtgtgacct 1020  
 ggtgacctgc tggaatgcgc agatgacagg gcggaacttg ccaagtacat gtgtgaaaac 1080  
 caggcgacta tctccagcaa actgcagact tgctgcgata aacctggtt gaagaaagcc 1140  
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&lt;210&gt; SEQ ID NO 50

&lt;211&gt; LENGTH: 2097

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL828-99- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 50

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ttcatcaaag aactgagagt gatcgagagc ggccctcact gcgccaacac cgagatcatc	180
gtgaaagtga gcgacggcag agagctgtgc ctggacccca aagaaaactg ggtgcagcgg	240
gtggtggaag agttcctgaa gcggggccgag aacagcggtg gaggcggtag cggagggcga	300
gggtcggaag cacacaagag tgagatcgcc catcgggata atgatttggg agaacaacat	360
ttcaaaggcc tagtcctgat tgccttttcc cagtatctcc agaaatgctc atacgatgag	420
catgccaat tagtgcagga agtaacagac ttgcaaaga cgtgtgttgc cgatgagtct	480
gccgccaact gtgacaaatc ccttcacact ctttttgagg ataagttgtg tgcattcca	540
aacctccgtg aaaactatgg tgaactggct gactgctgta caaaacaaga gcccgaaaga	600
aacgaatggt tcctgcaaca caaagatgac aaccccagcc tgccaccatt tgaaggcca	660
gaggtgaggg ccatgtgcac ctcccttaag gaaaacccaa ccacctttat gggacactat	720
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gagcagtaca atgagattct gaccagtggt tgtgcagagg ctgacaagga aagctgcctg	840
accccgaaagc ttgatggtgt gaaggagaaa gcattggtct catctgtccg tcagagaatg	900
aagtgctcca gtatgcagaa gtttgagag agagcttita aagcatgggc agtagctcgt	960
ctgagccaga cattcccaaa tgcctgactt gcagaaatca ccaaattggc aacagacctg	1020
accaaagtca acaaggagtg ctgccatggt gacctgctgg aatgcccaga tgacagggcg	1080
gaacttgcca agtacatgtg tgaaaaccag gcgactatct ccagcaaaact gcagacttgc	1140
tgcgataaac cactgttgaa gaaagcccac tgtcttagtg aggtggagca tgacaccatg	1200
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cctgattact ctgtatccct gttgctgaga cttgctaaga aatatgaagc cactctggaa	1380
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cctctttagg aagagcctaa gaacttggtc aaaaccaact gtgatcttta cgagaagctt	1500
ggagaatatg gattccaaaa tgccattcta gttcgtaca ccagaaagc acctcaggtg	1560
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tgcaaggctg ctgacaagga cacctgcttc tcgactgagg gtccaaacct tgtcactaga 2040
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<210> SEQ ID NO 51
<211> LENGTH: 2190
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL923-125-(Gly4Ser)2-
mouse SA-(Gly4Ser)-His6

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<400> SEQUENCE: 51
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ctccagtctc tgaaggacct gaagcagttc gccccagcc ccagctgcga gaagatcgag 180
attatcgcca cactgaaaaa cgggggtgcag acctgcctga accccgacag cgccgacgtg 240
aaagaactga tcaagaaatg ggagaaacag gtgtcccaga agaagaagca gaagaacgga 300
aagaagcacc agaaaaagaa agtgctgaaa gtgcggaagt cccagcggag ccggcagaag 360
aaaaccacag gtggaggcgg tagcggaggc ggagggctcg aagcacacaa gagtgagatc 420
gcccacgggt ataatgatth gggagaacaa catttcaaag gcctagtcct gattgccttt 480
tcccagatc tccagaaatg ctcatcagat gagcatgcca aattagtgca ggaagtaaca 540
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actctttttg gagataagtt gtgtgccatt ccaaacctcc gtgaaaacta tggatgaactg 660
gctgactgct gtacaaaaca agagcccga agaaaagcaat gtttctgca acacaaagat 720
gacaacccca gcctgccacc atttgaagg ccagaggctg aggcctatgt cacctccttt 780
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caggcgacta tctccagcaa actgcagact tgctgcgata aacctgtt gaagaaagcc 1260
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ggcacgttct tgtatgaata ttcaagaaga caccctgatt actctgtatc cctgttgctg 1440
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gctcttgctg agctgggtgaa gcacaagccc aaggctacag cggagcaact gaagactgtc 2040
atggatgact ttgcacagtt cctggataca tgttgcaagg ctgctgacaa ggacacctgc 2100
ttctcgactg agggtcacaa ccttgtcact agatgcaaag acgccttagc cggagggggc 2160
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&lt;210&gt; SEQ ID NO 52

&lt;211&gt; LENGTH: 2112

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL1022-98- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 52

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cccagaagcc tggaaaagct ggaatcacc cccgccagcc agttctgccc cagagtggaa 180
attatcgcca ccatgaagaa gaaaggcgag aagcggtgcc tgaacccga gagcaaggcc 240
atcaagaacc tgctgaaggc cgtgtccaaa gagcggagca agcggagccc aggtggaggc 300
ggtagcggag gcgagggtc ggaagcacac aagagtgaga tcgcccacg gtataatgat 360
ttgggagaac aacatttcaa aggcctagtc ctgattgcct tttcccagta tctccagaaa 420
tgctcatacg atgagcatgc caaattagtg caggaagtaa cagactttgc aaagacgtgt 480
gttgccgatg agtctgcgc caactgtgac aaatccctc acactctttt tggagataag 540
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caagagccc aaagaaacga atgtttctc caacacaaag atgacaaccc cagcctgcca 660
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ctttacgaga agcttgagaga atatggattc caaaatgcca ttctagtctg ctacaccag 1560
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tgcacacttc cagagaagga gaagcagatt aagaaacaaa cggctcttgc tgagctggtg 1920
aagcacaagc ccaaggctac agcggagcaa ctgaagactg tcatggatga ctttgcacag 1980
ttcctggata catgttgcaa ggetgtgac aaggacacct gcttctcgac tgagggtcca 2040
aaccttgtca ctagatgcaa agacgcctta gccggagggg gcggttccca ccatcaccac 2100
catcactgat aa 2112

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<210> SEQ ID NO 53
<211> LENGTH: 2100
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: gWiz-LS-hCXCL1122-94-(Gly4Ser)2-
mouse SA-(Gly4Ser)-His6

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<400> SEQUENCE: 53
atgaggggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60
tccccatgt tcaagcgggg cagatgcctg tgcacggcc ctggcgtgaa agcagtgaa 120
gtggccgata tcgagaaggc cagcatcatg taccocagca acaactgcga caagatcgaa 180
gtgatcatca ccctgaaaga gaacaagggc cagagatgcc tgaatcccaa gtccaagcag 240
gccccggctga tcacaaagaa ggtggaacgg aagaacttcg gtggaggcgg tagcggaggc 300
ggagggctcg aagcacacaa gactgagatc gcccatcggt ataatgattt gggagaacaa 360
catttcaaag gcctagtctt gattgccttt tcccagatc tccagaaatg ctacacgat 420
gagcatgcca aattagtgca ggaagtaaca gactttgcaa agacgtgtgt tgccgatgag 480
tctgcccga actgtgacaa atcccttcac actctttttg gagataagtt gtgtgccatt 540
ccaaacctcc gtgaaaacta tggatgaactg gctgactgct gtacaaaaca agagcccga 600
agaaacgaat gtttcctgca acacaaagat gacaacccca gcctgccacc atttgaag 660
ccagaggctg aggccatgtg cacctccttt aaggaaaacc caaccacctt tatgggacac 720
tatttgcag aagttgccc aagacatcct tatttctatg cccagaaact tctttactat 780
gctgagcagt acaatgagat tctgaccag tgttgtgac aggctgacaa ggaaagctgc 840
ctgacccca agcttgatgg tgtgaaggag aaagcattgg tctcatctgt ccgtcagaga 900
atgaagtgtc ccagtatgca gaagtttga gagagagctt ttaaagcatg ggcagtagct 960
cgtctgagcc agacattccc caatgctgac tttgcagaaa tcaccaaatt ggcaacagac 1020

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ctgaccaaag tcaacaagga gtgctgccat ggtgacctgc tggaaatgccc agatgacagg	1080
gcggaacttg ccaagtacat gtgtgaaaac caggcgacta tctccagcaa actgcagact	1140
tgctgcgata aacctctggt gaagaaagcc cactgtctta gtgagggtgga gcatgacacc	1200
atgcctgctg atctgcctgc cattgctgct gattttgttg aggaccagga agtgtgcaag	1260
aactatgctg aggccaagga tgtcttctctg ggcacgttct tgatgaata ttcaagaaga	1320
cacctgatt actctgtatc cctgttctg agacttgcta agaaatatga agccactctg	1380
gaaaagtgtc gcgctgaagc caatctccc gcatgctacg gcacagtgtc tgctgaattt	1440
cagcctcttg tagaagagcc taagaacttg gtcaaaaacca actgtgatct ttacgagaag	1500
cttgagaaat atggattcca aaatgccatt ctagtctgct acaccagaa agcacctcag	1560
gtgtcaacc ccaactctctg ggaggctgca agaaacctag gaagagtggg caccaagtgt	1620
tgtacacttc ctgaagatca gagactgcct tgtgtggaag actatctgct tgcaatcctg	1680
aacctgtgtg gtctgctgca tgagaagacc ccagtgagtg agcatgttac caagtgtgtg	1740
agtggatccc tgggtgaaag gcggccatgc ttctctgctc tgacagtga tgaacatat	1800
gtcccccagg agtttaaagc tgagaccttc acctccact ctgatctctg cacacttcca	1860
gagaaggaga agcagattaa gaaacaaacg gctcttctg agctgggtgaa gcacaagccc	1920
aaggctacag cggagcaact gaagactgtc atggatgact ttgcacagtt cctggatata	1980
tgttgcaagg ctgctgacaa ggacacctgc ttctcgactg aggggtccaaa ccttctcact	2040
agatgcaaag acgcttagc cggagggggc ggttcccacc atcaccacca tcaactgataa	2100

&lt;210&gt; SEQ ID NO 54

&lt;211&gt; LENGTH: 2097

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL125-96- (Gly4Ser)2-mouse SA- (Gly4Ser) -His6

&lt;400&gt; SEQUENCE: 54

atgaggggtcc cgcctcagct cctgggggctc ctgctgctct ggctcccagg tgcaacgatgt	60
gccccatttg ccaacgagct gcggtgccag tgccctgcaga ccatggccgg catccacctg	120
aagaacatcc agagcctgaa ggtgctgccc agcggccctc actgcaccca gaccgaagtg	180
atcgccaccc tgaagaacgg cagagaggcc tgccctggatc ccgaggcccc cctgggtgcag	240
aaaatcgtgc agaaaatgct gaagggcgctg cccaaggggtg gaggcggtag cggaggcgga	300
gggtcggaa gacacaagag tgagatcgcc catcggtata atgatttggg agaacaacat	360
ttcaaaaggcc tagtccctgat tgccctttcc cagtatctcc agaaatgctc atacgatgag	420
catgccaagt tagtgcagga agtaacagac tttgcaaaag cgtgtgttgc cgatgagtct	480
gccgccaact gtgacaaatc ccttcacact ctttttgag ataagttgtg tgccattcca	540
aacctccgtg aaaactatgg tgaactggct gactgctgta caaaacaaga gccgaaaga	600
aacgaatggt tcctgcaaca caaagatgac aaccccagcc tgccaccatt tgaaggcca	660
gaggctgagg ccatgtgcac ctcccttaag gaaaacccaa ccacctttat gggacactat	720
ttgcatgaag ttgccagaag acatccttat ttctatgccc cagaacttct ttactatgct	780
gagcagtaca atgagattct gaccagtggt tgtgcagagg ctgacaagga aagctgctctg	840
accccgaaag ttgatggtgt gaaggagaaa gcattggtct catctgtccg tcagagaatg	900

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aagtgctcca gtatgcagaa gtttgagag agagctttaa aagcatgggc agtagctcgt    960
ctgagccaga cattcccaa tgctgacttt gcagaaatca ccaaattggc aacagacctg    1020
accaaagtca acaaggagtg ctgccatggt gacctgctgg aatgocgaga tgacagggcg    1080
gaacttgcca agtacatgtg tgaaaaccag gcgactatct ccagcaaact gcagacttgc    1140
tgcgataaac cactgttgaa gaaagccac tgtcttagtg aggtggagca tgacaccatg    1200
cctgctgac  tgctgcat  tgctgctgat  tttgttgagg  accaggaagt  gtgcaagaac    1260
tatgctgagg ccaaggatgt cttcctgggc acgttcttgt atgaatattc aagaagacac    1320
cctgattact ctgtatccct gttgctgaga cttgctaaga aatatgaagc cactctggaa    1380
aagtgctcgc ctgaagccaa tcctcccgca tgctacggca cagtgcttgc tgaatctcag    1440
cctctttag  aagagcctaa  gaacttggtc  aaaaccaact  gtgatcttta  cgagaagctt    1500
ggagaatatg gattccaaaa tgccattcta gttcgtaca cccagaaagc acctcaggtg    1560
tcaaccccaa ctctcgtgga ggctgcaaga aacctaggaa gagtgggcac caagtgttgt    1620
acacttctg  aagatcagag  actgccttgt  gtggaagact  atctgtctgc  aatcctgaac    1680
cgtgtgtgtc tgctgcatga gaagaccca gtgagtgagc atgttaccaa gtgctgtagt    1740
ggatccctgg tggaaaggcg gccatgcttc tctgctctga cagttgatga aacatagtgc    1800
cccaaagagt ttaaagtga  gaccttcacc  ttccactctg  atatctgac  acttcagag    1860
aaggagaagc agattaagaa acaaacggct cttgctgagc tggatgaagca caagcccaag    1920
gctacagcgg agcaactgaa gactgtcatg gatgactttg cacagttcct ggatacatgt    1980
tgcaaggetg ctgacaagga cacctgcttc tcgactgagg gtccaaacct tgtcactaga    2040
tgcaaaagcg ccttagccgg agggggcggg tcccaccatc accaccatca ctgataa    2097

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&lt;210&gt; SEQ ID NO 55

&lt;211&gt; LENGTH: 2100

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL228-100- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 55

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atgaggggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt    60
gccgctcgtgg ccagcgagct gcggtgccag tgccctgaaa ccctgccccg ggtggacttc    120
aagaacatcc agagcctgag cgtgaccccc cctggccctc actgtgcccc gaccgaagtg    180
atcgccaccc tgaagggcgg ccagaaagtg tgccctggacc ccgagggccc cctggtgcag    240
aagatcatcc agaagatcct gaacaagggc aaggccaacg gtggaggcgg tagcggaggc    300
ggagggctcgg aagcacacaa gagtgagatc gcccatcggg ataatgattt gggagaacaa    360
catttcaaag gcctagtctt gattgccttt tcccagtatc tccagaaatg ctcatatgat    420
gagcatgcc  aattagtga  ggaagtaaca  gactttgcaa  agacgtgtgt  tgccgatgag    480
tctgcccgcc actgtgacaa atcccttcac actctttttg gagataagtt gtgtgccatt    540
ccaaacctcc gtgaaaacta tggatgaactg gctgactgct gtacaaaaca agagcccga    600
agaaacgaat gtttctctgca acacaagat gacaaccccc gcctgccacc atttgaaagg    660
ccagaggetg aggccatgtg cacctccttt aaggaaaacc caaccacctt tatgggacac    720

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tatttgcattg aagttgcccag aagacatcct tatttctatg ccccagaact tctttactat	780
gctgagcagt acaatgagat tctgacccag tgtttgtcag aggctgacaa ggaaagctgc	840
ctgaccccga agcttgatgg tgtgaaggag aaagcattgg tctcatctgt cegtacagaga	900
atgaagtgtc ccagtatgca gaagtttga gagagagctt ttaaagcatg ggcagtagct	960
cgtctgagcc agacattccc caatgctgac tttgcagaaa tcaccaaatt ggcaacagac	1020
ctgaccaaag tcaacaagga gtgctgccat ggtgacctgc tggaaatgccc agatgacagg	1080
gcggaacttg ccaagtaacat gtgtgaaaac caggcgacta tctccagcaa actgcagact	1140
tgctcgcgata aacctctgtt gaagaaagcc cactgtctta gtgaggtgga gcatgacacc	1200
atgcctgctg atctgcctgc cattgtgctt gattttgttg aggaccagga agtgtgcaag	1260
aactatgctg aggccaaagga tgtcttctct ggcacgttct tgtatgaata ttcaagaaga	1320
cacctgatt actctgtatc cctggtgctg agacttgcta agaaatatga agccactctg	1380
gaaaagtgtc gcgctgaagc caatcctccc gcatgctacg gcacagtgtc tgctgaattt	1440
cagcctcttg tagaagagcc taagaacttg gtcaaaacca actgtgatct ttacgagaag	1500
cttgagaat atggattcca aaatgccatt ctagtctcgt acaccagaa agcacctcag	1560
gtgtcaaccc caactctcgt ggaggtgca agaaacctag gaagagtggg caccaagtgt	1620
tgtacacttc ctgaagatca gagactgcct tgtgtggaag actatctgtc tgcaatcctg	1680
aacctgtgtg gtctgctgca tgagaagacc ccagtgagtg agcatgttac caagtgtgtg	1740
agtggatccc tgggtgaaag gcggccatgc ttctctgctc tgacagtga tgaacatat	1800
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gagaaggaga agcagattaa gaaacaaacg gctcttgctg agctggtgaa gcacaagccc	1920
aaggctacag cggagcaact gaagactgtc atggatgact ttgcacagtt cctggatata	1980
tgttgcaagg ctgctgacaa ggacacctgc ttctcgactg agggccaaa ccttgtcact	2040
agatgcaaaag acgcttagc cggagggggc ggttcccacc atcaccacca tcaactgataa	2100

&lt;210&gt; SEQ ID NO 56

&lt;211&gt; LENGTH: 2100

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL328-100-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 56

atgaggggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt	60
gctgtggtgg cctctgagct gagatgccag tgcctgaaca ccctgccccg ggtggacttc	120
gagacaatcc agagcctgac cgtgaccccc cctggccctc actgtaccca gacagaagtg	180
atcggccccc tgaaggacgg ccaggaagtg tgccctgaatc cccagggccc cagactccag	240
atcatcatca agaagatcct gaagtccggc aagagcagcg gtggaggcgg tagcggaggc	300
ggagggctcg aagcacacaa gagtgagatc gcccatcggg ataattgattt gggagaacaa	360
catttcaaag gcctagtcct gattgccttt tcccagatc tccagaaatg ctcatatgat	420
gagcatgcca aattagtgca ggaagtaaca gactttgcaa agacgtgtgt tgccgatgag	480
tctgccgcca actgtgacaa atcccctcac actctttttg gagataagtt gtgtgccatt	540
ccaaacctcc gtgaaaacta tggatgaactg gctgactgct gtacaaaaca agagcccga	600

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agaaacgaat gtttcctgca acacaaagat gacaacccca gcctgccacc atttgaaagg 660
ccagaggctg aggccatgtg cacctccttt aaggaaaacc caaccacctt tatgggacac 720
tatttgcatg aagttgcag aagacatcct tatttctatg cccagaact tctttactat 780
gctgagcagt acaatgagat tctgaccag tgtgtgagc aggctgacaa ggaaagctgc 840
ctgaccccgga agcttgatgg tgtgaaggag aaagcattgg tctcatctgt ccgtcagaga 900
atgaagtgtc ccagtatgca gaagtgtgga gagagagctt ttaaagcatg ggcaagtagct 960
cgtctgagcc agacattccc caatgtgac tttgcagaaa tcaccaaatt ggcaacagac 1020
ctgaccaaag tcaacaagga gtgctgccat ggtgacctgc tggaaatgagc agatgacagg 1080
gcggaacttg ccaagtacat gtgtgaaaac caggcgacta tctccagcaa actgcagact 1140
tgctgagata aacctgtt gaagaaagcc cactgtctta gtgaggtgga gcatgacacc 1200
atgcctgctg atctgcctgc cattgtgctt gattttgttg aggaccagga agtgtgcaag 1260
aactatgctg aggccaagga tgtcttctct ggcaagcttct tgatgaata ttcaagaaga 1320
cacctgatt actctgtatc cctgttctg agacttgcta agaaatatga agccactctg 1380
gaaaagtgtc gcgctgaagc caatcctccc gcatgctacg gcacagtgtc tgctgaattt 1440
cagcctcttg tagaagagcc taagaacttg gtcaaaaacca actgtgatct ttacgagaag 1500
cttgagaaat atggattoca aaatgccatt ctagtctgct acaccagaa agcacctcag 1560
gtgtcaaccc caactctctg ggaggctgca agaaacctag gaagagtggg caccaagtgt 1620
tgtacacttc ctgaagatca gagactgcct tgtgtggaag actatctgtc tgcaatcctg 1680
aacctgtgtg gtctgtgca tgagaagacc ccagtgtgtg agcatgttac caagtgtgtg 1740
agtggatccc tgggtgaaag gcgccatgc ttctctgtct tgacagtga tgaacatat 1800
gtccccaaag agtttaaagc tgagaccttc acctccact ctgatctctg cacacttcca 1860
gagaaggaga agcagattaa gaaacaaacg gctcttctg agctggtgaa gcacaagccc 1920
aaggctacag cggagcaact gaagactgtc atggatgact ttgcacagtt cctggatata 1980
tggtgcaagg ctgctgacaa ggacacctgc ttctcgactg aggggtccaaa ccttgtcact 2040
agatgcaaaag acgcttagc cggagggggc ggttccacc atcaccacca tcaactgataa 2100

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&lt;210&gt; SEQ ID NO 57

&lt;211&gt; LENGTH: 2109

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL430-105-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 57

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atgaggggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60
gtgacatctg ccggccctga ggaaagcagc ggcatctgt cttgctgtg cgtgaaaacc 120
atcagcagcg gcatccacct gaagcacatc accagcctgg aagtgatcaa ggccggcagg 180
cactgtgccg tgccctcagct gattgccacc ctgaagaacg gccggaagat ctgctggac 240
agacaggccc ccctgtacaa gaaagtgatt aagaagatcc tggaaagcgg tggaggcggg 300
agcggaggcg gaggtctgga agcacacaag agtgagatcg cccatcggta taatgatttg 360
ggagaacaac atttcaaagg cctagtctct attgcctttt cccagtatct ccagaaatgc 420

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tcatacgatg agcatgccaa attagtgcag gaagtaacag actttgcaaa gacgtgtgtt	480
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tgtgccattc caaacctocg tgaaaactat ggtgaactgg ctgactgctg tacaaaaaa	600
gagcccgaag gaaacgaatg tttcctgcaa cacaaagatg acaaccccag cctgccacca	660
tttgaaggc cagaggctga ggccatgtgc acctccttta aggaaaaccc aaccaccttt	720
atgggacact atttgcata agttgccaga agacatcctt atttctatgc cccagaactt	780
ctttactatg ctgagcagta caatgagatt ctgacccagt gttgtgcaga ggctgacaag	840
gaaagctgcc tgaccccga gcttgatggt gtgaaggaga aagcattggt ctcatctgtc	900
cgtcagagaa tgaagtgtc cagtatgcag aagtttgag agagagcttt taaagcatgg	960
gcagtagctc gtctgagcca gacattccc aatgctgact ttgcagaaat caccaaattg	1020
gcaacagacc tgaccaaagt caacaaggag tgctgccatg gtgacctgct ggaatgcgca	1080
gatgacaggg cggaaactgc caagtacatg tgtgaaaacc aggcgactat ctccagcaaa	1140
ctgcagactt gctgcgataa accactgttg aagaaagccc actgtcttag tgagggtggag	1200
catgacacca tgctgtctga tctgcctgcc attgctgctg attttgttga ggaccaggaa	1260
gtgtgcaaga actatgctga ggccaaggat gtcttctgg gcacgttctt gtatgaatat	1320
tcaagaagac accctgatta ctctgtatcc ctggtgctga gacttgctaa gaaatatgaa	1380
gccactctgg aaaagtgtg cgctgaagcc aatcctccc catgctacgg cacagtgtt	1440
gctgaatttc agcctctgtt agaagagcct aagaacttg tcaaaaccaa ctgtgatctt	1500
tacgagaagc ttggagaata tggattccaa aatgccattc tagttcgcta caccagaaa	1560
gcacctcagg tgtcaacccc aactctcgtg gagctgcaa gaaacctagg aagagtgggc	1620
accaagtgtt gtacacttcc tgaagatcag agactgcctt gtgtggaaga ctatctgtct	1680
gcaatcctga accgtgtgtg tctgctgcat gagaagaccc cagtgagtga gcatgttacc	1740
aagtgtgta gtggatccct ggtggaagg cggccatgct tctctgctct gacagtgtat	1800
gaaacatatg tccccaaaga gtttaagct gagaccttca ccttccactc tgatatctgc	1860
acacttccag agaaggagaa gcagattaag aaacaaacgg ctcttgctga gctggtgaag	1920
cacaagccca aggctacagc ggagcaactg aagactgtca tggatgactt tgcacagttc	1980
ctggatacat gttgcaaggc tctgacaag gacacctgct tctcgactga gggtcctaac	2040
cttgtcacta gatgcaaaga cgccttagcc ggagggggcg gttcccacca tcaccacat	2100
cactgataa	2109

&lt;210&gt; SEQ ID NO 58

&lt;211&gt; LENGTH: 2094

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL548-118- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 58

atgaggggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt	60
gccaccgagc tgagatgctg gtgcctgacc gtgaccccca agatcaaccc caagctgatc	120
gccaacctgg aagtgatccc tgccggcctt cagtgcccc ccgtggaagt gattgccaag	180
ctgaagaacc agaagaagt gtgcctggac cccgaggccc ccgtgatcaa gaagatcatc	240

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cagaagatcc tgggcagcga caagaagaaa gccggtggag gcggtagcgg aggcggaggg 300
tcggaagcac acaagagtga gatcgcccat cggataatg atttgggaga acaacatttc 360
aaaggcctag tcctgattgc cttttcccag tatctccaga aatgctcata cgatgagcat 420
gccaaattag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc 480
gccaaactgt acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac 540
ctccgtgaaa actatggtga actggctgac tgctgtacaa aacaagagcc cgaagaagaa 600
gaatgtttcc tgcaacacaa agatgacaac cccagcctgc caccatttga aaggccagag 660
gctgaggcca tgtgcacctc ctttaaggaa aaccaacca cctttatggg aactatttg 720
catgaagtgt ccagaagaca tccttatttc tatgcccag aacttcttta ctatgctgag 780
cagtacaatg agattctgac ccagtgtgtg gcagaggctg acaaggaaag ctgctgacc 840
ccgaagcttg atggtgtgaa ggagaaagca ttggtctcat ctgtccgtca gagaatgaag 900
tgctccagta tgcagaagtt tggagagaga gcttttaaag catgggcagt agctcgtctg 960
agccagacat tcccaatgc tgactttgca gaaatcacca aattggcaac agacctgacc 1020
aaagtcaaca aggagtgtg ccatggtgac ctgctggaat gcgcagatga cagggcggaa 1080
cttgccaagt acatgtgtga aaaccaggcg actatctcca gcaaactgca gacttctgctc 1140
gataaaccac tgttgaagaa agcccactgt cttagtgagg tggagcatga caccatgcct 1200
gctgatctgc ctgccattgc tgctgattt gttgaggacc aggaagtgtg caagaactat 1260
gctgaggcca aggatgtcct cctgggcacg ttcttgtatg aatattcaag aagacaccct 1320
gattactctg tatccctggt gctgagactt gctaagaaat atgaagccac tctggaaaag 1380
tgctgctgctg aagccaatcc tcccgcacgc tacggcacag tgcttctgga atttcagcct 1440
ctttagaag agcctaagaa cttggtcaaa accaactgtg atctttacga gaagcttggaa 1500
gaatatggat tccaaaatgc cattctagtt cgctacaccc agaaagcacc tcaggtgtca 1560
acccaactc tcgtggaggc tgcaagaaac ctaggaagag tgggcaccaa gtgttgtaca 1620
cttctgaag atcagagact gccttgtgtg gaagactatc tgtctgcaat cctgaaccgt 1680
gtgtgtctgc tgcagtagaa gaccccagtg agtgagcatg ttaccaagtg ctgtagtgga 1740
tccttgggtg aaaggcggcc atgcttctct gctctgacag ttgatgaaac atatgtcccc 1800
aaagagtta aagctgagac cttcaccttc cactctgata tctgcacact tccagagaag 1860
gagaagcaga ttaagaaaca aacggctcct gctgagctgg tgaagcacia gcccaaggct 1920
acagcggagc aactgaagac tgcctatgat gactttgcac agttcctgga tacatgttgc 1980
aaggctgctg acaaggacac ctgcttctcg actgagggtc caaaccttgt cactagatgc 2040
aaagacgct tagccggagg gggcgggtcc caccatcacc accatcactg ataa 2094

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&lt;210&gt; SEQ ID NO 59

&lt;211&gt; LENGTH: 2079

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL748-113- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 59

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atgagggctcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60

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atcgagctgc ggtgccggtg caccaacacc atcagcggca tccctttcaa cagcatcagc 120
ctcgtgaacg tgtacagacc cggcgtgcac tgcgccgacg tggaaagtgat tgctacactg 180
aagaatgggc agaaaacctg cctggacccc aacgcccctg gcgtgaagcg gatcgtgatg 240
aagattctgg aaggctacgg tggaggcggg agcggaggcg gagggtcggg agcacacaag 300
agtggagatcg cccatcggta taatgatttg ggagaacaac atttcaaagg cctagtccctg 360
attgcctttt cccagtatct ccagaaatgc tcatacagatg agcatgccaa attagtgcag 420
gaagtaacag actttgcaaa gacgtgtgtt gccgatgagt ctgccgccaa ctgtgacaaa 480
tcccttcaca ctcttttttg agataagttg tgtgccattc caaacctccg tgaaaactat 540
ggtgaactgg ctgactgctg tacaaaacaa gagcccgaag gaaacgaatg tttcctgcaa 600
cacaagatg acaaccccag cctgccacca tttgaaaggc cagaggctga ggccatgtgc 660
acctccttta aggaaaaccc aaccaccttt atgggacact atttgcatag agttgccaga 720
agacatcctt atttctatgc ccagaaactt ctttactatg ctgagcagta caatgagatt 780
ctgaccagtg gttgtgcaga ggctgacaag gaaagctgcc tgaccccgaag gcttgatggg 840
gtgaaggaga aagcattggg ctcatctgtc cgtcagagaa tgaagtgtcc cagtatgcag 900
aagtttgag agagagcttt taaagcatgg gcagttagctc gtctgagcca gacattcccc 960
aatgctgact ttgcagaaat caccaaattg gcaacagacc tgaccaaaagt caacaaggag 1020
tgctgccatg gtgacctgct ggaatcgcga gatgacaggg cggaacttgc caagtacatg 1080
tgtgaaaacc aggcgactat ctccagcaaa ctgcagactt gctgcgataa accactgttg 1140
aagaaagccc actgtcttag tgaggtggag catgacacca tgacctgctga tctgcctgcc 1200
attgctgctg attttgttga ggaccaggaa gtgtgcaaga actatgctga ggccaaggat 1260
gtcttctctg gcacgttctt gtatgaatat tcaagaagac acctgatta ctctgtatcc 1320
ctggttctga gacttgctaa gaaatatgaa gccactctgg aaaagtgtctg cgctgaagcc 1380
aatcctcccg catgctacgg cacagtgtt gctgaatttc agcctcttgt agaagagcct 1440
aagaacttgg tcaaaaccaa ctgtgatctt tacgagaagc ttggagaata tggattccaa 1500
aatgccattc tagttcgcta caccagaaa gcacctcagg tgtcaacccc aactctcgtg 1560
gaggctgcaa gaaacctagg aagagtgggc accaagtgtt gtacacttcc tgaagatcag 1620
agactgcctt gtgtggaaga ctatctgtct gcaatcctga accgtgtgtg tctgctgcat 1680
gagaagacc cagtgagtga gcatgttacc aagtgtgtg gtggatccct ggtggaagg 1740
cggccatgct tctctgtct gacagttgat gaaacatatg tccccaaga gtttaaagct 1800
gagaccttca ccttccactc tgatatctgc acacttccag agaaggagaa gcagattaag 1860
aaacaaacgg ctcttctgta gctggtgaag cacaagccca aggctacagc ggagcaactg 1920
aagactgtca tggatgactt tgcacagttc ctggatacat gttgcaaggc tgctgacaag 1980
gacacctgct tctcgactga ggttccaaac cttgtcacta gatgcaaga cgccttagcc 2040
ggagggggcg gttcccacca tcaccacat cactgataa 2079

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&lt;210&gt; SEQ ID NO 60

&lt;211&gt; LENGTH: 2196

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL922-126-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

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<400> SEQUENCE: 60

atgaggggtcc cgcctcagct cctgggggtc ctgctgctct ggctcccagg tgcacgatgt 60  
accctcgtga tccggaacgc ccggtgcagc tgtatcagca ccagcagagg caccatccac 120  
tacaagagcc tgaaggatct gaagcagttc gccccagcc ccaactgcaa caagaccgag 180  
attatcgcca cactgaaaaa cggggaccag acctgtctgg accccgacag cgccaactg 240  
aagaaactga tgaaggaatg ggagaagaag atcagccaga agaagaagca gaagcggggc 300  
aagaaacacc agaaaaacat gaagaaccgg aagcccaaga cccccagag cggcgggaga 360  
tccagaaaga ccacaggtgg aggcggtagc ggagcggag ggtcggaagc acacaagagt 420  
gagatcgcgc atcgggtataa tgatttggga gaacaacatt tcaaaggcct agtcctgatt 480  
gccttttccc agtatctcca gaaatgctca tacgatgagc atgccaatt agtgcaggaa 540  
gtaacagact ttgcaaagac gtgtgtgccc gatgagctg cgcccaactg tgacaaatcc 600  
cttcacactc tttttggaga taagttgtgt gccattccaa acctcctga aaactatggt 660  
gaactggctg actgctgtac aaaacaagag cccgaaagaa acgaatgttt cctgcaacac 720  
aaagatgaca accccagcct gccaccattt gaaaggccag aggctgaggc catgtgcacc 780  
tcctttaagg aaaacccaac cacctttatg ggacactatt tgcatgaagt tgccagaaga 840  
catccttatt tctatgcccc agaacttctt tactatgctg agcagtacaa tgagattctg 900  
accagtggtt gtgcagaggc tgacaaggaa agctgcctga ccccgaaagt tgatggtgtg 960  
aaggagaaaag cattggtctc atctgtccgt cagagaatga agtgctccag tatgcagaag 1020  
tttgagagaga gagcttttaa agcatgggca gtagctctgc tgagccagac attcccaat 1080  
gctgactttg cagaaatcac caaattggca acagacctga ccaaagtcaa caaggagtgc 1140  
tgccatgggt acctgctgga atgcgcagat gacaggcggg aacttgccaa gtacatgtgt 1200  
gaaaaccagg cgactatctc cagcaaacctg cagacttgct gcgataaacc actggtgaag 1260  
aaagcccact gtcttagtga ggtggagcat gacaccatgc ctgctgatct gcctgccatt 1320  
gctgctgatt ttgttgagga ccaggaagtg tgcaagaact atgctgaggc caaggatgtc 1380  
ttcctgggca cgttcttgta tgaatattca agaagacacc ctgattactc tgtatccctg 1440  
ttgctgagac ttgctaagaa atatgaagcc actctggaag agtgctgcgc tgaagccaat 1500  
cctcccgcct gctacggcac agtgcctgct gaatttcagc ctctttaga agagcctaag 1560  
aacttggtca aaaccaactg tgatctttac gagaagcttg gagaatatgg attccaaaat 1620  
gccattctag ttcgctacac ccagaaagca cctcaggtgt caacccaac tctcgtggag 1680  
gctgcaagaa acctaggaag agtgggcacc aagtgttga cacttcctga agatcagaga 1740  
ctgccttggt tggaaagacta tctgtctgca atcctgaacc gtgtgtgtct gctgcatgag 1800  
aagaccccag tgagttagca tgttaccaag tgctgtagtg gatccctggt ggaaaggcgg 1860  
ccatgcttct ctgctctgac agttgatgaa acatatgtcc ccaagagtt taaagctgag 1920  
accttcacct tccactctga tatctgcaca cttccagaga aggagaagca gattaagaaa 1980  
caaacggctc ttgctgagct ggtgaagcac aagcccaagg ctacagcggg gcaactgaag 2040  
actgtcatgg atgactttgc acagttctg gatacatggt gcaaggctgc tgacaaggac 2100  
acctgcttct cgactgaggg tccaaaacct gtcactagat gcaagacgc cttagccgga 2160  
ggggcggtt cccaccatca ccaccatcac tgataa 2196

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<210> SEQ ID NO 61  
<211> LENGTH: 2112  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL1022-98- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

<400> SEQUENCE: 61

atgagggctcc cgcgtcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60  
atccccactgg ccagaaccgt gcggtgcaac tgcacccaca tcgacgatgg ccccgtagcg 120  
atgagagcca tcggcaagct ggaatcctc cccgccagcc tgagctgccc cagagtggaa 180  
attatcgcca ccatgaagaa gaacgacgag cagcgggtgcc tgaaccccca gagcaagacc 240  
atcaagaacc tgatgaaggc ctttagccag aagcggagca agagggcccc aggtggaggc 300  
ggtagcggag gcggagggtc ggaagcacac aagagtgaga tcgcccctcg gtataatgat 360  
ttgggagaac aacatttcaa aggcctagtc ctgattgcct tttcccagta tctccagaaa 420  
tgctcatacg atgagcatgc caaattagtg caggaagtaa cagactttgc aaagacgtgt 480  
gttgccgatg agtctgccc caactgtgac aaatccctc acactctttt tggagataag 540  
ttgtgtgcca ttccaaacct ccgtgaaaac tatggtgaac tggctgactg ctgtacaaaa 600  
caagagcccc aaagaaacga atgtttcctg caacacaaag atgacaaccc cagcctgcca 660  
ccatttgaag ggccagaggc tgaggccatg tgcacctcct ttaaggaaaa cccaaccacc 720  
tttatgggac actatttgca tgaagttgcc agaagacatc cttatctcta tgccccagaa 780  
cttctttact atgctgagca gtacaatgag attctgacct agtgttctgc agaggctgac 840  
aaggaaagct gcctgacccc gaagcttgat ggtgtgaagg agaaagcatt ggtctcatct 900  
gtccgtcaga gaatgaagtg ctccagtatg cagaagttg gagagagagc ttttaaagca 960  
tgggcagtag ctgctctgag ccagacattc cccaatgctg actttgcaga aatcaccaaa 1020  
ttggcaacag acctgaccaa agtcaacaag gagtgtgccc atggtgacct gctggaatgc 1080  
gcagatgaca gggcggaaact tgccaagtac atgtgtgaaa accagggcagc tatctccagc 1140  
aaactgcaga cttgctgcga taaacctctg ttgaagaaag cccactgtct tagtgagggtg 1200  
gagcatgaca ccatgctgct tgatctgctt gccattgctg ctgattttgt tgaggaccag 1260  
gaagtgtgca agaactatgc tgaggccaag gatgtcttcc tgggcacggt cttgtatgaa 1320  
tattcaagaa gacacctga ttactctgta tccctgttgc tgagacttgc taagaaat 1380  
gaagccactc tggaaaagtg ctgcgctgaa gccaatcctc ccgatgcta cggcacagtg 1440  
cttgctgaat ttcagcctct tgtagaagag cctaagaact tggcctcctc caactgtgat 1500  
ctttacgaga agcttgagaga atatggattc caaaatgcca ttctagtctg ctacaccag 1560  
aaagcacctc aggtgtcaac cccaactctc gtggaggctg caagaaacct aggaagagtg 1620  
ggcaccagt gttgtacact tctgaagat cagagactgc cttgtgtgga agactatctg 1680  
tctgcaatcc tgaacctgtg gtgtctgctg catgagaaga cccagtgag tgagcatggt 1740  
accaagtgtc gtagtgatc cctggtggaa aggcggccat gcttctctgc tctgacagtt 1800  
gatgaaacat atgtcccca agagtttaa gctgagacct tcaccttcca ctctgatatc 1860  
tgcacacttc cagagaagga gaagcagatt aagaaacaaa cggctcttgc tgagctgggtg 1920

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aagcacaagc ccaaggctac agcggagcaa ctgaagactg tcatggatga cttgacacag 1980
ttcctggata catgttgcaa ggctgctgac aaggacacct gcttctcgac tgagggtcca 2040
aaccttgta ctatagtgaa agacgcctta gccggagggg gcggttccca ccatcaccac 2100
catcactgat aa 2112

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&lt;210&gt; SEQ ID NO 62

&lt;211&gt; LENGTH: 2118

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mCXCL1122-100- (Gly4Ser)2-  
mouse SA- (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 62

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atgagggtcc ccgctcagct cctggggctc ctgctgctct ggctcccagg tgcacgatgt 60
ttcctgatgt tcaagcaggg ccggtgctg tgcacggcc ctggaatgaa ggccgtgaa 120
atggccgaga tcgagaaggc cagcgtgatc taccacagca acggctgcga caagtgtaa 180
gtgatcgtga ccatgaaggc ccacaagcg cagagatgcc tggaccccag atccaagcag 240
gccccgctga tcatgcaggc tatcgagaag aagaatttcc tgcggcggca gaacatgggt 300
ggaggcggta gcggaggcgg agggctcggaa gcacacaaga gtgagatcgc ccatcgggat 360
aatgatattg gagaacaaca tttcaaagc ctagtctga ttgccttttc ccagtatctc 420
cagaaatgct catacagatg gcatgccaac ttagtgcagg aagtaacaga ctttgcaaag 480
acgtgtgttg ccgatgagtc tgcgccaac tgtgacaaat cccttcacac tctttttgga 540
gataagttgt gtgccattcc aaacctcctg gaaaactatg gtgaactggc tgactgctgt 600
acaaaacaag agcccgaag aaacgaatgt ttcctgcaac acaaagatga caaccccagc 660
ctgccacat ttgaaaggcc agaggctgag gccatgtgca cctcctttaa ggaaaaccca 720
accaccttta tgggacacta tttgcatgaa gttgccagaa gacatcctta tttctatgcc 780
ccagaacttc tttactatgc tgagcagtac aatgagattc tgacccagtg ttgtgcagag 840
gctgacaagg aaagctgcct gaccccgaag cttgatggtg tgaaggagaa agcattggtc 900
tcatctgtcc gtcagagaat gaagtgtccc agtatgcaga agtttgagaa gagagctttt 960
aaagcatggg cagtagctcg tctgagccag acattcccca atgctgactt tgcagaaatc 1020
accaaattgg caacagacct gaccaaagtc aacaaggagt gctgccatgg tgacctgctg 1080
gaatgcgcag atgacagggc ggaacttgc aagtacatgt gtgaaaacca ggcgactatc 1140
tccagcaaac tgcagacttg ctgcgataaa ccactgttga agaaagccca ctgtcttagt 1200
gaggtggagc atgacacatc gctgctgat ctgcctgcca ttgctgctga tttgtgtgag 1260
gaccaggaag tgtgcaagaa ctatgctgag gccaaaggatg tcttctggg cacgttcttg 1320
tatgaatatt caagaagaca cctgattac tctgtatccc tgttgtgag acttgctaag 1380
aaatatgaag ccactctgga aaagtgtgc gctgaagcca atcctccgc atgctacggc 1440
acagtgcttg ctgaatttca gcctcttgta gaagagccta agaacttggc caaaaaccaac 1500
tgtgatcttt acgagaagct tggagaatat ggattccaaa atgccattct agttcgtctc 1560
accagaaaag cacctcaggt gtaacaccca actctcgtgg aggctgcaag aaacctagga 1620
agagtgggca ccaagtgttg tacacttctc gaagatcaga gactgccttg tgtggaagac 1680
tatctgtctg caatcctgaa ccgtgtgtgt ctgctgcatg agaagacccc agtgagtgag 1740

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catgttacca agtgctgtag tggatccctg gtggaaggc ggccatgctt ctctgctctg 1800
acagttgatg aaacatatgt ccccaaagag tttaaagctg agaccttcac ctccactct 1860
gatatctgca cacttccaga gaaggagaag cagattaaga aacaaacggc tcttgctgag 1920
ctggtgaagc acaagcccaa ggctacagcg gagcaactga agactgtcat ggatgacttt 1980
gcacagttoc tggatacatg ttgcaaggct gctgacaagg acacctgctt ctcgactgag 2040
ggtccaaacc ttgtcactag atgcaaagac gccttagccg gagggggcgg ttcccacat 2100
caccaccatc actgataa 2118

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<210> SEQ ID NO 63
<211> LENGTH: 698
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: LS-hCXCL135-107-(Gly4Ser)2-mouse SA-
(Gly4Ser)-His6

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<400> SEQUENCE: 63

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Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro
1           5           10           15
Gly Ala Arg Cys Ala Ser Val Ala Thr Glu Leu Arg Cys Gln Cys Leu
20          25          30
Gln Thr Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val
35          40          45
Lys Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu
50          55          60
Lys Asn Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys
65          70          75          80
Lys Ile Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn Gly Gly Gly
85          90          95
Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His
100         105         110
Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile
115        120        125
Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys
130        135        140
Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu
145        150        155        160
Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys
165        170        175
Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp
180        185        190
Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His
195        200        205
Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu
210        215        220
Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His
225        230        235        240
Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
245        250        255
Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys
260        265        270

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Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val  
 275 280 285

Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser  
 290 295 300

Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala  
 305 310 315 320

Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys  
 325 330 335

Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp  
 340 345 350

Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys  
 355 360 365

Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys  
 370 375 380

Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr  
 385 390 395 400

Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln  
 405 410 415

Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr  
 420 425 430

Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu  
 435 440 445

Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys  
 450 455 460

Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe  
 465 470 475 480

Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp  
 485 490 495

Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val  
 500 505 510

Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu  
 515 520 525

Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro  
 530 535 540

Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu  
 545 550 555 560

Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val  
 565 570 575

Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser  
 580 585 590

Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu  
 595 600 605

Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys  
 610 615 620

Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro  
 625 630 635 640

Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln  
 645 650 655

Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser  
 660 665 670

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 Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly  
                   675  680  685

 Gly Gly Gly Ser His His His His His His  
       690  695

&lt;210&gt; SEQ ID NO 64

&lt;211&gt; LENGTH: 698

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-hCXCL235-107-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 64

 Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro  
   1                  5  10  15

 Gly Ala Arg Cys Ala Pro Leu Ala Thr Glu Leu Arg Cys Gln Cys Leu  
                   20  25  30

 Gln Thr Leu Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val Lys Val  
                   35  40  45

 Lys Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu  
   50  55  60

 Lys Asn Gly Gln Lys Ala Cys Leu Asn Pro Ala Ser Pro Met Val Lys  
   65  70  75  80

 Lys Ile Ile Glu Lys Met Leu Lys Asn Gly Lys Ser Asn Gly Gly Gly  
                   85  90  95

 Gly Ser Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His  
                   100  105  110

 Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile  
                   115  120  125

 Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys  
   130  135  140

 Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu  
   145  150  155  160

 Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys  
                   165  170  175

 Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp  
                   180  185  190

 Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His  
                   195  200  205

 Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu  
   210  215  220

 Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His  
   225  230  235  240

 Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu  
                   245  250  255

 Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys  
                   260  265  270

 Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val  
                   275  280  285

 Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser  
   290  295  300

 Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala  
   305  310  315  320

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Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys  
325 330 335

Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp  
340 345 350

Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys  
355 360 365

Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys  
370 375 380

Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr  
385 390 395 400

Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln  
405 410 415

Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr  
420 425 430

Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu  
435 440 445

Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys  
450 455 460

Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe  
465 470 475 480

Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp  
485 490 495

Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val  
500 505 510

Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu  
515 520 525

Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro  
530 535 540

Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu  
545 550 555 560

Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val  
565 570 575

Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser  
580 585 590

Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu  
595 600 605

Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys  
610 615 620

Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro  
625 630 635 640

Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln  
645 650 655

Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser  
660 665 670

Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly  
675 680 685

Gly Gly Gly Ser His His His His His His  
690 695

&lt;210&gt; SEQ ID NO 65

&lt;211&gt; LENGTH: 698

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<212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL335-107-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

<400> SEQUENCE: 65

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro  
 1 5 10 15  
 Gly Ala Arg Cys Ala Ser Val Val Thr Glu Leu Arg Cys Gln Cys Leu  
 20 25 30  
 Gln Thr Leu Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val Asn Val  
 35 40 45  
 Arg Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu  
 50 55 60  
 Lys Asn Gly Lys Lys Ala Cys Leu Asn Pro Ala Ser Pro Met Val Gln  
 65 70 75 80  
 Lys Ile Ile Glu Lys Ile Leu Asn Lys Gly Ser Thr Asn Gly Gly Gly  
 85 90 95  
 Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His  
 100 105 110  
 Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile  
 115 120 125  
 Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys  
 130 135 140  
 Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu  
 145 150 155 160  
 Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys  
 165 170 175  
 Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp  
 180 185 190  
 Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His  
 195 200 205  
 Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu  
 210 215 220  
 Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His  
 225 230 235 240  
 Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu  
 245 250 255  
 Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys  
 260 265 270  
 Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val  
 275 280 285  
 Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser  
 290 295 300  
 Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala  
 305 310 315 320  
 Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys  
 325 330 335  
 Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp  
 340 345 350  
 Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys  
 355 360 365

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Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys  
 370 375 380  
 Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr  
 385 390 395 400  
 Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln  
 405 410 415  
 Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr  
 420 425 430  
 Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu  
 435 440 445  
 Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys  
 450 455 460  
 Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe  
 465 470 475 480  
 Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp  
 485 490 495  
 Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val  
 500 505 510  
 Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu  
 515 520 525  
 Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro  
 530 535 540  
 Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu  
 545 550 555 560  
 Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val  
 565 570 575  
 Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser  
 580 585 590  
 Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu  
 595 600 605  
 Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys  
 610 615 620  
 Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro  
 625 630 635 640  
 Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln  
 645 650 655  
 Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser  
 660 665 670  
 Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly  
 675 680 685  
 Gly Gly Gly Ser His His His His His His  
 690 695

&lt;210&gt; SEQ ID NO 66

&lt;211&gt; LENGTH: 695

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-hCXCL432-101-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 66

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro

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1	5	10	15
Gly Ala Arg Cys Glu Ala Glu Glu Asp Gly Asp Leu Gln Cys Leu Cys	20	25	30
Val Lys Thr Thr Ser Gln Val Arg Pro Arg His Ile Thr Ser Leu Glu	35	40	45
Val Ile Lys Ala Gly Pro His Cys Pro Thr Ala Gln Leu Ile Ala Thr	50	55	60
Leu Lys Asn Gly Arg Lys Ile Cys Leu Asp Leu Gln Ala Pro Leu Tyr	65	70	75
Lys Lys Ile Ile Lys Lys Leu Leu Glu Ser Gly Gly Gly Ser Gly	85	90	95
Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn	100	105	110
Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser	115	120	125
Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln	130	135	140
Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala	145	150	155
Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala	165	170	175
Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr	180	185	190
Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp	195	200	205
Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys	210	215	220
Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His	225	230	235
Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr	245	250	255
Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala	260	265	270
Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys	275	280	285
Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln	290	295	300
Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser	305	310	315
Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr	325	330	335
Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu	340	345	350
Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln	355	360	365
Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu	370	375	380
Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala	385	390	395
Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys	405	410	415

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Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr  
                   420                                  425                                  430  
 Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg  
                   435                                  440                                  445  
 Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala  
                   450                                  455                                  460  
 Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu  
                   465                                  470                                  475                                  480  
 Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu  
                                   485                                  490                                  495  
 Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr  
                                   500                                  505                                  510  
 Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg  
                                   515                                  520                                  525  
 Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln  
                   530                                  535                                  540  
 Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val  
                   545                                  550                                  555                                  560  
 Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys  
                                   565                                  570                                  575  
 Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr  
                                   580                                  585                                  590  
 Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr  
                                   595                                  600                                  605  
 Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys  
                   610                                  615                                  620  
 Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr  
                   625                                  630                                  635                                  640  
 Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp  
                                   645                                  650                                  655  
 Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly  
                                   660                                  665                                  670  
 Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly  
                   675                                  680                                  685  
 Ser His His His His His His  
                   690                                  695

&lt;210&gt; SEQ ID NO 67

&lt;211&gt; LENGTH: 696

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

 <223> OTHER INFORMATION: Synthetic: LS-hCXCL544-114-(Gly4Ser)2-mouse SA-  
 (Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 67

 Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro  
 1                  5                                  10                                  15

 Gly Ala Arg Cys Leu Arg Glu Leu Arg Cys Val Cys Leu Gln Thr Thr  
 20                                  25                                  30

 Gln Gly Val His Pro Lys Met Ile Ser Asn Leu Gln Val Phe Ala Ile  
 35                                  40                                  45

Gly Pro Gln Cys Ser Lys Val Glu Val Val Ala Ser Leu Lys Asn Gly



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50		55			60										
Lys 65	Glu	Ile	Cys	Leu	Asp 70	Pro	Glu	Ala	Pro	Phe 75	Leu	Lys	Lys	Val	Ile 80
Gln	Lys	Ile	Leu	Asp 85	Gly	Gly	Asn	Lys	Glu 90	Asn	Gly	Gly	Gly	Gly	Ser 95
Gly	Gly	Gly	Gly	Ser 100	Glu	Ala	His	Lys 105	Ser	Glu	Ile	Ala	His	Arg	Tyr 110
Asn	Asp	Leu	Gly	Glu	Gln	His	Phe 120	Lys	Gly	Leu	Val	Leu	Ile	Ala	Phe 125
Ser	Gln	Tyr	Leu	Gln	Lys 135	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu	Val 140
Gln	Glu	Val	Thr	Asp 145	Phe	Ala	Lys	Thr	Cys 150	Val	Ala	Asp	Glu	Ser	Ala 160
Ala	Asn	Cys	Asp	Lys 165	Ser	Leu	His	Thr	Leu 170	Phe	Gly	Asp	Lys	Leu	Cys 175
Ala	Ile	Pro	Asn	Leu	Arg	Glu	Asn 180	Tyr	Gly 185	Glu	Leu	Ala	Asp	Cys	Cys 190
Thr	Lys	Gln	Glu	Pro	Glu	Arg	Asn 200	Glu	Cys	Phe	Leu	Gln	His	Lys	Asp 205
Asp	Asn	Pro	Ser	Leu	Pro	Pro	Phe 215	Glu	Arg	Pro	Glu	Ala	Glu	Ala	Met 220
Cys	Thr	Ser	Phe	Lys 225	Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr	Leu 240
His	Glu	Val	Ala	Arg 245	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu 255
Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu 260	Ile	Leu 265	Thr	Gln	Cys	Cys	Ala	Glu 270
Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr 280	Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu 285
Lys	Ala	Leu	Val	Ser	Ser	Val	Arg 295	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met 300
Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe 310	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu 320
Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp 325	Phe	Ala 330	Glu	Ile	Thr	Lys	Leu	Ala 335
Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys 340	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu 350
Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu 360	Leu	Ala	Lys	Tyr	Met	Cys	Glu	Asn 365
Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu 370	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu 380
Leu	Lys	Lys	Ala	His	Cys	Leu	Ser 385	Glu	Val	Glu	His	Asp	Thr	Met	Pro 400
Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala 405	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val 415
Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys 420	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu 430
Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro 435	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu 445
Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala 450	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu 460

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Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro  
465 470 475 480

Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr  
485 490 495

Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr  
500 505 510

Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala  
515 520 525

Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp  
530 535 540

Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg  
545 550 555 560

Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr Lys  
565 570 575

Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu  
580 585 590

Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe  
595 600 605

Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile  
610 615 620

Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala  
625 630 635 640

Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu  
645 650 655

Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu  
660 665 670

Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly  
675 680 685

Gly Ser His His His His His His  
690 695

&lt;210&gt; SEQ ID NO 68

&lt;211&gt; LENGTH: 697

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-hCXCL643-114-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 68

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro  
1 5 10 15

Gly Ala Arg Cys Val Leu Thr Glu Leu Arg Cys Thr Cys Leu Arg Val  
20 25 30

Thr Leu Arg Val Asn Pro Lys Thr Ile Gly Lys Leu Gln Val Phe Pro  
35 40 45

Ala Gly Pro Gln Cys Ser Lys Val Glu Val Val Ala Ser Leu Lys Asn  
50 55 60

Gly Lys Gln Val Cys Leu Asp Pro Glu Ala Pro Phe Leu Lys Lys Val  
65 70 75 80

Ile Gln Lys Ile Leu Asp Ser Gly Asn Lys Lys Asn Gly Gly Gly Gly  
85 90 95

Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg

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100					105					110					
Tyr	Asn	Asp	Leu	Gly	Glu	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala
	115						120					125			
Phe	Ser	Gln	Tyr	Leu	Gln	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu
	130					135					140				
Val	Gln	Glu	Val	Thr	Asp	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser
145					150					155					160
Ala	Ala	Asn	Cys	Asp	Lys	Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	Lys	Leu
				165					170					175	
Cys	Ala	Ile	Pro	Asn	Leu	Arg	Glu	Asn	Tyr	Gly	Glu	Leu	Ala	Asp	Cys
			180					185						190	
Cys	Thr	Lys	Gln	Glu	Pro	Glu	Arg	Asn	Glu	Cys	Phe	Leu	Gln	His	Lys
		195					200						205		
Asp	Asp	Asn	Pro	Ser	Leu	Pro	Pro	Phe	Glu	Arg	Pro	Glu	Ala	Glu	Ala
	210					215					220				
Met	Cys	Thr	Ser	Phe	Lys	Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr
225					230					235					240
Leu	His	Glu	Val	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu
				245					250					255	
Leu	Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala
			260				265						270		
Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys
		275					280					285			
Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser
	290					295					300				
Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg
305					310					315					320
Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu
				325					330					335	
Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu
			340					345					350		
Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu
		355					360					365			
Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro
	370					375					380				
Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met
385					390					395					400
Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu
				405					410					415	
Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe
			420					425					430		
Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu
		435					440					445			
Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala
	450					455					460				
Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln
465					470					475					480
Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu
				485					490					495	
Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg
			500					505					510		

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Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala
    515                                520                                525

Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu
    530                                535                                540

Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn
    545                                550                                555                                560

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr
                                565                                570                                575

Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala
    580                                585                                590

Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr
    595                                600                                605

Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln
    610                                615                                620

Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys
    625                                630                                635                                640

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe
    645                                650                                655

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr
    660                                665                                670

Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly
    675                                680                                685

Gly Gly Ser His His His His His His
    690                                695

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&lt;210&gt; SEQ ID NO 69

&lt;211&gt; LENGTH: 688

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-hCXCL759-121-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 69

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Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro
  1                                5                                10                                15

Gly Ala Arg Cys Ala Glu Leu Arg Cys Met Cys Ile Lys Thr Thr Ser
    20                                25                                30

Gly Ile His Pro Lys Asn Ile Gln Ser Leu Glu Val Ile Gly Lys Gly
    35                                40                                45

Thr His Cys Asn Gln Val Glu Val Ile Ala Thr Leu Lys Asp Gly Arg
    50                                55                                60

Lys Ile Cys Leu Asp Pro Asp Ala Pro Arg Ile Lys Lys Ile Val Gln
    65                                70                                75                                80

Lys Lys Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ala His
    85                                90                                95

Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe
    100                               105                               110

Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser
    115                               120                               125

Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys
    130                               135                               140

Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His

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145	150	155	160
Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn	165	170	175
Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn	180	185	190
Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe	195	200	205
Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro	210	215	220
Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro	225	230	235
Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu	245	250	255
Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr	260	265	270
Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser Ser Val Arg	275	280	285
Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu Arg Ala Phe	290	295	300
Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp	305	310	315
Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys	325	330	335
Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu	340	345	350
Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu	355	360	365
Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser	370	375	380
Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala	385	390	395
Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys	405	410	415
Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro	420	425	430
Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala	435	440	445
Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly	450	455	460
Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro Lys Asn Leu	465	470	475
Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe	485	490	495
Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser	500	505	510
Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly Thr	515	520	525
Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp	530	535	540
Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr	545	550	555
			560

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Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu
      565                               570                               575
Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro
      580                               585                               590
Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr
      595                               600                               605
Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu
      610                               615                               620
Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val
      625                               630                               635                               640
Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp
      645                               650                               655
Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg Cys
      660                               665                               670
Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser His His His His His His
      675                               680                               685

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<210> SEQ ID NO 70
<211> LENGTH: 697
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: LS-hCXCL828-99- (Gly4Ser)2-mouse SA-
(Gly4Ser)-His6

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<400> SEQUENCE: 70

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```

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro
 1      5      10      15
Gly Ala Arg Cys Ser Ala Lys Glu Leu Arg Cys Gln Cys Ile Lys Thr
 20      25      30
Tyr Ser Lys Pro Phe His Pro Lys Phe Ile Lys Glu Leu Arg Val Ile
 35      40      45
Glu Ser Gly Pro His Cys Ala Asn Thr Glu Ile Ile Val Lys Leu Ser
 50      55      60
Asp Gly Arg Glu Leu Cys Leu Asp Pro Lys Glu Asn Trp Val Gln Arg
 65      70      75      80
Val Val Glu Lys Phe Leu Lys Arg Ala Glu Asn Ser Gly Gly Gly Gly
 85      90      95
Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg
100      105      110
Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
115      120      125
Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
130      135      140
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
145      150      155      160
Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
165      170      175
Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys
180      185      190
Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
195      200      205
Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala

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210			215			220									
Met	Cys	Thr	Ser	Phe	Lys	Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr
225					230					235					240
Leu	His	Glu	Val	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu
				245					250					255	
Leu	Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala
			260					265					270		
Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys
		275					280					285			
Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser
290					295						300				
Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg
305					310					315					320
Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu
				325					330					335	
Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu
		340						345					350		
Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu
		355					360					365			
Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro
370					375						380				
Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met
385					390						395				400
Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu
				405					410					415	
Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe
			420						425				430		
Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu
		435					440					445			
Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala
450					455						460				
Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln
465					470					475					480
Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu
				485					490					495	
Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg
			500					505					510		
Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala
		515					520						525		
Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu
530					535						540				
Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn
545					550					555					560
Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr
				565					570					575	
Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala
			580						585				590		
Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr
		595						600					605		
Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln
610						615							620		

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Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys
625                               630                               635                               640

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe
                               645                               650                               655

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr
                               660                               665                               670

Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly
                               675                               680                               685

Gly Gly Ser His His His His His His
690                               695

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<210> SEQ ID NO 71
<211> LENGTH: 728
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: LS-hCXCL923-115-(Gly4Ser)2-mouse SA-
(Gly4Ser)-His6

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<400> SEQUENCE: 71

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Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro
1                               5                               10                               15

Gly Ala Arg Cys Thr Pro Val Val Arg Lys Gly Arg Cys Ser Cys Ile
                               20                               25                               30

Ser Thr Asn Gln Gly Thr Ile His Leu Gln Ser Leu Lys Asp Leu Lys
                               35                               40                               45

Gln Phe Ala Pro Ser Pro Ser Cys Glu Lys Ile Glu Ile Ile Ala Thr
50                               55                               60

Leu Lys Asn Gly Val Gln Thr Cys Leu Asn Pro Asp Ser Ala Asp Val
65                               70                               75                               80

Lys Glu Leu Ile Lys Lys Trp Glu Lys Gln Val Ser Gln Lys Lys Lys
                               85                               90                               95

Gln Lys Asn Gly Lys Lys His Gln Lys Lys Lys Val Leu Lys Val Arg
100                              105                              110

Lys Ser Gln Arg Ser Arg Gln Lys Lys Thr Thr Gly Gly Gly Gly Ser
115                              120                              125

Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr
130                              135                              140

Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe
145                              150                              155                              160

Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val
165                              170                              175

Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala
180                              185                              190

Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys
195                              200                              205

Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys
210                              215                              220

Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp
225                              230                              235                              240

Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met
245                              250                              255

Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu

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260					265					270					
His	Glu	Val	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu
	275						280					285			
Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala	Glu
	290					295					300				
Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu
305					310					315					320
Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met
				325					330						335
Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu
			340						345						350
Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu	Ala
			355				360						365		
Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu
370						375					380				
Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu	Asn
385					390					395					400
Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu
				405					410						415
Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met	Pro
			420					425						430	
Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val
		435					440					445			
Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu
450						455					460				
Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu
465					470					475					480
Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu
				485					490						495
Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro
			500					505						510	
Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr
		515					520						525		
Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr
530						535					540				
Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala
545					550					555					560
Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	Asp
				565					570						575
Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn	Arg
			580					585						590	
Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr	Lys
		595					600						605		
Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu
610						615					620				
Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	Phe
625					630					635					640
Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile
				645					650						655
Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala
				660				665							670

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Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu  
675 680 685

Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu  
690 695 700

Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly  
705 710 715 720

Gly Ser His His His His His His  
725

<210> SEQ ID NO 72  
<211> LENGTH: 702  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: LS-hCXCL1022-98-(Gly4Ser)2-mouse SA-  
(Gly4Ser)-His6

<400> SEQUENCE: 72

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro  
1 5 10 15

Gly Ala Arg Cys Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys Ile  
20 25 30

Ser Ile Ser Asn Gln Pro Val Asn Pro Arg Ser Leu Glu Lys Leu Glu  
35 40 45

Ile Ile Pro Ala Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala Thr  
50 55 60

Met Lys Lys Lys Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser Lys Ala  
65 70 75 80

Ile Lys Asn Leu Leu Lys Ala Val Ser Lys Glu Arg Ser Lys Arg Ser  
85 90 95

Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser  
100 105 110

Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly  
115 120 125

Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp  
130 135 140

Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys  
145 150 155 160

Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu  
165 170 175

Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly  
180 185 190

Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys  
195 200 205

Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg  
210 215 220

Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr  
225 230 235 240

Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe  
245 250 255

Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu  
260 265 270

Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys

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275					280					285					
Leu	Asp	Gly	Val	Lys	Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg
290					295					300					
Met	Lys	Cys	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala
305					310					315					320
Trp	Ala	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala
				325					330					335	
Glu	Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys
			340					345					350		
Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala
		355					360					365			
Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr
	370					375					380				
Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val
385					390					395					400
Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe
				405					410					415	
Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val
			420					425					430		
Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr
		435					440					445			
Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu
	450					455					460				
Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val
465					470					475					480
Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys
				485					490					495	
Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn
			500					505					510		
Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro
		515					520					525			
Thr	Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys
	530					535					540				
Cys	Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu
545					550					555					560
Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val
				565					570					575	
Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg
		580						585					590		
Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu
		595					600					605			
Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro
	610					615					620				
Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val
625					630					635					640
Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp
				645					650					655	
Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp
			660					665					670		
Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp
		675					680						685		

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Ala Leu Ala Gly Gly Gly Gly Ser His His His His His His  
690 695 700

&lt;210&gt; SEQ ID NO 73

&lt;211&gt; LENGTH: 698

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-hCXCL1122-94-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 73

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro  
1 5 10 15

Gly Ala Arg Cys Phe Pro Met Phe Lys Arg Gly Arg Cys Leu Cys Ile  
20 25 30

Gly Pro Gly Val Lys Ala Val Lys Val Ala Asp Ile Glu Lys Ala Ser  
35 40 45

Ile Met Tyr Pro Ser Asn Asn Cys Asp Lys Ile Glu Val Ile Ile Thr  
50 55 60

Leu Lys Glu Asn Lys Gly Gln Arg Cys Leu Asn Pro Lys Ser Lys Gln  
65 70 75 80

Ala Arg Leu Ile Ile Lys Lys Val Glu Arg Lys Asn Phe Gly Gly Gly  
85 90 95

Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His  
100 105 110

Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile  
115 120 125

Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys  
130 135 140

Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu  
145 150 155 160

Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys  
165 170 175

Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp  
180 185 190

Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His  
195 200 205

Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu  
210 215 220

Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His  
225 230 235 240

Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu  
245 250 255

Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys  
260 265 270

Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val  
275 280 285

Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser  
290 295 300

Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala  
305 310 315 320

Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys

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325				330				335							
Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp
			340						345				350		
Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys
		355					360						365		
Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys
	370					375					380				
Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr
	385				390					395					400
Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln
			405						410						415
Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr
			420						425						430
Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu
	435						440						445		
Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys
	450					455					460				
Ala	Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe
	465				470					475					480
Gln	Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp
			485						490						495
Leu	Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val
			500						505				510		
Arg	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu
		515					520						525		
Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro
	530					535					540				
Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu
	545				550					555					560
Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val
			565							570					575
Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser
			580							585					590
Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu
		595					600						605		
Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys
	610					615					620				
Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro
	625					630					635				640
Lys	Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln
			645							650					655
Phe	Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser
		660							665						670
Thr	Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly
		675					680						685		
Gly	Gly	Gly	Ser	His	His	His	His	His	His	His	His				
	690						695								

&lt;210&gt; SEQ ID NO 74

&lt;211&gt; LENGTH: 697

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

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&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: LS-mCXCL125-96- (Gly4Ser)2-mouse SA-  
(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 74

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Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro
1          5          10          15
Gly Ala Arg Cys Ala Pro Ile Ala Asn Glu Leu Arg Cys Gln Cys Leu
20          25          30
Gln Thr Met Ala Gly Ile His Leu Lys Asn Ile Gln Ser Leu Lys Val
35          40          45
Leu Pro Ser Gly Pro His Cys Thr Gln Thr Glu Val Ile Ala Thr Leu
50          55          60
Lys Asn Gly Arg Glu Ala Cys Leu Asp Pro Glu Ala Pro Leu Val Gln
65          70          75          80
Lys Ile Val Gln Lys Met Leu Lys Gly Val Pro Lys Gly Gly Gly Gly
85          90          95
Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His Arg
100         105         110
Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
115         120         125
Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
130         135         140
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
145         150         155         160
Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
165         170         175
Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys
180         185         190
Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
195         200         205
Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala
210         215         220
Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr
225         230         235         240
Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
245         250         255
Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala
260         265         270
Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys
275         280         285
Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser
290         295         300
Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
305         310         315         320
Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu
325         330         335
Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu
340         345         350
Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu
355         360         365
Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro

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370			375			380									
Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met
385				390					395						400
Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu
			405						410					415	
Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe
			420					425					430		
Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu
		435					440					445			
Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala
	450					455					460				
Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln
465				470						475					480
Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu
			485						490					495	
Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg
		500						505					510		
Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala
		515					520					525			
Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu
	530					535					540				
Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn
545				550						555					560
Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr
			565						570					575	
Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala
			580					585					590		
Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr
		595					600					605			
Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln
	610					615					620				
Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys
625					630					635					640
Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe
			645						650					655	
Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr
		660						665					670		
Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly	Gly
		675					680					685			
Gly	Gly	Ser	His	His	His	His	His	His							
	690					695									

<210> SEQ ID NO 75  
 <211> LENGTH: 698  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mCXCL228-100-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6  
 <400> SEQUENCE: 75

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro  
 1 5 10 15

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Gly Ala Arg Cys Ala Val Val Ala Ser Glu Leu Arg Cys Gln Cys Leu  
                   20                                  25                                  30  
 Lys Thr Leu Pro Arg Val Asp Phe Lys Asn Ile Gln Ser Leu Ser Val  
                   35                                  40                                  45  
 Thr Pro Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu  
                   50                                  55                                  60  
 Lys Gly Gly Gln Lys Val Cys Leu Asp Pro Glu Ala Pro Leu Val Gln  
                   65                                  70                                  75                                  80  
 Lys Ile Ile Gln Lys Ile Leu Asn Lys Gly Lys Ala Asn Gly Gly Gly  
                   85                                  90                                  95  
 Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His  
                   100                                  105                                  110  
 Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile  
                   115                                  120                                  125  
 Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys  
                   130                                  135                                  140  
 Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu  
                   145                                  150                                  155                                  160  
 Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys  
                   165                                  170                                  175  
 Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp  
                   180                                  185                                  190  
 Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His  
                   195                                  200                                  205  
 Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu  
                   210                                  215                                  220  
 Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His  
                   225                                  230                                  235                                  240  
 Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu  
                   245                                  250                                  255  
 Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys  
                   260                                  265                                  270  
 Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val  
                   275                                  280                                  285  
 Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser  
                   290                                  295                                  300  
 Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala  
                   305                                  310                                  315                                  320  
 Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys  
                   325                                  330                                  335  
 Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp  
                   340                                  345                                  350  
 Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys  
                   355                                  360                                  365  
 Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys  
                   370                                  375                                  380  
 Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr  
                   385                                  390                                  395                                  400  
 Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln  
                   405                                  410                                  415  
 Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr



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      420          425          430
Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu
   435                      440          445
Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys
   450                      455          460
Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe
   465                      470          475          480
Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp
   485                      490          495
Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val
   500                      505          510
Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu
   515                      520          525
Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro
   530                      535          540
Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu
   545                      550          555          560
Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val
   565                      570          575
Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser
   580                      585          590
Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu
   595                      600          605
Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys
   610                      615          620
Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro
   625                      630          635          640
Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln
   645                      650          655
Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser
   660                      665          670
Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly
   675                      680          685
Gly Gly Gly Ser His His His His His His
   690                      695

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&lt;210&gt; SEQ ID NO 76

&lt;211&gt; LENGTH: 698

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-mCXCL328-100-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 76

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Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro
 1          5          10          15
Gly Ala Arg Cys Ala Val Val Ala Ser Glu Leu Arg Cys Gln Cys Leu
 20          25          30
Asn Thr Leu Pro Arg Val Asp Phe Glu Thr Ile Gln Ser Leu Thr Val
 35          40          45
Thr Pro Pro Gly Pro His Cys Thr Gln Thr Glu Val Ile Ala Thr Leu
 50          55          60

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Lys Asp Gly Gln Glu Val Cys Leu Asn Pro Gln Gly Pro Arg Leu Gln  
 65 70 75 80

Ile Ile Ile Lys Lys Ile Leu Lys Ser Gly Lys Ser Ser Gly Gly Gly  
 85 90 95

Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu Ile Ala His  
 100 105 110

Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile  
 115 120 125

Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys  
 130 135 140

Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu  
 145 150 155 160

Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys  
 165 170 175

Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp  
 180 185 190

Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His  
 195 200 205

Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu  
 210 215 220

Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His  
 225 230 235 240

Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu  
 245 250 255

Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys  
 260 265 270

Ala Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val  
 275 280 285

Lys Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser  
 290 295 300

Ser Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala  
 305 310 315 320

Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys  
 325 330 335

Leu Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp  
 340 345 350

Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys  
 355 360 365

Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys  
 370 375 380

Pro Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr  
 385 390 395 400

Met Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln  
 405 410 415

Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr  
 420 425 430

Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu  
 435 440 445

Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys  
 450 455 460

Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe

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465              470              475              480
Gln Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp
              485              490              495
Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val
              500              505              510
Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu
              515              520              525
Ala Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro
              530              535              540
Glu Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu
545              550              555              560
Asn Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val
              565              570              575
Thr Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser
              580              585              590
Ala Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu
595              600              605
Thr Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys
610              615              620
Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro
625              630              635              640
Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln
645              650              655
Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser
660              665              670
Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly
675              680              685
Gly Gly Gly Ser His His His His His His
690              695

<210> SEQ ID NO 77
<211> LENGTH: 701
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: LS-mCXCL430-105-(Gly4Ser)2-mouse SA-
(Gly4Ser)-His6

<400> SEQUENCE: 77
Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro
1              5              10              15
Gly Ala Arg Cys Val Thr Ser Ala Gly Pro Glu Glu Ser Asp Gly Asp
20              25              30
Leu Ser Cys Val Cys Val Lys Thr Ile Ser Ser Gly Ile His Leu Lys
35              40              45
His Ile Thr Ser Leu Glu Val Ile Lys Ala Gly Arg His Cys Ala Val
50              55              60
Pro Gln Leu Ile Ala Thr Leu Lys Asn Gly Arg Lys Ile Cys Leu Asp
65              70              75              80
Arg Gln Ala Pro Leu Tyr Lys Lys Val Ile Lys Lys Ile Leu Glu Ser
85              90              95
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser Glu
100             105             110

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Ile	Ala	His	Arg	Tyr	Asn	Asp	Leu	Gly	Glu	Gln	His	Phe	Lys	Gly	Leu
		115					120					125			
Val	Leu	Ile	Ala	Phe	Ser	Gln	Tyr	Leu	Gln	Lys	Cys	Ser	Tyr	Asp	Glu
	130					135					140				
His	Ala	Lys	Leu	Val	Gln	Glu	Val	Thr	Asp	Phe	Ala	Lys	Thr	Cys	Val
145					150					155					160
Ala	Asp	Glu	Ser	Ala	Ala	Asn	Cys	Asp	Lys	Ser	Leu	His	Thr	Leu	Phe
				165					170					175	
Gly	Asp	Lys	Leu	Cys	Ala	Ile	Pro	Asn	Leu	Arg	Glu	Asn	Tyr	Gly	Glu
			180					185					190		
Leu	Ala	Asp	Cys	Cys	Thr	Lys	Gln	Glu	Pro	Glu	Arg	Asn	Glu	Cys	Phe
		195					200					205			
Leu	Gln	His	Lys	Asp	Asp	Asn	Pro	Ser	Leu	Pro	Pro	Phe	Glu	Arg	Pro
	210					215					220				
Glu	Ala	Glu	Ala	Met	Cys	Thr	Ser	Phe	Lys	Glu	Asn	Pro	Thr	Thr	Phe
225					230					235					240
Met	Gly	His	Tyr	Leu	His	Glu	Val	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr
				245					250					255	
Ala	Pro	Glu	Leu	Leu	Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr
			260					265					270		
Gln	Cys	Cys	Ala	Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu
			275				280					285			
Asp	Gly	Val	Lys	Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met
	290					295					300				
Lys	Cys	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp
305					310					315					320
Ala	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu
				325					330					335	
Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys
			340					345					350		
His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys
		355					360					365			
Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys
	370				375						380				
Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu
385					390					395					400
His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val
				405					410					415	
Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe
			420					425					430		
Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser
		435					440					445			
Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu
	450					455					460				
Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu
465					470					475					480
Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr
				485					490					495	
Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala
			500					505					510		
Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr

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515					520					525					
Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys
530						535					540				
Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser
545					550					555					560
Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser
				565					570						575
Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro
			580					585						590	
Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe
		595					600						605		
Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu
610						615						620			
Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys
625					630					635					640
His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp	Asp
				645					650						655
Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp	Thr
			660						665						670
Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp	Ala
		675					680							685	
Leu	Ala	Gly	Gly	Gly	Gly	Ser	His	His	His	His	His	His			
690						695						700			

<210> SEQ ID NO 78  
 <211> LENGTH: 696  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mCXCL548-118-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

<400> SEQUENCE: 78

Met	Arg	Val	Pro	Ala	Gln	Leu	Leu	Gly	Leu	Leu	Leu	Leu	Trp	Leu	Pro
1				5					10					15	
Gly	Ala	Arg	Cys	Ala	Thr	Glu	Leu	Arg	Cys	Val	Cys	Leu	Thr	Val	Thr
			20						25					30	
Pro	Lys	Ile	Asn	Pro	Lys	Leu	Ile	Ala	Asn	Leu	Glu	Val	Ile	Pro	Ala
			35				40						45		
Gly	Pro	Gln	Cys	Pro	Thr	Val	Glu	Val	Ile	Ala	Lys	Leu	Lys	Asn	Gln
			50				55					60			
Lys	Glu	Val	Cys	Leu	Asp	Pro	Glu	Ala	Pro	Val	Ile	Lys	Lys	Ile	Ile
65					70					75					80
Gln	Lys	Ile	Leu	Gly	Ser	Asp	Lys	Lys	Lys	Ala	Gly	Gly	Gly	Gly	Ser
				85						90					95
Gly	Gly	Gly	Gly	Ser	Glu	Ala	His	Lys	Ser	Glu	Ile	Ala	His	Arg	Tyr
				100					105						110
Asn	Asp	Leu	Gly	Glu	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala	Phe
				115					120						125
Ser	Gln	Tyr	Leu	Gln	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu	Val
		130					135							140	
Gln	Glu	Val	Thr	Asp	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser	Ala
145					150								155		160

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Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys  
165 170 175

Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys  
180 185 190

Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp  
195 200 205

Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met  
210 215 220

Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu  
225 230 235 240

His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu  
245 250 255

Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu  
260 265 270

Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu  
275 280 285

Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met  
290 295 300

Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu  
305 310 315 320

Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala  
325 330 335

Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu  
340 345 350

Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn  
355 360 365

Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu  
370 375 380

Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met Pro  
385 390 395 400

Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val  
405 410 415

Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu  
420 425 430

Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu  
435 440 445

Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu  
450 455 460

Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro  
465 470 475 480

Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr  
485 490 495

Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr  
500 505 510

Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala  
515 520 525

Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp  
530 535 540

Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg  
545 550 555 560

Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr Lys

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          565          570          575
Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu
      580          585          590
Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe
      595          600          605
Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile
      610          615          620
Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala
      625          630          635          640
Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu
      645          650          655
Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu
      660          665          670
Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly
      675          680          685
Gly Ser His His His His His His
      690          695

<210> SEQ ID NO 79
<211> LENGTH: 691
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: LS-mCXCL748-113-(Gly4Ser)2-mouse SA-
      (Gly4Ser)-His6

<400> SEQUENCE: 79
Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro
 1          5          10          15
Gly Ala Arg Cys Ile Glu Leu Arg Cys Arg Cys Thr Asn Thr Ile Ser
      20          25          30
Gly Ile Pro Phe Asn Ser Ile Ser Leu Val Asn Val Tyr Arg Pro Gly
      35          40          45
Val His Cys Ala Asp Val Glu Val Ile Ala Thr Leu Lys Asn Gly Gln
      50          55          60
Lys Thr Cys Leu Asp Pro Asn Ala Pro Gly Val Lys Arg Ile Val Met
      65          70          75          80
Lys Ile Leu Glu Gly Tyr Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
      85          90          95
Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu
      100          105          110
Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln
      115          120          125
Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp
      130          135          140
Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys
      145          150          155          160
Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu
      165          170          175
Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro
      180          185          190
Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu
      195          200          205

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Pro	Pro	Phe	Glu	Arg	Pro	Glu	Ala	Glu	Ala	Met	Cys	Thr	Ser	Phe	Lys
	210					215					220				
Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr	Leu	His	Glu	Val	Ala	Arg
225					230					235					240
Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu	Tyr	Tyr	Ala	Glu	Gln
				245					250					255	
Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala	Glu	Ala	Asp	Lys	Glu	Ser
		260						265					270		
Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu	Lys	Ala	Leu	Val	Ser
		275					280					285			
Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu
	290					295					300				
Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro
305					310					315					320
Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys
				325					330					335	
Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp
			340					345					350		
Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser
		355					360					365			
Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His
	370					375					380				
Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala
385					390					395					400
Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala
				405					410					415	
Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg
			420					425					430		
Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys
		435					440					445			
Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala
	450					455					460				
Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro
465					470					475					480
Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu
				485					490					495	
Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro
			500					505					510		
Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg
			515				520					525			
Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys
	530					535					540				
Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His
545					550					555					560
Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser
				565					570					575	
Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr
			580				585						590		
Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp
		595					600					605			
Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala



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610	615	620
Leu Ala Glu Leu Val	Lys His Lys Pro Lys	Ala Thr Ala Glu Gln Leu
625	630	635 640
Lys Thr Val Met Asp	Asp Phe Ala Gln Phe	Leu Asp Thr Cys Cys Lys
645	650	655
Ala Ala Asp Lys Asp	Thr Cys Phe Ser Thr	Glu Gly Pro Asn Leu Val
660	665	670
Thr Arg Cys Lys Asp	Ala Leu Ala Gly Gly	Gly Ser His His His
675	680	685
His His His		
690		
<210> SEQ ID NO 80		
<211> LENGTH: 730		
<212> TYPE: PRT		
<213> ORGANISM: Artificial Sequence		
<220> FEATURE:		
<223> OTHER INFORMATION: Synthetic: LS-mCXCL922-126-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6		
<400> SEQUENCE: 80		
Met Arg Val Pro Ala	Gln Leu Leu Gly	Leu Leu Leu Trp Leu Pro
1	5	10 15
Gly Ala Arg Cys Thr	Leu Val Ile Arg	Asn Ala Arg Cys Ser Cys Ile
20	25	30
Ser Thr Ser Arg Gly	Thr Ile His Tyr	Lys Ser Leu Lys Asp Leu Lys
35	40	45
Gln Phe Ala Pro Ser	Pro Asn Cys Asn	Lys Thr Glu Ile Ile Ala Thr
50	55	60
Leu Lys Asn Gly Asp	Gln Thr Cys Leu	Asp Pro Asp Ser Ala Asn Val
65	70	75 80
Lys Lys Leu Met Lys	Glu Trp Glu Lys	Lys Ile Ser Gln Lys Lys Lys
85	90	95
Gln Lys Arg Gly Lys	Lys His Gln Lys	Asn Met Lys Asn Arg Lys Pro
100	105	110
Lys Thr Pro Gln Ser	Arg Arg Ser Arg	Lys Thr Thr Gly Gly Gly
115	120	125
Gly Ser Gly Gly Gly	Gly Ser Glu Ala	His Lys Ser Glu Ile Ala His
130	135	140
Arg Tyr Asn Asp Leu	Gly Glu Gln His	Phe Lys Gly Leu Val Leu Ile
145	150	155 160
Ala Phe Ser Gln Tyr	Leu Gln Lys Cys	Ser Tyr Asp Glu His Ala Lys
165	170	175
Leu Val Gln Glu Val	Thr Asp Phe Ala	Lys Thr Cys Val Ala Asp Glu
180	185	190
Ser Ala Ala Asn Cys	Asp Lys Ser Leu	His Thr Leu Phe Gly Asp Lys
195	200	205
Leu Cys Ala Ile Pro	Asn Leu Arg Glu	Asn Tyr Gly Glu Leu Ala Asp
210	215	220
Cys Cys Thr Lys Gln	Glu Pro Glu Arg	Asn Glu Cys Phe Leu Gln His
225	230	235 240
Lys Asp Asp Asn Pro	Ser Leu Pro Pro	Phe Glu Arg Pro Glu Ala Glu
245	250	255

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Ala	Met	Cys	Thr	Ser	Phe	Lys	Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His
			260					265					270		
Tyr	Leu	His	Glu	Val	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu
		275					280					285			
Leu	Leu	Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys
	290					295					300				
Ala	Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val
305					310					315					320
Lys	Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser
				325					330					335	
Ser	Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala
		340						345					350		
Arg	Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys
		355					360					365			
Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp
	370					375					380				
Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys
385					390					395					400
Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys
				405					410					415	
Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr
			420					425					430		
Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln
		435					440					445			
Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr
	450					455					460				
Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu
465					470					475					480
Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys
				485					490					495	
Ala	Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe
			500					505					510		
Gln	Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp
		515					520					525			
Leu	Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val
	530					535					540				
Arg	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu
545					550					555					560
Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro
				565					570					575	
Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu
			580					585					590		
Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val
		595					600					605			
Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser
	610					615						620			
Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu
625					630					635					640
Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys
				645					650					655	
Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro

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660	665	670
Lys Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln		
675	680	685
Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser		
690	695	700
Thr Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly		
705	710	715
Gly Gly Gly Ser His His His His His His		
	725	730

&lt;210&gt; SEQ ID NO 81

&lt;211&gt; LENGTH: 702

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-mCXCL1022-98-(Gly4Ser)2-mouse SA-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 81

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro		
1	5	10
Gly Ala Arg Cys Ile Pro Leu Ala Arg Thr Val Arg Cys Asn Cys Ile		
	20	25
His Ile Asp Asp Gly Pro Val Arg Met Arg Ala Ile Gly Lys Leu Glu		
	35	40
Ile Ile Pro Ala Ser Leu Ser Cys Pro Arg Val Glu Ile Ile Ala Thr		
	50	55
Met Lys Lys Asn Asp Glu Gln Arg Cys Leu Asn Pro Glu Ser Lys Thr		
65	70	75
Ile Lys Asn Leu Met Lys Ala Phe Ser Gln Lys Arg Ser Lys Arg Ala		
	85	90
Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ala His Lys Ser		
	100	105
Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly		
	115	120
Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp		
	130	135
Glu His Ala Lys Leu Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys		
145	150	155
Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu		
	165	170
Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly		
	180	185
Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys		
	195	200
Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg		
	210	215
Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr		
225	230	235
Phe Met Gly His Tyr Leu His Glu Val Ala Arg Arg His Pro Tyr Phe		
	245	250
Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu		
	260	265
		270

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Thr	Gln	Cys	Cys	Ala	Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys
		275					280					285			
Leu	Asp	Gly	Val	Lys	Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg
	290					295					300				
Met	Lys	Cys	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala
305					310					315					320
Trp	Ala	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala
				325					330					335	
Glu	Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys
			340					345					350		
Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala
		355					360					365			
Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr
	370					375					380				
Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val
385					390					395					400
Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe
				405					410					415	
Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val
			420					425					430		
Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr
		435					440					445			
Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu
	450					455					460				
Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val
465					470					475					480
Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys
				485					490					495	
Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn
			500					505					510		
Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro
		515					520					525			
Thr	Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys
	530					535					540				
Cys	Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu
545					550					555					560
Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val
				565					570					575	
Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg
			580					585					590		
Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu
		595					600					605			
Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro
	610					615					620				
Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val
625					630					635					640
Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp
				645				650						655	
Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp
		660						665					670		
Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp

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675	680	685													
Ala	Leu	Ala	Gly	Gly	Gly	Gly	Ser	His	His	His	His	His	His	His	
690						695							700		
<p>&lt;210&gt; SEQ ID NO 82                  &lt;211&gt; LENGTH: 704                  &lt;212&gt; TYPE: PRT                  &lt;213&gt; ORGANISM: Artificial Sequence                  &lt;220&gt; FEATURE:                  &lt;223&gt; OTHER INFORMATION: Synthetic: LS-mCXCL1122-100-(Gly4Ser)2-mouse                  SA-(Gly4Ser)-His6</p>															
<p>&lt;400&gt; SEQUENCE: 82</p>															
Met	Arg	Val	Pro	Ala	Gln	Leu	Leu	Gly	Leu	Leu	Leu	Leu	Trp	Leu	Pro
1				5					10					15	
Gly	Ala	Arg	Cys	Phe	Leu	Met	Phe	Lys	Gln	Gly	Arg	Cys	Leu	Cys	Ile
			20					25					30		
Gly	Pro	Gly	Met	Lys	Ala	Val	Lys	Met	Ala	Glu	Ile	Glu	Lys	Ala	Ser
			35				40					45			
Val	Ile	Tyr	Pro	Ser	Asn	Gly	Cys	Asp	Lys	Val	Glu	Val	Ile	Val	Thr
	50					55					60				
Met	Lys	Ala	His	Lys	Arg	Gln	Arg	Cys	Leu	Asp	Pro	Arg	Ser	Lys	Gln
65					70					75					80
Ala	Arg	Leu	Ile	Met	Gln	Ala	Ile	Glu	Lys	Lys	Asn	Phe	Leu	Arg	Arg
				85					90					95	
Gln	Asn	Met	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Ala	His
			100					105					110		
Lys	Ser	Glu	Ile	Ala	His	Arg	Tyr	Asn	Asp	Leu	Gly	Glu	Gln	His	Phe
		115					120					125			
Lys	Gly	Leu	Val	Leu	Ile	Ala	Phe	Ser	Gln	Tyr	Leu	Gln	Lys	Cys	Ser
	130					135					140				
Tyr	Asp	Glu	His	Ala	Lys	Leu	Val	Gln	Glu	Val	Thr	Asp	Phe	Ala	Lys
145					150					155					160
Thr	Cys	Val	Ala	Asp	Glu	Ser	Ala	Ala	Asn	Cys	Asp	Lys	Ser	Leu	His
				165					170					175	
Thr	Leu	Phe	Gly	Asp	Lys	Leu	Cys	Ala	Ile	Pro	Asn	Leu	Arg	Glu	Asn
			180					185					190		
Tyr	Gly	Glu	Leu	Ala	Asp	Cys	Cys	Thr	Lys	Gln	Glu	Pro	Glu	Arg	Asn
		195				200						205			
Glu	Cys	Phe	Leu	Gln	His	Lys	Asp	Asp	Asn	Pro	Ser	Leu	Pro	Pro	Phe
	210					215					220				
Glu	Arg	Pro	Glu	Ala	Glu	Ala	Met	Cys	Thr	Ser	Phe	Lys	Glu	Asn	Pro
225					230					235					240
Thr	Thr	Phe	Met	Gly	His	Tyr	Leu	His	Glu	Val	Ala	Arg	Arg	His	Pro
			245						250					255	
Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu	Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu
			260					265					270		
Ile	Leu	Thr	Gln	Cys	Cys	Ala	Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr
		275					280						285		
Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg
	290					295					300				
Gln	Arg	Met	Lys	Cys	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe
305					310						315				320

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Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro Asn Ala Asp  
 325 330 335

Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys Val Asn Lys  
 340 345 350

Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Glu  
 355 360 365

Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser Ser Lys Leu  
 370 375 380

Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His Cys Leu Ser  
 385 390 395 400

Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala Ile Ala Ala  
 405 410 415

Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala Glu Ala Lys  
 420 425 430

Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg Arg His Pro  
 435 440 445

Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys Tyr Glu Ala  
 450 455 460

Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala Cys Tyr Gly  
 465 470 475 480

Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro Lys Asn Leu  
 485 490 495

Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu Tyr Gly Phe  
 500 505 510

Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro Gln Val Ser  
 515 520 525

Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg Val Gly Thr  
 530 535 540

Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys Val Glu Asp  
 545 550 555 560

Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His Glu Lys Thr  
 565 570 575

Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser Leu Val Glu  
 580 585 590

Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr Tyr Val Pro  
 595 600 605

Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp Ile Cys Thr  
 610 615 620

Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala Leu Ala Glu  
 625 630 635 640

Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu Lys Thr Val  
 645 650 655

Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys Ala Ala Asp  
 660 665 670

Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val Thr Arg Cys  
 675 680 685

Lys Asp Ala Leu Ala Gly Gly Gly Ser His His His His His  
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<210> SEQ ID NO 83  
 <211> LENGTH: 2652  
 <212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv
(VL-VH) CK138-(Gly4Ser)-His6

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ttcaaaggcc tagtcctgat tgccttttcc cagtatctcc agaaatgctc atacgatgag    180
catgccaaat tagtgcagga agtaacagac tttgcaaaga cgtgtgttgc cgatgagtct    240
gccgccaact gtgacaaatc ccttcacact ctttttgag ataagttgtg tgccattcca    300
aacctccgtg aaaactatgg tgaactggct gactgctgta caaaacaaga gcccgaaaga    360
aacgaatggt tcctgcaaca caaagatgac aaccccagcc taccaccatt tgaaggcca    420
gaggctgagg ccatgtgcac ctcccttaag gaaaaccaa ccacctttat gggacactat    480
ttgcatgaag ttgccagaag acatccttat ttctatgcc cagaacttct ttactatgct    540
gagcagtaca atgagattct gaccagtggt tgtgcagagg ctgacaagga aagctgctg    600
acccgaagc ttgatggtgt gaaggagaaa gcattggtct catctgtccg tcagagaatg    660
aagtgtctca gtatgcagaa gtttgagag agagcttta aagcatgggc agtagctcgt    720
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tatgtctgag ccaaggatgt ctccctgggc acgttctgt atgaatattc aagaagacac    1080
cctgattact ctgtatccct gttgctgaga cttgctaaga aatatgaagc cactctggaa    1140
aagtgtctgc ctgaagccaa tcctcccgca tgctacggca cagtgtctgc tgaatttcag    1200
cctctttag aagagcctaa gaacttggtc aaaaccaact gtgatcttta cgagaagctt    1260
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aaggagaagc agattaagaa acaaacggct cttgctgagc tgggtgaagca caagcccaag    1680
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accatcacct gccgtgccag tcagtaccac gacggttctg cagcctggta tcaacagaaa    1980
ccagaaaaag ctccgaagct tctgatttac ggtgcatcct acctctactc tggagtccct    2040
tcccgtctct ctggtagccg ttccgggagc gatttcactc tgaccatcag cagtctgcag    2100

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ccggaagact tcgcaactta ttactgtcag caatcttctt attctctgat cecgttcgga 2160
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agcagtgggtg ccgaggttca gctgggtggag tctgacgggtg gcctgggtgca gccagggggc 2280
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tacacttctt atgccgatag cgtcaagggc cgtttcacta taagcgcaga cacatccaaa 2460
aacacagcct acctacaaat gaacagctta agagctgagg acaactgccg ctactattgt 2520
gctcgtctg gttacagtta ctctccgat tattcttggg tctctgctgg tatgaactac 2580
tggggtaac gagccctggg caccgtctcc tcgggagggg gcggttccca ccatcaccac 2640
catcactgat ag 2652

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&lt;210&gt; SEQ ID NO 84

&lt;211&gt; LENGTH: 2625

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv (VL-VH) CK157-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 84

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agatgcgaag cacacaagag tgagatcgcc catcgggata atgatttggg agaacaacat 120
ttcaaaggcc tagtctgat tgccttttcc cagtatctcc agaaatgctc atacgatgag 180
catgccaagt tagtgcagga agtaacagac ttgcaaaga cgtgtgttgc cgatgagtct 240
gccgccaact gtgacaaatc ccttcacact ctttttggag ataagttgtg tgccattcca 300
aacctccgtg aaaactatgg tgaactggct gactgctgta caaaacaaga gccgaaaga 360
aacgaatggt tcctgcaaca caaagatgac aaccccagcc taccaccatt tgaaggcca 420
gaggtgagg ccatgtgac ctcctttaag gaaaaccaa ccaccttat gggacactat 480
ttgcatgaag ttgccagaag acatccttat ttctatgccc cagaacttct ttactatgct 540
gagcagtaca atgagattct gaccagtggt tgtgcagagg ctgacaagga aagctgcctg 600
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cgtgtgtgtc	tgctgcatga	gaagacccca	gtgagtgagc	atgttaccaa	gtgctgtagt	1500
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cgccattact	actggtacga	tgtactgac	tactggggtc	aaggaacct	ggtcacccgtc	2580
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&lt;210&gt; SEQ ID NO 85

&lt;211&gt; LENGTH: 2646

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv  
(VL-VH) CK129-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 85

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ttcaaaggcc	tagtcctgat	tgccctttcc	cagtatctcc	agaaatgctc	atcagatgag	180
catgccaaat	tagtgcagga	agtaacagac	tttgcaaga	cgtgtgttgc	cgatgagtct	240
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gagcagtaca	atgagattct	gacccagtgt	tgtgcagagg	ctgacaagga	aagctgcctg	600
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accaaagtca	acaaggagtg	ctgccatggt	gacctgctgg	aatgocgaga	tgacagggcg	840
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cctgctgatc	tgctgcat	tgctgctgat	ttgttgagg	accaggaagt	gtgcaagaac	1020
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cagccggaag	acttcgcaac	ttattactgt	cagcgaggtc	atgctctgat	cacgttcgga	2160
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tgatag						2646

&lt;210&gt; SEQ ID NO 86

&lt;211&gt; LENGTH: 2652

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv

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(VL-VH) CK138-ds1 (VL100Q&gt;C / VH44G&gt;C) - (Gly4Ser) - His6

&lt;400&gt; SEQUENCE: 86

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ttcaaaggcc tagtctgat tgccttttcc cagtatctcc agaaatgctc atacgatgag	180
catgccaaat tagtgcagga agtaacagac tttgcaaaga cgtgtgttgc cgatgagtct	240
gccgccaact gtgacaaate ccttcacact ctttttgag ataagttgtg tgccattcca	300
aacctccgtg aaaactatgg tgaactggct gactgctgta caaaacaaga gcccgaaaga	360
aacgaatgtt tcctgcaaca caaagatgac aaccccagcc taccaccatt tgaaggcca	420
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ttgcatgaag ttgccagaag acatccttat ttctatgccc cagaacttct ttactatgct	540
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accccgaaagc ttgatggtgt gaaggagaaa gcattggtct catctgtccg tcagagaatg	660
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accaaagtca acaaggagtg ctgccatggt gacctgctgg aatgcccaga tgacagggcg	840
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cccaaagagt ttaaagctga gacctcacc ttcactctg atatctgcac acttccagag	1620
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&lt;210&gt; SEQ ID NO 87

&lt;211&gt; LENGTH: 2658

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv  
(VL-VH) CK138-ds2 (VL43A>C / VH105Q>C)-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 87

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&lt;210&gt; SEQ ID NO 88

&lt;211&gt; LENGTH: 2625

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

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<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv
(VL-VH) CK157-ds1 (VL100Q>C / VH44E>C) - (Gly4Ser)-His6

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&lt;400&gt; SEQUENCE: 88

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&lt;210&gt; SEQ ID NO 89

&lt;211&gt; LENGTH: 2625

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv  
 (VL-VH) CK157-ds2 (VL43A>C / VH105Q>C)-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 89

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<210> SEQ ID NO 90  
 <211> LENGTH: 2217  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)-VL  
 CK157-His6

<400> SEQUENCE: 90

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&lt;210&gt; SEQ ID NO 91

&lt;211&gt; LENGTH: 2265

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)-VH  
CK157-His6

&lt;400&gt; SEQUENCE: 91

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cctgctgatc tgctgccaat tgctgctgat tttgttgagg accaggaagt gtgcaagaac 1020
tatgctgagg ccaaggatgt cttcctgggc acgttcttgt atgaatatc aagaagacac 1080
cctgattact ctgtatccct gttgctgaga cttgctaaga aatatgaagc cactctggaa 1140
aagtgtctcg ctgaagccaa tctcccgcga tgctacggca cagtgttgc tgaatttcag 1200
cctctttag aagagcctaa gaacttggtc aaaaccaact gtgatctta cgagaagctt 1260
ggagaatatg gattccaaaa tgccattcta gttcgtaca ccagaaagc acctcaggtg 1320

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tcaaccccaa ctctcgtgga ggctgcaaga aacctaggaa gagtgggcac caagtgttgt 1380
acacttctcg aagatcagag actgccttgt gtggaagact atctgtctgc aatcctgaac 1440
cgtgtgtgtc tgctgcatga gaagacccca gtgagtgagc atgttaccaa gtgctgtagt 1500
ggateccctg tggaaaggcg gccatgcttc tctgctctga cagttgatga aacatatgtc 1560
cccaaagagt ttaaagctga gaccttcacc ttccactctg atatctgcac acttccagag 1620
aaggagaagc agattaagaa acaaacggct cttgctgagc tggatgaagca caagcccaag 1680
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cgccattact actggtacga tgctactgac tactggggtc aaggaacct ggtcaccgtc 2220
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<210> SEQ ID NO 92
<211> LENGTH: 2640
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv
(VL-VH) CK129-ds1 (VL100Q>C / VH44G>C) - (Gly4Ser) - His6

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<400> SEQUENCE: 92
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ttcaaaggcc tagtcctgat tgccttttcc cagtatctcc agaatgctc atacgatgag 180
catgccaat tagtgcagga agtaacagac tttgcaaaga cgtgtgttgc cgatgagtct 240
gccgccaact gtgacaaate ccttcacact ctttttgag ataagttgtg tgccattcca 300
aacctccgtg aaaactatgg tgaactggct gactgctgta caaacaaga gccgaaaga 360
aacgaatgtt tcctgcaaca caaagatgac aaccccagcc taccaccatt tgaaggcca 420
gaggctgagg ccatgtgcac ctcccttaag gaaaacccaa ccaccttat gggacactat 480
ttgcatgaag ttgccagaag acatccttat ttctatgccc cagaacttct ttactatgct 540
gagcagtaca atgagattct gaccagtggt tgtgcagagg ctgacaagga aagctgcctg 600
acccggaagc ttgatggtgt gaaggagaaa gcattggtct catctgtccg tcagagaatg 660
aagtgtcca gtatgcagaa gtttgagag agagctttaa aagcatgggc agtagctcgt 720
ctgagccaga cattcccaaa tgctgacttt gcagaaatca ccaaattggc aacagacctg 780
accaaagtca acaaggagtg ctgccatggt gacctgctgg aatgocgaga tgacagggag 840
gaacttgcca agtacatgtg tgaaaaccag gcgactatct ccagcaact gcagacttgc 900
tgcgataaac cactgttgaa gaaagccac tgtcttagtg aggtggagca tgacaccatg 960

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cctgctgac tgccctgcat tgctgctgat tttgttgagg accaggaagt gtgcaagaac 1020
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cctgattact ctgtatccct gttgctgaga cttgctaaga aatatgaagc cactctggaa 1140
aagtgctgog ctgaagccaa tcctcccgca tgctacggca cagtgcttgc tgaatttcag 1200
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cgtggttacg gtcctggtga cgttactct tacttgcctt tggactactg gggtaagga 2580
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&lt;210&gt; SEQ ID NO 93

&lt;211&gt; LENGTH: 2640

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv  
(VL-VH) CK129-ds2 (VL43A>C / VH105Q>C)-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 93

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agatgcgaag cacacaagag tgagatgcc catcgggata atgatttggg agaacaacat 120
ttcaaaggcc tagtctgat tgccttttcc cagtatctcc agaaatgctc atacgatgag 180
catgccaaat tagtgcagga agtaacagac tttgcaaaga cgtgtgttgc cgatgagtct 240
gccgccaact gtgacaaatc ccttcacact ctttttgag ataagttgtg tgccattcca 300

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ttgcatgaag	ttgccagaag	acatccttat	ttctatgccc	cagaacttct	ttactatgct	540
gagcagtaca	atgagattct	gacccagtgt	tgtgcagagg	ctgacaagga	aagctgctctg	600
accccgaaagc	ttgatgggtg	gaaggagaaa	gcattgggtc	catctgtccg	tcagagaatg	660
aagtgtctcca	gtatgcagaa	gtttgagag	agagctttta	aagcatgggc	agtagctcgt	720
ctgagccaga	cattccccaa	tgctgacttt	gcagaaatca	ccaaattggc	aacagactctg	780
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<210> SEQ ID NO 94

<211> LENGTH: 2625

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: gWiz-LS-mouse SA-(Gly4Ser)3-scFv  
(VH-VL) sm3E-ds (VH44R>G / VL100G>C)-(Gly4Ser)-His6

<400> SEQUENCE: 94

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ttcaaaggcc tagtcctgat tgccttttcc cagtatctcc agaaatgctc atacgatgag 180

catgccaaat tagtgcagga agtaacagac ttgcaaaga cgtgtgttgc cgatgagtct 240

gccgccaaact gtgacaaatc ccttcacact ctttttggag ataagttgtg tgccattcca 300

aacctccgtg aaaactatgg tgaactggct gactgctgta caaaacaaga gcccgaaaga 360

aacgaatggt tcctgcaaca caaagatgac aaccccagcc taccaccatt tgaaggcca 420

gaggtgagg ccatgtgcac ctctttaaag gaaaaccaa ccaccttat gggacactat 480

ttgcatgaag ttgccagaag acatccttat ttctatgccc cagaacttct ttactatgct 540

gagcagtaca atgagattct gaccagtggt tgtgcagagg ctgacaagga aagctgcctg 600

accccgaaagc ttgatggtgt gaaggagaaa gcattggtct catctgtccg tcagagaatg 660

aagtgtcca gtatgcagaa gtttgagag agagctttaa aagcatgggc agtagctcgt 720

ctgagccaga cattccccaa tgcctgacttt gcagaaatca ccaaattggc aacagacctg 780

accaaagtca acaaggagtg ctgccatggt gacctgctgg aatgcccaga tgacagggcg 840

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tgcgataaac cactgttgaa gaaagcccac tgtcttagtg aggtggagca tgacaccatg 960

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tcgcaagtta aactggaaca gtcggtgct gaagttgtca aaccaggtgc ttcggtgaag 1920
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tacttgggct tatcttctt gagaccagag gacactgccg tatactactg caacgaaggg 2160
acaccaactg gtccttacta tttcgactac tggggacaag gtacottagt tactgtctct 2220
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gcatecteta gtgtccata tatgcactgg cttcaacaga agccaggtaa aagcccaaag 2400
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&lt;210&gt; SEQ ID NO 95

&lt;211&gt; LENGTH: 884

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

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<223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)
CK138-(Gly4Ser)-His6

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&lt;400&gt; SEQUENCE: 95

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1          5          10          15
Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg
20        25        30
Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
35        40        45
Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
50        55        60
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
65        70        75        80
Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
85        90        95
Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys
100       105       110
Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
115       120       125
Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala
130       135       140
Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr
145       150       155       160
Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
165       170       175
Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala
180       185       190
Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys
195       200       205

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Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	210	215	220	
Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	225	230	235	240
Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu	245	250	255	
Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu	260	265	270	
Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu	275	280	285	
Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro	290	295	300	
Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met	305	310	315	320
Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	325	330	335	
Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	340	345	350	
Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	355	360	365	
Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	370	375	380	
Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	385	390	395	400
Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	405	410	415	
Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	420	425	430	
Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	435	440	445	
Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	450	455	460	
Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn	465	470	475	480
Arg	Val	Cys	Leu	Leu	His	Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr	485	490	495	
Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala	500	505	510	
Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	515	520	525	
Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	530	535	540	
Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	545	550	555	560
Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	565	570	575	
Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	580	585	590	
Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly	Gly	595	600	605	
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ala	Ser	Ala				

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610		615		620																
Ile	Gln	Met	Thr	Arg	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	Asp					
625					630					635					640					
Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Tyr	His	Asp	Gly	Ser	Ala					
				645						650					655					
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr					
			660					665						670						
Gly	Ala	Ser	Tyr	Leu	Tyr	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser					
		675					680					685								
Arg	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu					
	690					695					700									
Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ser	Tyr	Ser	Leu	Ile	Thr					
705					710					715					720					
Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys	Gly	Thr	Thr	Ala	Ala	Ser					
				725					730						735					
Gly	Ser	Ser	Gly	Gly	Ser	Ser	Ser	Gly	Ala	Glu	Val	Gln	Leu	Val	Glu					
			740					745						750						
Ser	Asp	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	Ser	Leu	Arg	Leu	Ser	Cys					
		755					760					765								
Ala	Ala	Ser	Gly	Phe	Asn	Leu	Ser	Tyr	Tyr	Gly	Met	His	Trp	Val	Arg					
	770				775						780									
Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Tyr	Ile	Ala	Ser	Tyr					
785					790					795					800					
Pro	Gly	Tyr	Thr	Ser	Tyr	Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile					
				805						810					815					
Ser	Ala	Asp	Thr	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Ser	Leu					
			820					825					830							
Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Ser	Gly	Tyr	Ser					
		835					840					845								
Tyr	Ser	Pro	Tyr	Tyr	Ser	Trp	Phe	Ser	Ala	Gly	Met	Asn	Tyr	Trp	Gly					
	850					855					860									
Gln	Gly	Ala	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	His	His					
865					870						875				880					

His His His His

&lt;210&gt; SEQ ID NO 96

&lt;211&gt; LENGTH: 875

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK157-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 96

Met	Asp	Met	Arg	Val	Pro	Ala	Gln	Leu	Leu	Gly	Leu	Leu	Leu	Leu	Trp					
1				5					10					15						
Leu	Pro	Gly	Ala	Arg	Cys	Glu	Ala	His	Lys	Ser	Glu	Ile	Ala	His	Arg					
			20					25					30							
Tyr	Asn	Asp	Leu	Gly	Glu	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala					
		35					40						45							
Phe	Ser	Gln	Tyr	Leu	Gln	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu					
	50					55					60									
Val	Gln	Glu	Val	Thr	Asp	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser					



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65	70					75					80				
Ala	Ala	Asn	Cys	Asp	Lys	Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	Lys	Leu
				85					90					95	
Cys	Ala	Ile	Pro	Asn	Leu	Arg	Glu	Asn	Tyr	Gly	Glu	Leu	Ala	Asp	Cys
			100					105						110	
Cys	Thr	Lys	Gln	Glu	Pro	Glu	Arg	Asn	Glu	Cys	Phe	Leu	Gln	His	Lys
		115					120						125		
Asp	Asp	Asn	Pro	Ser	Leu	Pro	Pro	Phe	Glu	Arg	Pro	Glu	Ala	Glu	Ala
	130					135					140				
Met	Cys	Thr	Ser	Phe	Lys	Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr
	145				150					155					160
Leu	His	Glu	Val	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu
				165					170						175
Leu	Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala
			180					185						190	
Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys
		195					200						205		
Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser
	210					215					220				
Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg
	225				230					235					240
Leu	Ser	Gln	Thr	Phe	Pro	Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu
				245					250						255
Ala	Thr	Asp	Leu	Thr	Lys	Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu
		260						265						270	
Leu	Glu	Cys	Ala	Asp	Asp	Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu
		275				280							285		
Asn	Gln	Ala	Thr	Ile	Ser	Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro
	290					295					300				
Leu	Leu	Lys	Lys	Ala	His	Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met
	305				310					315					320
Pro	Ala	Asp	Leu	Pro	Ala	Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu
				325					330						335
Val	Cys	Lys	Asn	Tyr	Ala	Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe
			340					345						350	
Leu	Tyr	Glu	Tyr	Ser	Arg	Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu
		355					360						365		
Leu	Arg	Leu	Ala	Lys	Lys	Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala
	370					375					380				
Glu	Ala	Asn	Pro	Pro	Ala	Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln
	385				390					395					400
Pro	Leu	Val	Glu	Glu	Pro	Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu
				405					410						415
Tyr	Glu	Lys	Leu	Gly	Glu	Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg
			420					425						430	
Tyr	Thr	Gln	Lys	Ala	Pro	Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala
		435					440						445		
Ala	Arg	Asn	Leu	Gly	Arg	Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu
	450					455						460			
Asp	Gln	Arg	Leu	Pro	Cys	Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn
	465				470					475					480

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Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495  
 Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
 500 505 510  
 Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
 515 520 525  
 Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
 530 535 540  
 Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
 545 550 555 560  
 Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
 565 570 575  
 Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
 580 585 590  
 Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
 595 600 605  
 Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp  
 610 615 620  
 Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp  
 625 630 635 640  
 Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Tyr Gly Gly Val Ala  
 645 650 655  
 Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser  
 660 665 670  
 Ala Ser Tyr Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg  
 675 680 685  
 Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp  
 690 695 700  
 Phe Ala Thr Tyr Tyr Cys Gln Gln Pro Ser His Leu Ile Thr Phe Gly  
 705 710 715 720  
 Gln Gly Thr Glu Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser  
 725 730 735  
 Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly  
 740 745 750  
 Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala  
 755 760 765  
 Ser Gly Ser Asn Pro Tyr Tyr Tyr Gly Gly Thr His Trp Val Arg Gln  
 770 775 780  
 Ala Pro Gly Glu Glu Leu Glu Trp Val Ala Ser Ile Gly Ser Tyr Pro  
 785 790 795 800  
 Gly Tyr Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser  
 805 810 815  
 Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg  
 820 825 830  
 Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg His Tyr Tyr Trp Tyr  
 835 840 845  
 Asp Ala Thr Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
 850 855 860  
 Gly Gly Gly Gly Ser His His His His His His  
 865 870 875

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<210> SEQ ID NO 97  
 <211> LENGTH: 880  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)  
 CK129-(Gly4Ser)-His6

<400> SEQUENCE: 97

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp  
 1 5 10 15  
 Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg  
 20 25 30  
 Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala  
 35 40 45  
 Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu  
 50 55 60  
 Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser  
 65 70 75 80  
 Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu  
 85 90 95  
 Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys  
 100 105 110  
 Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys  
 115 120 125  
 Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala  
 130 135 140  
 Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr  
 145 150 155 160  
 Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu  
 165 170 175  
 Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala  
 180 185 190  
 Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys  
 195 200 205  
 Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser  
 210 215 220  
 Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg  
 225 230 235 240  
 Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
 245 250 255  
 Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
 260 265 270  
 Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
 275 280 285  
 Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
 290 295 300  
 Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
 305 310 315 320  
 Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
 325 330 335  
 Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
 340 345 350

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Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
355 360 365

Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
370 375 380

Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
385 390 395 400

Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
405 410 415

Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
420 425 430

Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
435 440 445

Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
450 455 460

Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
465 470 475 480

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
485 490 495

Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
500 505 510

Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
515 520 525

Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
530 535 540

Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
545 550 555 560

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
565 570 575

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
580 585 590

Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
595 600 605

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp  
610 615 620

Ile Gln Met Thr Gln Ser Pro Ser Pro Leu Ser Ala Ser Val Gly Asp  
625 630 635 640

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Gly Gly Tyr Val Ala  
645 650 655

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly  
660 665 670

Ala Ser Leu Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Gly Arg  
675 680 685

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp  
690 695 700

Phe Ala Thr Tyr Tyr Cys Gln Arg Gly His Ala Leu Ile Thr Phe Gly  
705 710 715 720

Gln Gly Thr Lys Val Glu Ile Glu Gly Thr Thr Ala Ala Ser Gly Ser  
725 730 735

Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly  
740 745 750

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Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala  
755 760 765

Ser Gly Phe Asn Ile Ser Ser Tyr Gly Ser Met His Trp Val Arg Gln  
770 775 780

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Tyr Pro Tyr Ser  
785 790 795 800

Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser  
805 810 815

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg  
820 825 830

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Tyr Gly Pro Trp  
835 840 845

Tyr Ala Tyr Ser Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu  
850 855 860

Val Thr Val Ser Ser Gly Gly Gly Gly Ser His His His His His His  
865 870 875 880

&lt;210&gt; SEQ ID NO 98

&lt;211&gt; LENGTH: 884

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK138-ds1 (VL100Q>C / VH44G>C) - (Gly4Ser) -His6

&lt;400&gt; SEQUENCE: 98

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp  
1 5 10 15

Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg  
20 25 30

Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala  
35 40 45

Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu  
50 55 60

Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser  
65 70 75 80

Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu  
85 90 95

Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys  
100 105 110

Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys  
115 120 125

Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala  
130 135 140

Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr  
145 150 155 160

Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu  
165 170 175

Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala  
180 185 190

Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys  
195 200 205

Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser  
210 215 220

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Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg  
 225 230 235 240  
 Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
 245 250 255  
 Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
 260 265 270  
 Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
 275 280 285  
 Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
 290 295 300  
 Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
 305 310 315 320  
 Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
 325 330 335  
 Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
 340 345 350  
 Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
 355 360 365  
 Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
 370 375 380  
 Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
 385 390 395 400  
 Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
 405 410 415  
 Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
 420 425 430  
 Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
 435 440 445  
 Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
 450 455 460  
 Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
 465 470 475 480  
 Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495  
 Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
 500 505 510  
 Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
 515 520 525  
 Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
 530 535 540  
 Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
 545 550 555 560  
 Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
 565 570 575  
 Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
 580 585 590  
 Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
 595 600 605  
 Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Ala  
 610 615 620

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Ile Gln Met Thr Arg Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
625                               630                               635                               640

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr His Asp Gly Ser Ala
                               645                               650                               655

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
                               660                               665                               670

Gly Ala Ser Tyr Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
                               675                               680                               685

Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
690                               695                               700

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ser Tyr Ser Leu Ile Thr
705                               710                               715                               720

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Gly Thr Thr Ala Ala Ser
                               725                               730                               735

Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu
740                               745                               750

Ser Asp Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
755                               760                               765

Ala Ala Ser Gly Phe Asn Leu Ser Tyr Tyr Gly Met His Trp Val Arg
770                               775                               780

Gln Ala Pro Gly Lys Cys Leu Glu Trp Val Ala Tyr Ile Ala Ser Tyr
785                               790                               795                               800

Pro Gly Tyr Thr Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile
805                               810                               815

Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu
820                               825                               830

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Tyr Ser
835                               840                               845

Tyr Ser Pro Tyr Tyr Ser Trp Phe Ser Ala Gly Met Asn Tyr Trp Gly
850                               855                               860

Gln Gly Ala Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser His His
865                               870                               875                               880

His His His His
    
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<210> SEQ ID NO 99
<211> LENGTH: 884
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)
        CK138-ds2 (VL43A>C / VH105Q>C) - (Gly4Ser)-His6
    
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<400> SEQUENCE: 99

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1                               5                               10                               15

Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg
20                               25                               30

Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
35                               40                               45

Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
50                               55                               60

Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
65                               70                               75                               80
    
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Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu  
85 90 95

Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys  
100 105 110

Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys  
115 120 125

Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala  
130 135 140

Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr  
145 150 155 160

Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu  
165 170 175

Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala  
180 185 190

Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys  
195 200 205

Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser  
210 215 220

Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg  
225 230 235 240

Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
245 250 255

Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
260 265 270

Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
275 280 285

Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
290 295 300

Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
305 310 315 320

Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
325 330 335

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
340 345 350

Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
355 360 365

Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
370 375 380

Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
385 390 395 400

Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
405 410 415

Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
420 425 430

Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
435 440 445

Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
450 455 460

Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
465 470 475 480

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr



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485					490					495					
Lys	Cys	Cys	Ser	Gly	Ser	Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala
			500					505					510		
Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr
		515					520					525			
Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln
		530				535					540				
Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys
	545					550					555				560
Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe
			565						570					575	
Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr
			580					585					590		
Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly	Gly
		595					600					605			
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ala	Ser	Ala
	610					615					620				
Ile	Gln	Met	Thr	Arg	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	Asp
	625					630					635				640
Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Tyr	His	Asp	Gly	Ser	Ala
			645						650					655	
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Cys	Pro	Lys	Leu	Leu	Ile	Tyr
			660					665						670	
Gly	Ala	Ser	Tyr	Leu	Tyr	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser
		675					680					685			
Arg	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu
	690					695					700				
Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ser	Tyr	Ser	Leu	Ile	Thr
	705					710					715				720
Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys	Gly	Thr	Thr	Ala	Ala	Ser
			725						730					735	
Gly	Ser	Ser	Gly	Gly	Ser	Ser	Ser	Gly	Ala	Glu	Val	Gln	Leu	Val	Glu
			740					745					750		
Ser	Asp	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	Ser	Leu	Arg	Leu	Ser	Cys
		755					760					765			
Ala	Ala	Ser	Gly	Phe	Asn	Leu	Ser	Tyr	Tyr	Gly	Met	His	Trp	Val	Arg
		770				775					780				
Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Tyr	Ile	Ala	Ser	Tyr
	785					790					795				800
Pro	Gly	Tyr	Thr	Ser	Tyr	Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile
			805						810					815	
Ser	Ala	Asp	Thr	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Ser	Leu
			820					825					830		
Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Ser	Gly	Tyr	Ser
		835					840						845		
Tyr	Ser	Pro	Tyr	Tyr	Ser	Trp	Phe	Ser	Ala	Gly	Met	Asn	Tyr	Trp	Gly
	850					855							860		
Cys	Gly	Ala	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	His	His
	865					870					875				880
His	His	His	His												

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<210> SEQ ID NO 100  
 <211> LENGTH: 875  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)  
 CK157-ds1 (VL100Q>C / VH44E>C)-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 100

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp  
 1 5 10 15

Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg  
 20 25 30

Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala  
 35 40 45

Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu  
 50 55 60

Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser  
 65 70 75 80

Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu  
 85 90 95

Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys  
 100 105 110

Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys  
 115 120 125

Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala  
 130 135 140

Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr  
 145 150 155 160

Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu  
 165 170 175

Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala  
 180 185 190

Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys  
 195 200 205

Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser  
 210 215 220

Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg  
 225 230 235 240

Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
 245 250 255

Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
 260 265 270

Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
 275 280 285

Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
 290 295 300

Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
 305 310 315 320

Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
 325 330 335

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
 340 345 350

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Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
 355 360 365  
 Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
 370 375 380  
 Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
 385 390 395 400  
 Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
 405 410 415  
 Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
 420 425 430  
 Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
 435 440 445  
 Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
 450 455 460  
 Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
 465 470 475 480  
 Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495  
 Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
 500 505 510  
 Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
 515 520 525  
 Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
 530 535 540  
 Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
 545 550 555 560  
 Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
 565 570 575  
 Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
 580 585 590  
 Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
 595 600 605  
 Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp  
 610 615 620  
 Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp  
 625 630 635 640  
 Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Tyr Gly Gly Val Ala  
 645 650 655  
 Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser  
 660 665 670  
 Ala Ser Tyr Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg  
 675 680 685  
 Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp  
 690 695 700  
 Phe Ala Thr Tyr Tyr Cys Gln Gln Pro Ser His Leu Ile Thr Phe Gly  
 705 710 715 720  
 Cys Gly Thr Glu Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser  
 725 730 735  
 Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly  
 740 745 750

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Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala  
755 760 765

Ser Gly Ser Asn Pro Tyr Tyr Tyr Gly Gly Thr His Trp Val Arg Gln  
770 775 780

Ala Pro Gly Glu Cys Leu Glu Trp Val Ala Ser Ile Gly Ser Tyr Pro  
785 790 795 800

Gly Tyr Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser  
805 810 815

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg  
820 825 830

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg His Tyr Tyr Trp Tyr  
835 840 845

Asp Ala Thr Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
850 855 860

Gly Gly Gly Gly Ser His His His His His His  
865 870 875

<210> SEQ ID NO 101  
<211> LENGTH: 875  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK157-ds2 (VL43A>C / VH105Q>C) - (Gly4Ser) -His6

<400> SEQUENCE: 101

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp  
1 5 10 15

Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg  
20 25 30

Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala  
35 40 45

Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu  
50 55 60

Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser  
65 70 75 80

Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu  
85 90 95

Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys  
100 105 110

Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys  
115 120 125

Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala  
130 135 140

Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr  
145 150 155 160

Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu  
165 170 175

Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala  
180 185 190

Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys  
195 200 205

Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser  
210 215 220

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Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg  
 225 230 235 240  
 Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
 245 250 255  
 Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
 260 265 270  
 Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
 275 280 285  
 Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
 290 295 300  
 Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
 305 310 315 320  
 Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
 325 330 335  
 Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
 340 345 350  
 Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
 355 360 365  
 Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
 370 375 380  
 Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
 385 390 395 400  
 Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
 405 410 415  
 Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
 420 425 430  
 Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
 435 440 445  
 Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
 450 455 460  
 Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
 465 470 475 480  
 Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495  
 Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
 500 505 510  
 Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
 515 520 525  
 Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
 530 535 540  
 Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
 545 550 555 560  
 Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
 565 570 575  
 Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
 580 585 590  
 Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
 595 600 605  
 Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp  
 610 615 620

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Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
625                               630                               635                               640

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Tyr Gly Gly Val Ala
                               645                               650                               655

Trp Tyr Gln Gln Lys Pro Gly Lys Cys Pro Lys Leu Leu Ile Tyr Ser
                               660                               665                               670

Ala Ser Tyr Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg
                               675                               680                               685

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
690                               695                               700

Phe Ala Thr Tyr Tyr Cys Gln Gln Pro Ser His Leu Ile Thr Phe Gly
705                               710                               715                               720

Gln Gly Thr Glu Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser
                               725                               730                               735

Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly
740                               745                               750

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala
755                               760                               765

Ser Gly Ser Asn Pro Tyr Tyr Tyr Gly Gly Thr His Trp Val Arg Gln
770                               775                               780

Ala Pro Gly Glu Glu Leu Glu Trp Val Ala Ser Ile Gly Ser Tyr Pro
785                               790                               795                               800

Gly Tyr Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
                               805                               810                               815

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
                               820                               825                               830

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg His Tyr Tyr Trp Tyr
835                               840                               845

Asp Ala Thr Asp Tyr Trp Gly Cys Gly Thr Leu Val Thr Val Ser Ser
850                               855                               860

Gly Gly Gly Gly Ser His His His His His His
865                               870                               875
    
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<210> SEQ ID NO 102
<211> LENGTH: 739
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)-VL CK157-His6
    
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<400> SEQUENCE: 102

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Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1                               5                               10                               15

Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg
20                               25                               30

Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
35                               40                               45

Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
50                               55                               60

Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
65                               70                               75                               80

Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
85                               90                               95
    
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Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys  
 100 105 110

Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys  
 115 120 125

Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala  
 130 135 140

Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr  
 145 150 155 160

Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu  
 165 170 175

Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala  
 180 185 190

Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys  
 195 200 205

Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser  
 210 215 220

Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg  
 225 230 235 240

Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
 245 250 255

Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
 260 265 270

Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
 275 280 285

Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
 290 295 300

Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
 305 310 315 320

Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
 325 330 335

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
 340 345 350

Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
 355 360 365

Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
 370 375 380

Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
 385 390 395 400

Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
 405 410 415

Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
 420 425 430

Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
 435 440 445

Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
 450 455 460

Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
 465 470 475 480

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495

Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala

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500				505				510							
Leu	Thr	Val	Asp	Glu	Thr	Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr
		515						520					525		
Phe	Thr	Phe	His	Ser	Asp	Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln
	530						535				540				
Ile	Lys	Lys	Gln	Thr	Ala	Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys
	545					550					555				560
Ala	Thr	Ala	Glu	Gln	Leu	Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe
				565					570						575
Leu	Asp	Thr	Cys	Cys	Lys	Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr
			580						585					590	
Glu	Gly	Pro	Asn	Leu	Val	Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly	Gly
		595					600							605	
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ala	Ser	Asp
	610					615						620			
Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	Asp
	625					630					635				640
Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ser	Tyr	Gly	Gly	Val	Ala
				645						650					655
Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Ser
			660						665					670	
Ala	Ser	Tyr	Leu	Tyr	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Arg
		675						680						685	
Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp
	690						695						700		
Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Pro	Ser	His	Leu	Ile	Thr	Phe	Gly
	705					710					715				720
Gln	Gly	Thr	Glu	Val	Glu	Ile	Lys	Gly	Gly	Gly	Gly	Ser	His	His	His
				725					730						735
His His His															
<210> SEQ ID NO 103															
<211> LENGTH: 755															
<212> TYPE: PRT															
<213> ORGANISM: Artificial Sequence															
<220> FEATURE:															
<223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)-VH CK157-His6															
<400> SEQUENCE: 103															
Met	Asp	Met	Arg	Val	Pro	Ala	Gln	Leu	Leu	Gly	Leu	Leu	Leu	Leu	Trp
1				5					10						15
Leu	Pro	Gly	Ala	Arg	Cys	Glu	Ala	His	Lys	Ser	Glu	Ile	Ala	His	Arg
		20						25					30		
Tyr	Asn	Asp	Leu	Gly	Glu	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala
		35					40						45		
Phe	Ser	Gln	Tyr	Leu	Gln	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu
	50						55					60			
Val	Gln	Glu	Val	Thr	Asp	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser
	65					70				75					80
Ala	Ala	Asn	Cys	Asp	Lys	Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	Lys	Leu
				85						90					95
Cys	Ala	Ile	Pro	Asn	Leu	Arg	Glu	Asn	Tyr	Gly	Glu	Leu	Ala	Asp	Cys
			100						105						110



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Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys  
 115 120 125  
 Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala  
 130 135 140  
 Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr  
 145 150 155 160  
 Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu  
 165 170 175  
 Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala  
 180 185 190  
 Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys  
 195 200 205  
 Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser  
 210 215 220  
 Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg  
 225 230 235 240  
 Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
 245 250 255  
 Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
 260 265 270  
 Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
 275 280 285  
 Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
 290 295 300  
 Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
 305 310 315 320  
 Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
 325 330 335  
 Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
 340 345 350  
 Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
 355 360 365  
 Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
 370 375 380  
 Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
 385 390 395 400  
 Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
 405 410 415  
 Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
 420 425 430  
 Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
 435 440 445  
 Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
 450 455 460  
 Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
 465 470 475 480  
 Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495  
 Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
 500 505 510

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Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
 515 520 525

Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
 530 535 540

Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
 545 550 555 560

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
 565 570 575

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
 580 585 590

Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
 595 600 605

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Ala  
 610 615 620

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
 625 630 635 640

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Asn Pro Tyr Tyr Tyr  
 645 650 655

Gly Gly Thr His Trp Val Arg Gln Ala Pro Gly Glu Glu Leu Glu Trp  
 660 665 670

Val Ala Ser Ile Gly Ser Tyr Pro Gly Tyr Thr Asp Tyr Ala Asp Ser  
 675 680 685

Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala  
 690 695 700

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr  
 705 710 715 720

Cys Ala Arg His Tyr Tyr Trp Tyr Asp Ala Thr Asp Tyr Trp Gly Gln  
 725 730 735

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser His His His  
 740 745 750

His His His  
 755

<210> SEQ ID NO 104  
 <211> LENGTH: 880  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)  
 CK129-ds1 (VL100Q>C / VH44G>C) - (Gly4Ser) -His6

<400> SEQUENCE: 104

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp  
 1 5 10 15

Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg  
 20 25 30

Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala  
 35 40 45

Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu  
 50 55 60

Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser  
 65 70 75 80

Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu  
 85 90 95

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Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys  
 100 105 110  
 Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys  
 115 120 125  
 Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala  
 130 135 140  
 Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr  
 145 150 155 160  
 Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu  
 165 170 175  
 Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala  
 180 185 190  
 Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys  
 195 200 205  
 Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser  
 210 215 220  
 Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg  
 225 230 235 240  
 Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
 245 250 255  
 Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
 260 265 270  
 Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
 275 280 285  
 Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
 290 295 300  
 Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
 305 310 315 320  
 Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
 325 330 335  
 Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
 340 345 350  
 Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
 355 360 365  
 Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
 370 375 380  
 Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
 385 390 395 400  
 Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
 405 410 415  
 Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
 420 425 430  
 Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
 435 440 445  
 Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
 450 455 460  
 Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
 465 470 475 480  
 Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495

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Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
 500 505 510

Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
 515 520 525

Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
 530 535 540

Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
 545 550 560

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
 565 570 575

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
 580 585 590

Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
 595 600 605

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp  
 610 615 620

Ile Gln Met Thr Gln Ser Pro Ser Pro Leu Ser Ala Ser Val Gly Asp  
 625 630 635 640

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Gly Gly Tyr Val Ala  
 645 650 655

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly  
 660 665 670

Ala Ser Leu Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Gly Arg  
 675 680 685

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp  
 690 695 700

Phe Ala Thr Tyr Tyr Cys Gln Arg Gly His Ala Leu Ile Thr Phe Gly  
 705 710 715 720

Cys Gly Thr Lys Val Glu Ile Glu Gly Thr Thr Ala Ala Ser Gly Ser  
 725 730 735

Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly  
 740 745 750

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala  
 755 760 765

Ser Gly Phe Asn Ile Ser Ser Tyr Gly Ser Met His Trp Val Arg Gln  
 770 775 780

Ala Pro Gly Lys Cys Leu Glu Trp Val Ala Ser Ile Tyr Pro Tyr Ser  
 785 790 795 800

Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser  
 805 810 815

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg  
 820 825 830

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Tyr Gly Pro Trp  
 835 840 845

Tyr Ala Tyr Ser Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu  
 850 855 860

Val Thr Val Ser Ser Gly Gly Gly Ser His His His His His His  
 865 870 875 880

<210> SEQ ID NO 105  
 <211> LENGTH: 880  
 <212> TYPE: PRT

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&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VL-VH)

CK129-ds2 (VL43A&gt;C / VH105Q&gt;C) - (Gly4Ser) - His6

&lt;400&gt; SEQUENCE: 105

```

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1          5          10          15
Leu Pro Gly Ala Arg Cys Glu Ala His Lys Ser Glu Ile Ala His Arg
20        25        30
Tyr Asn Asp Leu Gly Glu Gln His Phe Lys Gly Leu Val Leu Ile Ala
35        40        45
Phe Ser Gln Tyr Leu Gln Lys Cys Ser Tyr Asp Glu His Ala Lys Leu
50        55        60
Val Gln Glu Val Thr Asp Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
65        70        75        80
Ala Ala Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
85        90        95
Cys Ala Ile Pro Asn Leu Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys
100       105       110
Cys Thr Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
115       120       125
Asp Asp Asn Pro Ser Leu Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala
130       135       140
Met Cys Thr Ser Phe Lys Glu Asn Pro Thr Thr Phe Met Gly His Tyr
145       150       155       160
Leu His Glu Val Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
165       170       175
Leu Tyr Tyr Ala Glu Gln Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala
180       185       190
Glu Ala Asp Lys Glu Ser Cys Leu Thr Pro Lys Leu Asp Gly Val Lys
195       200       205
Glu Lys Ala Leu Val Ser Ser Val Arg Gln Arg Met Lys Cys Ser Ser
210       215       220
Met Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
225       230       235       240
Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu
245       250       255
Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu
260       265       270
Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu
275       280       285
Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro
290       295       300
Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met
305       310       315       320
Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu
325       330       335
Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe
340       345       350
Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu
355       360       365

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Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
 370 375 380

Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
 385 390 400

Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
 405 410 415

Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
 420 425 430

Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
 435 440 445

Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
 450 455 460

Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
 465 470 475 480

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495

Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
 500 505 510

Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
 515 520 525

Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
 530 535 540

Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
 545 550 555 560

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
 565 570 575

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
 580 585 590

Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
 595 600 605

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp  
 610 615 620

Ile Gln Met Thr Gln Ser Pro Ser Pro Leu Ser Ala Ser Val Gly Asp  
 625 630 635 640

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Tyr Gly Gly Tyr Val Ala  
 645 650 655

Trp Tyr Gln Gln Lys Pro Gly Lys Cys Pro Lys Leu Leu Ile Tyr Gly  
 660 665 670

Ala Ser Leu Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Gly Arg  
 675 680 685

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp  
 690 695 700

Phe Ala Thr Tyr Tyr Cys Gln Arg Gly His Ala Leu Ile Thr Phe Gly  
 705 710 715 720

Gln Gly Thr Lys Val Glu Ile Glu Gly Thr Thr Ala Ala Ser Gly Ser  
 725 730 735

Ser Gly Gly Ser Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Gly  
 740 745 750

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala  
 755 760 765

Ser Gly Phe Asn Ile Ser Ser Tyr Gly Ser Met His Trp Val Arg Gln

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770					775					780					
Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	Ala	Ser	Ile	Tyr	Pro	Tyr	Ser
785					790					795					800
Ser	Ser	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser
				805					810					815	
Ala	Asp	Thr	Ser	Lys	Asn	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg
			820					825					830		
Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Gly	Tyr	Gly	Pro	Trp
		835					840					845			
Tyr	Ala	Tyr	Ser	Tyr	Phe	Ala	Leu	Asp	Tyr	Trp	Gly	Cys	Gly	Thr	Leu
	850					855					860				
Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	His	His	His	His	His	His
865					870					875					880

&lt;210&gt; SEQ ID NO 106

&lt;211&gt; LENGTH: 875

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: LS-mouse SA-(Gly4Ser)3-scFv (VH-VL)  
sm3E-ds (VH44R>C / VL100G>C)-(Gly4Ser)-His6

&lt;400&gt; SEQUENCE: 106

Met	Asp	Met	Arg	Val	Pro	Ala	Gln	Leu	Leu	Gly	Leu	Leu	Leu	Trp	
1				5					10					15	
Leu	Pro	Gly	Ala	Arg	Cys	Glu	Ala	His	Lys	Ser	Glu	Ile	Ala	His	Arg
			20					25					30		
Tyr	Asn	Asp	Leu	Gly	Glu	Gln	His	Phe	Lys	Gly	Leu	Val	Leu	Ile	Ala
		35					40					45			
Phe	Ser	Gln	Tyr	Leu	Gln	Lys	Cys	Ser	Tyr	Asp	Glu	His	Ala	Lys	Leu
	50					55					60				
Val	Gln	Glu	Val	Thr	Asp	Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser
65				70							75			80	
Ala	Ala	Asn	Cys	Asp	Lys	Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	Lys	Leu
			85						90					95	
Cys	Ala	Ile	Pro	Asn	Leu	Arg	Glu	Asn	Tyr	Gly	Glu	Leu	Ala	Asp	Cys
			100					105						110	
Cys	Thr	Lys	Gln	Glu	Pro	Glu	Arg	Asn	Glu	Cys	Phe	Leu	Gln	His	Lys
			115					120					125		
Asp	Asp	Asn	Pro	Ser	Leu	Pro	Pro	Phe	Glu	Arg	Pro	Glu	Ala	Glu	Ala
	130					135					140				
Met	Cys	Thr	Ser	Phe	Lys	Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr
145				150							155				160
Leu	His	Glu	Val	Ala	Arg	Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu
			165						170					175	
Leu	Tyr	Tyr	Ala	Glu	Gln	Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala
			180					185						190	
Glu	Ala	Asp	Lys	Glu	Ser	Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys
		195					200						205		
Glu	Lys	Ala	Leu	Val	Ser	Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser
	210					215					220				
Met	Gln	Lys	Phe	Gly	Glu	Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg
225					230					235					240

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Leu Ser Gln Thr Phe Pro Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu  
 245 250 255

Ala Thr Asp Leu Thr Lys Val Asn Lys Glu Cys Cys His Gly Asp Leu  
 260 265 270

Leu Glu Cys Ala Asp Asp Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu  
 275 280 285

Asn Gln Ala Thr Ile Ser Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro  
 290 295 300

Leu Leu Lys Lys Ala His Cys Leu Ser Glu Val Glu His Asp Thr Met  
 305 310 315 320

Pro Ala Asp Leu Pro Ala Ile Ala Ala Asp Phe Val Glu Asp Gln Glu  
 325 330 335

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Thr Phe  
 340 345 350

Leu Tyr Glu Tyr Ser Arg Arg His Pro Asp Tyr Ser Val Ser Leu Leu  
 355 360 365

Leu Arg Leu Ala Lys Lys Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala  
 370 375 380

Glu Ala Asn Pro Pro Ala Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln  
 385 390 400

Pro Leu Val Glu Glu Pro Lys Asn Leu Val Lys Thr Asn Cys Asp Leu  
 405 410 415

Tyr Glu Lys Leu Gly Glu Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg  
 420 425 430

Tyr Thr Gln Lys Ala Pro Gln Val Ser Thr Pro Thr Leu Val Glu Ala  
 435 440 445

Ala Arg Asn Leu Gly Arg Val Gly Thr Lys Cys Cys Thr Leu Pro Glu  
 450 455 460

Asp Gln Arg Leu Pro Cys Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn  
 465 470 475 480

Arg Val Cys Leu Leu His Glu Lys Thr Pro Val Ser Glu His Val Thr  
 485 490 495

Lys Cys Cys Ser Gly Ser Leu Val Glu Arg Arg Pro Cys Phe Ser Ala  
 500 505 510

Leu Thr Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr  
 515 520 525

Phe Thr Phe His Ser Asp Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln  
 530 535 540

Ile Lys Lys Gln Thr Ala Leu Ala Glu Leu Val Lys His Lys Pro Lys  
 545 550 555 560

Ala Thr Ala Glu Gln Leu Lys Thr Val Met Asp Asp Phe Ala Gln Phe  
 565 570 575

Leu Asp Thr Cys Cys Lys Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr  
 580 585 590

Glu Gly Pro Asn Leu Val Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly  
 595 600 605

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ser Gln  
 610 615 620

Val Lys Leu Glu Gln Ser Gly Ala Glu Val Val Lys Pro Gly Ala Ser  
 625 630 635 640

Val Lys Leu Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Ser Tyr



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645			650			655									
Met	His	Trp	Leu	Arg	Gln	Gly	Pro	Gly	Gln	Cys	Leu	Glu	Trp	Ile	Gly
			660					665				670			
Trp	Ile	Asp	Pro	Glu	Asn	Gly	Asp	Thr	Glu	Tyr	Ala	Pro	Lys	Phe	Gln
		675					680					685			
Gly	Lys	Ala	Thr	Phe	Thr	Thr	Asp	Thr	Ser	Ala	Asn	Thr	Ala	Tyr	Leu
	690					695					700				
Gly	Leu	Ser	Ser	Leu	Arg	Pro	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Asn
	705				710					715					720
Glu	Gly	Thr	Pro	Thr	Gly	Pro	Tyr	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly
				725						730				735	
Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly
		740						745						750	
Ser	Gly	Gly	Gly	Gly	Ser	Glu	Asn	Val	Leu	Thr	Gln	Ser	Pro	Ser	Ser
		755					760						765		
Met	Ser	Val	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Ala	Cys	Ser	Ala	Ser
	770					775					780				
Ser	Ser	Val	Pro	Tyr	Met	His	Trp	Leu	Gln	Gln	Lys	Pro	Gly	Lys	Ser
	785				790						795				800
Pro	Lys	Leu	Leu	Ile	Tyr	Leu	Thr	Ser	Asn	Leu	Ala	Ser	Gly	Val	Pro
			805							810				815	
Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Ser	Leu	Thr	Ile
		820						825						830	
Ser	Ser	Val	Gln	Pro	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Arg
		835					840						845		
Ser	Ser	Tyr	Pro	Leu	Thr	Phe	Gly	Cys	Gly	Thr	Lys	Leu	Glu	Ile	Lys
	850					855					860				
Gly	Gly	Gly	Gly	Ser	His	His	His	His	His	His	His				
	865				870						875				

<210> SEQ ID NO 107  
 <211> LENGTH: 573  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL138-107-G3-c-myc-Aga2

<400> SEQUENCE: 107

```

atgaagggtt tgattgtctt gttggctatc ttcgctgctt tgccattggc cttagctcaa    60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagagccacc    120
gagctgagat gccagtgcct gcagaccctg cagggcatcc accccaagaa catccagagc    180
gtgaacgtga agtcccctgg cccccactgc gccagaccg aagtgatcgc caccctgaag    240
aacggccgga aggctgcct gaaccccgcc agccccatcg tgaagaaaat catcgagaag    300
atgctgaaca gcgacaagag caacggcgga ggccaacaaa agcttatctc cgaagaagac    360
ttgcaggaac tgacaactat atgcgagcaa atcccctcac caactttaga atcgacgccc    420
tactctttgt caacgactac tattttggcc aacgggaagg caatgcaagg agtttttgaa    480
tattacaaat cagtaacgtt tgcagtaat tgcggttctc acccctcaac aactagcaaa    540
ggcagcccca taaacacaca gtatgttttt taa                                573
    
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<210> SEQ ID NO 108

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<211> LENGTH: 573
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL238-107-G3-c-myc-Aga2

<400> SEQUENCE: 108
atgaagggttt tgattgtcctt gttggctatc ttcgctgctt tgccattggc cttagctcaa    60
cgggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagagccaca    120
gagctgagat gccagtgcct ccagacactc cagggcatcc acctgaagaa catccagagc    180
gtgaaagtga agtcccctgg cccccactgc gccagacag aagtgatcgc caccctgaag    240
aatggccaga aggctgcct gaaccccgcc agccctatgg tcaagaaaat catcgagaag    300
atgctgaaga acggcaagag caacggcgga ggcaacaaa agcttatctc cgaagaagac    360
ttgcaggaac tgacaactat atcgagcaa atccccctcac caactttaga atcgacgccg    420
tactctttgt caacgactac tattttggcc aacgggaagg caatgcaagg agtttttgaa    480
tattacaaat cagtaacgtt tgcagtaat tgcggttctc acccctcaac aactagcaaa    540
ggcagcccca taaacacaca gtatgttttt taa                                573

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<210> SEQ ID NO 109
<211> LENGTH: 573
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL338-107-G3-c-myc-Aga2

<400> SEQUENCE: 109
atgaagggttt tgattgtcctt gttggctatc ttcgctgctt tgccattggc cttagctcaa    60
cgggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagagtgacc    120
gagctgagat gccagtgcct ccagacactc cagggcatcc acctgaagaa catccagagc    180
gtgaacgtgc ggagccctgg ccctcattgt gccagacag aagtgatcgc caccctgaag    240
aatggcaaga aggctgcct gaaccccgcc agccctatgg tgcagaagat catcgagaag    300
atcctgaaca agggcagcac caacggcgga ggcaacaaa agcttatctc cgaagaagac    360
ttgcaggaac tgacaactat atcgagcaa atccccctcac caactttaga atcgacgccg    420
tactctttgt caacgactac tattttggcc aacgggaagg caatgcaagg agtttttgaa    480
tattacaaat cagtaacgtt tgcagtaat tgcggttctc acccctcaac aactagcaaa    540
ggcagcccca taaacacaca gtatgttttt taa                                573

```

```

<210> SEQ ID NO 110
<211> LENGTH: 573
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL432-101-G3-c-myc-Aga2

<400> SEQUENCE: 110
atgaagggttt tgattgtcctt gttggctatc ttcgctgctt tgccattggc cttagctcaa    60
cgggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagagaggct    120
gaagaggacg gcgatctcca gtgcctgtgc gtgaaaacca ccagccaagt gcgggccaga    180
cacatcacca gcctggaagt gatcaaggcc ggacccact gtcctaccgc ccagctgatt    240

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gccaccctga agaacggcgg gaagatctgc ctggacctcc agggccccct gtacaagaag 300
atcatcaaga agctgctgga aagcggcggga ggccaacaaa agcttatctc cgaagaagac 360
ttgcaggaac tgacaactat atgcgagcaa atccccctac caactttaga atcgacgccc 420
tactctttgt caacgactac tattttggcc aacgggaagg caatgcaagg agtttttgaa 480
tattacaaat cagtaacggt tgtcagtaat tgcggttctc acccctcaac aactagcaaa 540
ggcagcccca taaacacaca gtatgttttt taa 573

```

```

<210> SEQ ID NO 111
<211> LENGTH: 576
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL544-114-G3-c-myc-Aga2

```

&lt;400&gt; SEQUENCE: 111

```

atgaaggttt tgattgtctt gttggetatc ttcgctgctt tgccattggc cttagctcaa 60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaa gagactgccc 120
gagctgagat gcgtgtgcct gcagaccacc cagggcgtgc accccaagat gatcagcaac 180
ctccagggtg tgcctatcgg cccccagtgc agcaagggtg aagtgggtgg cagcctgaag 240
aacggcaaag agatctgcct ggaccccgag gccccattcc tgaagaaagt gatccagaag 300
atcctggacg gcggaacaaa agagaacggc ggaggcgaac aaaagcttat ctccgaagaa 360
gacttgacag aactgacaac tatatgcgag caaatccct caccaacttt agaatcgacg 420
ccgtactctt tgtcaacgac tactattttg gccaacggga aggcaatgca aggagttttt 480
gaatattaca aatcagtaac gtttgcagc aattgcgggt ctcacccctc aacaactagc 540
aaaggcagcc ccataaacac acagtatggt ttttaa 576

```

```

<210> SEQ ID NO 112
<211> LENGTH: 576
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL644-114-G3-c-myc-Aga2

```

&lt;400&gt; SEQUENCE: 112

```

atgaaggttt tgattgtctt gttggetatc ttcgctgctt tgccattggc cttagctcaa 60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaa gagactgacc 120
gagctgagggt gcacctgtct gagagtgacc ctgacgctga accccaagac catcggaag 180
ctccagggtg tcctgcccgg cctcagtgcc agcaagggtg aagtgggtgg cagcctgaaa 240
aacggaaaac aagtgtgcct ggaccccgag gccccattcc tgaagaaagt gatccagaag 300
atcctggaca gcggaacaaa gaagaacggc ggaggcgaac aaaagcttat ctccgaagaa 360
gacttgacag aactgacaac tatatgcgag caaatccct caccaacttt agaatcgacg 420
ccgtactctt tgtcaacgac tactattttg gccaacggga aggcaatgca aggagttttt 480
gaatattaca aatcagtaac gtttgcagc aattgcgggt ctcacccctc aacaactagc 540
aaaggcagcc ccataaacac acagtatggt ttttaa 576

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<210> SEQ ID NO 113
<211> LENGTH: 552
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL759-121-G3-c-myc-Aga2

<400> SEQUENCE: 113
atgaaggttt tgattgtctt gttggctatc ttcgctgctt tgccattggc cttagetcaa    60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaaa gagagccgag    120
ctgcggtgca tgtgcatcaa gaccaccagc ggaatccacc ccaagaatat ccagtccctg    180
gaagtgattg gcaagggcac cactgcaac caggtggaag tgattgccac actgaaagac    240
ggccggaaga tctgcctgga ccctgacgcc ccagaatca agaaaatcgt gcagaaaaag    300
ctgggcccgg gcaaacaaaa gcttatctcc gaagaagact tgcaggaact gacaactata    360
tgcgagcaaa tcccctcacc aactttagaa tcgacgccgt actctttgtc aacgactact    420
atthttggcca acgggaaggc aatgcaagga gtttttgaat attacaaatc agtaacgttt    480
gtcagtaatt gcggttctca cccctcaaca actagcaaaag gcagccccat aaacacacag    540
tatgtttttt aa                                                    552

<210> SEQ ID NO 114
<211> LENGTH: 576
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL829-99-G3-c-myc-Aga2

<400> SEQUENCE: 114
atgaaggttt tgattgtctt gttggctatc ttcgctgctt tgccattggc cttagetcaa    60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaaa gagagccaaa    120
gaactgcggt gccagtgcac caagacctac agcaagccct tccaccccaa gttcatcaaa    180
gaactgagag tgatcgagag cggccctcac tgcgccaaca ccgagatcat cgtgaagctg    240
agcgacggca gagagctgtg cctggacccc aaagaaaact ggggtgcagcg ggtggtgaa    300
aagttcctga agcggggcca gaacagcggc ggaggcgaac aaaagcttat ctccgaagaa    360
gacttgacgg aactgacaac tatatgcgag caaatcccct caccaacttt agaatcgacg    420
ccgtactctt tgtcaacgac tactatthttg gccaacggga aggcaatgca aggagthttt    480
gaatattaca aatcagtaac gtttgcagc aattgcgggt ctcaccctc aacaactagc    540
aaaggcagcc ccataaacac acagtatggt ttttaa                                                    576

<210> SEQ ID NO 115
<211> LENGTH: 672
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL923-115-G3-c-myc-Aga2

<400> SEQUENCE: 115
atgaaggttt tgattgtctt gttggctatc ttcgctgctt tgccattggc cttagetcaa    60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaaa gagaaccccc    120
gtcgtgcgga agggcagatg cagctgtatc agcaccaacc agggaccat ccatctccag    180
tctctgaagg acctgaagca gttcgcccc agccccagct gcgagaagat cgagattatc    240
gccacactga aaaacggggg gcagacctgc ctgaaccccg acagcgcgca cgtgaaagaa    300

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ctgatcaaga aatgggagaa acaggtgtcc cagaagaaga agcagaagaa cggaaagaag   360
caccagaaaa agaaagtgct gaaagtgcgg aagtcccagc ggagccggca gaagaaaacc   420
acaggcggag gcgaacaaaa gcttatctcc gaagaagact tgcaggaact gacaactata   480
tgcgagcaaa tcccctcacc aactttagaa tcgacgccgt actctttgtc aacgactact   540
atthtggcca acgggaaggg aatgcaagga gtttttgaat attacaaatc agtaacgttt   600
gtcagtaatt gcggttctca cccctcaaca actagcaaag gcagcccat aaacacacag   660
tatgtttttt aa                                                           672

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&lt;210&gt; SEQ ID NO 116

&lt;211&gt; LENGTH: 594

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL1022-98-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 116

```

atgaaggttt tgattgtctt gttggctatc ttcgctgctt tgccattggc cttagctcaa   60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaaa gagagtgcct   120
ctgagcagaa ccgtgcgggt cacctgtatc agcatcagca accagcccggt gaaccccaga   180
agcctgaaaa agctggaat catccccgcc agccagttct gcccagagt ggaattatc   240
gccaccatga agaagaaagg cgagaagcgg tgcctgaacc ccgagagcaa ggcatcaag   300
aacctgctga aggccgtgtc caaagagcgg agcaagcggg gccagcggg aggcgaacaa   360
aagcttatct ccgaagaaga cttgcaggaa ctgacaacta tatgcgagca aatcccctca   420
ccaactttag aatcgacgcc gtactctttg tcaacgacta ctattttggc caacgggaag   480
gcaatgcaag gagtttttga atattacaaa tcagtaacct ttgtcagtaa ttgcggttct   540
caccctcaa caactagcaa aggcagcccc ataacacac agtatgtttt ttaa           594

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&lt;210&gt; SEQ ID NO 117

&lt;211&gt; LENGTH: 582

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL1122-94-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 117

```

atgaaggttt tgattgtctt gttggctatc ttcgctgctt tgccattggc cttagctcaa   60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaaa gagattcccc   120
atgttcaagc ggggcagatg cctgtgcatc ggcctggcgg tgaaagccgt gaaggtggcc   180
gatatcgaga aggccagcat catgtacccc agcaacaact gcgacaagat cgaagtgatc   240
atcaccctga aagagaacaa gggccagaga tgcctgaatc ccaagtccaa gcaggcccgg   300
ctgatcatca agaaggtgga acggaagaac ttcggcggag gcgaacaaaa gcttatctcc   360
gaagaagact tgcaggaact gacaactata tgcgagcaaa tcccctcacc aactttagaa   420
tcgacgccgt actctttgtc aacgactact atthtggcca acgggaaggg aatgcaagga   480
gtttttgaat attacaaatc agtaacgttt gtcagtaatt gcggttctca cccctcaaca   540
actagcaaag gcagcccat aaacacacag tatgtttttt aa                       582

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&lt;210&gt; SEQ ID NO 118

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<211> LENGTH: 570
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL128-96-G3-c-myc-Aga2

<400> SEQUENCE: 118
atgaagggttt tgattgtcctt gttggctatc ttcgctgctt tgccattggc cttagctcaa      60
cgggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagagccaac      120
gagctgcggt gccagtgcct gcagaccatg gccggcatcc acctgaagaa catccagagc      180
ctgaagggtgc tgcccagcgg ccctcactgc acccagaccg aagtgatcgc caccctgaag      240
aacggcagag aggctgcct ggatcccag gccccctgg tgcagaaaat cgtgcagaaa      300
atgctgaagg gcgtgcccac gggcggaggc gaacaaaagc ttatctccga agaagacttg      360
caggaactga caactatatg cgagcaaatc cctcaccacaa ctttagaatc gacgccttac      420
tctttgtcaa cgactactat tttggccaac ggggaaggcaa tgcaaggagt ttttgaatat      480
tacaatcag taacgtttgt cagtaattgc gtttctcacc cctcaacaac tagcaaaggc      540
agccccataa acacacagta tgttttttaa      570

<210> SEQ ID NO 119
<211> LENGTH: 573
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL231-100-G3-c-myc-Aga2

<400> SEQUENCE: 119
atgaagggttt tgattgtcctt gttggctatc ttcgctgctt tgccattggc cttagctcaa      60
cgggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagagccagc      120
gagctgcggt gccagtgcct gaaaaccctg ccccggtggg acttcaagaa catccagagc      180
ctgagcgtga cccccctgg ccctcactgt gcccagaccg aagtgatcgc caccctgaag      240
ggcggccaga aagtgtgcct ggaccccag gccccctgg tgcagaagat catccagaag      300
atcctgaaca agggcaaggc caacggcgga ggcaacaaa agcttatctc cgaagaagac      360
ttgcaggaac tgacaactat atcgagacaa atcccctcac caactttaga atcgacgccg      420
tactctttgt caacgactac tattttggcc aacgggaagg caatgcaagg agtttttgaa      480
tattacaaat cagtaacgtt tgcagtaat tgcggttctc acccctcaac aactagcaaa      540
ggcagcccca taaacacaca gtatgttttt taa      573

<210> SEQ ID NO 120
<211> LENGTH: 573
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL331-100-G3-c-myc-Aga2

<400> SEQUENCE: 120
atgaagggttt tgattgtcctt gttggctatc ttcgctgctt tgccattggc cttagctcaa      60
cgggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagagcctct      120
gagctgagat gccagtgcct gaacaccctg ccccggtggg acttccagac aatccagagc      180
ctgaccgtga cccccctgg ccctcactgt acccagacag aagtgatcgc caccctgaag      240

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gacggccagg aagtgtgctt gaatccccag ggccccagac tccagatcat catcaagaag 300
atcctgaagt cggcaagag cagcggcggga ggccaacaaa agcttatctc cgaagaagac 360
ttgcaggaac tgacaactat atgcgagcaa atccccctac caactttaga atcgacgccc 420
tactctttgt caacgactac tattttggcc aacgggaagg caatgcaagg agtttttgaa 480
tattacaaat cagtaacggt tgtaagtaat tgcggttctc acccctcaac aactagcaaa 540
ggcagcccca taaacacaca gtatgttttt taa 573

```

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<210> SEQ ID NO 121
<211> LENGTH: 591
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL430-105-G3-c-myc-Aga2

```

&lt;400&gt; SEQUENCE: 121

```

atgaaggttt tgattgtctt gttggetatc ttcgctgctt tgccattggc cttagetcaa 60
cgggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaa gagagtgaca 120
tctgcccggc ctgaggaaag cgacggcgat ctgtcttgcg tgtgcgtgaa aaccatcagc 180
agcggcatcc acctgaagca catcaccagc ctggaagtga tcaaggccgg caggcactgt 240
gccgtgctc agctgattgc caccctgaag aacggccgga agatctgcct ggacagacag 300
gccccctgt acaagaaagt gattaagaag atcctggaaa gcggcggagg cgaacaaaag 360
cttatctcgg aagaagactt gcaggaactg acaactatat gcgagcaaat cccctcacca 420
actttagaat cgacgccgta ctctttgtca acgactacta ttttgccaa cggaaggca 480
atgcaaggag tttttgaata ttacaaatca gtaacgtttg tcagtaattg cggttctcac 540
ccctcaacaa ctagcaaaagg cagccccata aacacacagt atgtttttta a 591

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<210> SEQ ID NO 122
<211> LENGTH: 576
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL548-118-G3-c-myc-Aga2

```

&lt;400&gt; SEQUENCE: 122

```

atgaaggttt tgattgtctt gttggetatc ttcgctgctt tgccattggc cttagetcaa 60
cgggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaa gagagccacc 120
gagctgagat gcgtgtgctt gaccgtgacc cccaagatca accccaagct gatcgccaac 180
ctggaagtga tccttgccgg cctcagtgcc cccaccgtgg aagtgattgc caagctgaag 240
aaccagaaag aagtgtgctt ggaccccgag gccccctgta tcaagaagat catccagaag 300
atcctgggca gcgacaagaa gaaagccggc ggaggcgaac aaaagcttat ctccgaagaa 360
gacttgaggc aactgacaac tatatgagag caaatccctt caccaacttt agaatcgacg 420
ccgtactctt tgtcaacgac tactatcttg gccaacggga aggcaatgca aggagttttt 480
gaatattaca aatcagtaac gtttgcagc aattgcgggt ctcaccctc aacaactagc 540
aaaggcagcc ccataaacac acagtatggt ttttaa 576

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<210> SEQ ID NO 123
<211> LENGTH: 561
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL748-113-G3-c-myc-Aga2

<400> SEQUENCE: 123

atgaaggttt tgattgtott gttggctatc ttcgctgctt tgccattggc cttagctcaa    60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagaatcgag    120
ctgcggtgcc ggtgcaccaa caccatcagc ggcacccctt tcaacagcat cagcctcgtg    180
aacgtgtaca gaccggcggt gactgcgcc gacgtggaag tgattgctac actgaagaat    240
gggcagaaaa cctgcctgga cccaacgcc cctggcgtga agcggatcgt gatgaagatt    300
ctggaaggct acggcggagg cgaacaaaag cttatctccg aagaagactt gcaggaactg    360
acaactatat gcgagcaaat cccctcacca actttagaat cgacgccgta ctctttgtca    420
acgactacta ttttggccaa cgggaaggca atgcaaggag tttttgaata ttacaaatca    480
gtaacgtttg tcagtaattg cgtttctcac cctcaacaa ctagcaaagg cagccccata    540
aacacacagt atgtttttta a                                         561

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<210> SEQ ID NO 124
<211> LENGTH: 678
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL922-126-G3-c-myc-Aga2

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<400> SEQUENCE: 124

atgaaggttt tgattgtott gttggctatc ttcgctgctt tgccattggc cttagctcaa    60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagaaccctc    120
gtgatccgga acgcccgggt cagctgtatc agcaccagca gaggcaccat ccaactacaag    180
agcctgaagg atctgaagca gttcgcoccc agccccaact gcaacaagac cgagattatc    240
gccacactga aaaacgggga ccagacctgt ctggaccccg acagcgccaa cgtgaagaaa    300
ctgatgaagg aatgggagaa gaagatcagc cagaagaaga agcagaagcg gggcaagaaa    360
caccagaaaa acatgaagaa ccggaagccc aagaccccc agagccggcg gagatccaga    420
aagaccacag gcggaggcga acaaaagctt atctccgaag aagacttgca ggaactgaca    480
actatatgcg agcaaatccc ctacccaact ttagaatcga cgccgtactc tttgtcaacg    540
actactatth tggccaacgg gaaggcaatg caaggagttt ttgaatatta caaatcagta    600
acgtttgtea gtaattgcyg ttctcaccoc tcaacaacta gcaaaggcag ccccataaac    660
acacagtatg ttttttaa                                         678

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<210> SEQ ID NO 125
<211> LENGTH: 594
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL1022-98-G3-c-myc-Aga2

```

```

<400> SEQUENCE: 125

atgaaggttt tgattgtott gttggctatc ttcgctgctt tgccattggc cttagctcaa    60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagaatccca    120
ctggccagaa ccgtgcgggt caactgcac cacatcgacg atggccccgt gcggatgaga    180

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gccatcgga agctggaat catccccgc agcctgagct gccccagagt gaaattatc 240
gccaccatga agaagaacga cgagcagcgg tgcctgaacc ccgagagcaa gaccatcaag 300
aacctgatga aggcccttag ccagaagcgg agcaagaggg ccccaggcgg aggcgaaaca 360
aagcttatct ccgaagaaga cttgcaggaa ctgacaacta tatgagagca aatcccctca 420
ccaactttag aatcgagcgc gtactctttg tcaacgacta ctattttggc caacgggaag 480
gcaatgcaag gagtttttga atattacaaa tcagtaacct ttgtcagtaa ttgcggttct 540
caccctcaa caactagcaa aggcagcccc ataaacacac agtatgtttt ttaa 594

```

&lt;210&gt; SEQ ID NO 126

&lt;211&gt; LENGTH: 600

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: pCHA-LS-mCXCL1122-100-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 126

```

atgaaggttt tgattgtott gttggctatc ttcgctgctt tgccattggc cttagctcaa 60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttggacaa gagattcctg 120
atggtcaagc agggccgggt cctgtgcac gccctggaa tgaaggccgt gaagatggcc 180
gagatcgaga aggccagcgt gatctacccc agcaacggct gcgacaaggt ggaagtgatc 240
gtgaccatga agggccacaa gcggcagaga tgcctggacc ccagatccaa gcaggcccgg 300
ctgatcatgc aggtatcga gaagaagaat ttcctgcggc ggcagaacat gggcgagggc 360
gaacaaaagc ttatctccga agaagacttg caggaactga caactatatg cgagcaaatc 420
ccctacacaa ctttagaatc gacgccgtac tctttgtcaa cgactactat tttggccaac 480
gggaaggcaa tgcaaggagt ttttgaatat tacaatcag taacgtttgt cagtaattgc 540
ggttctcacc cctcaacaac tagcaaggc agccccataa acacacagta tgttttttaa 600

```

&lt;210&gt; SEQ ID NO 127

&lt;211&gt; LENGTH: 190

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-hCXCL138-107-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 127

```

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu
1           5           10          15
Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu
20          25          30
Gly Ser Leu Asp Lys Arg Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln
35          40          45
Thr Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys
50          55          60
Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys
65          70          75          80
Asn Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys
85          90          95
Ile Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn Gly Gly Gly Glu
100         105         110
Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys

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115	120	125
Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser 130 135 140		
Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu 145 150 155 160		
Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser 165 170 175		
Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe 180 185 190		

<210> SEQ ID NO 128  
 <211> LENGTH: 190  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL238-107-G3-c-myc-Aga2

<400> SEQUENCE: 128

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu 1 5 10 15		
Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu 20 25 30		
Gly Ser Leu Asp Lys Arg Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln 35 40 45		
Thr Leu Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val Lys Val Lys 50 55 60		
Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys 65 70 75 80		
Asn Gly Gln Lys Ala Cys Leu Asn Pro Ala Ser Pro Met Val Lys Lys 85 90 95		
Ile Ile Glu Lys Met Leu Lys Asn Gly Lys Ser Asn Gly Gly Gly Glu 100 105 110		
Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys 115 120 125		
Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser 130 135 140		
Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu 145 150 155 160		
Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser 165 170 175		
Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe 180 185 190		

<210> SEQ ID NO 129  
 <211> LENGTH: 190  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL338-107-G3-c-myc-Aga2

<400> SEQUENCE: 129

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu 1 5 10 15		
Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu 20 25 30		

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Gly Ser Leu Asp Lys Arg Val Thr Glu Leu Arg Cys Gln Cys Leu Gln  
           35                                  40                                  45  
 Thr Leu Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val Asn Val Arg  
   50                                  55                                  60  
 Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys  
   65                                  70                                  75                                  80  
 Asn Gly Lys Lys Ala Cys Leu Asn Pro Ala Ser Pro Met Val Gln Lys  
                                   85                                  90                                  95  
 Ile Ile Glu Lys Ile Leu Asn Lys Gly Ser Thr Asn Gly Gly Gly Glu  
                                   100                                  105                                  110  
 Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys  
                                   115                                  120                                  125  
 Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser  
   130                                  135                                  140  
 Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu  
   145                                  150                                  155                                  160  
 Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser  
                                   165                                  170                                  175  
 Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
                                   180                                  185                                  190

&lt;210&gt; SEQ ID NO 130

&lt;211&gt; LENGTH: 190

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-hCXCL432-101-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 130

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
   1                                  5                                  10                                  15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
                                   20                                  25                                  30  
 Gly Ser Leu Asp Lys Arg Glu Ala Glu Glu Asp Gly Asp Leu Gln Cys  
                                   35                                  40                                  45  
 Leu Cys Val Lys Thr Thr Ser Gln Val Arg Pro Arg His Ile Thr Ser  
   50                                  55                                  60  
 Leu Glu Val Ile Lys Ala Gly Pro His Cys Pro Thr Ala Gln Leu Ile  
   65                                  70                                  75                                  80  
 Ala Thr Leu Lys Asn Gly Arg Lys Ile Cys Leu Asp Leu Gln Ala Pro  
                                   85                                  90                                  95  
 Leu Tyr Lys Lys Ile Ile Lys Lys Leu Leu Glu Ser Gly Gly Gly Glu  
                                   100                                  105                                  110  
 Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys  
                                   115                                  120                                  125  
 Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser  
   130                                  135                                  140  
 Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu  
   145                                  150                                  155                                  160  
 Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser  
                                   165                                  170                                  175  
 Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
                                   180                                  185                                  190

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<210> SEQ ID NO 131  
 <211> LENGTH: 191  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL544-114-G3-c-myc-Aga2

<400> SEQUENCE: 131

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
 1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
 20 25 30  
 Gly Ser Leu Asp Lys Arg Leu Arg Glu Leu Arg Cys Val Cys Leu Gln  
 35 40 45  
 Thr Thr Gln Gly Val His Pro Lys Met Ile Ser Asn Leu Gln Val Phe  
 50 55 60  
 Ala Ile Gly Pro Gln Cys Ser Lys Val Glu Val Val Ala Ser Leu Lys  
 65 70 75 80  
 Asn Gly Lys Glu Ile Cys Leu Asp Pro Glu Ala Pro Phe Leu Lys Lys  
 85 90 95  
 Val Ile Gln Lys Ile Leu Asp Gly Gly Asn Lys Glu Asn Gly Gly Gly  
 100 105 110  
 Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile  
 115 120 125  
 Cys Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu  
 130 135 140  
 Ser Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe  
 145 150 155 160  
 Glu Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro  
 165 170 175  
 Ser Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
 180 185 190

<210> SEQ ID NO 132  
 <211> LENGTH: 191  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL644-114-G3-c-myc-Aga2

<400> SEQUENCE: 132

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
 1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
 20 25 30  
 Gly Ser Leu Asp Lys Arg Leu Thr Glu Leu Arg Cys Thr Cys Leu Arg  
 35 40 45  
 Val Thr Leu Arg Val Asn Pro Lys Thr Ile Gly Lys Leu Gln Val Phe  
 50 55 60  
 Pro Ala Gly Pro Gln Cys Ser Lys Val Glu Val Val Ala Ser Leu Lys  
 65 70 75 80  
 Asn Gly Lys Gln Val Cys Leu Asp Pro Glu Ala Pro Phe Leu Lys Lys  
 85 90 95  
 Val Ile Gln Lys Ile Leu Asp Ser Gly Asn Lys Lys Asn Gly Gly Gly  
 100 105 110

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Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile  
 115 120 125  
 Cys Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu  
 130 135 140  
 Ser Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe  
 145 150 155 160  
 Glu Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro  
 165 170 175  
 Ser Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
 180 185 190

<210> SEQ ID NO 133  
 <211> LENGTH: 183  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL759-121-G3-c-myc-Aga2

<400> SEQUENCE: 133

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
 1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
 20 25 30  
 Gly Ser Leu Asp Lys Arg Ala Glu Leu Arg Cys Met Cys Ile Lys Thr  
 35 40 45  
 Thr Ser Gly Ile His Pro Lys Asn Ile Gln Ser Leu Glu Val Ile Gly  
 50 55 60  
 Lys Gly Thr His Cys Asn Gln Val Glu Val Ile Ala Thr Leu Lys Asp  
 65 70 75 80  
 Gly Arg Lys Ile Cys Leu Asp Pro Asp Ala Pro Arg Ile Lys Lys Ile  
 85 90 95  
 Val Gln Lys Lys Leu Gly Gly Gly Glu Gln Lys Leu Ile Ser Glu Glu  
 100 105 110  
 Asp Leu Gln Glu Leu Thr Thr Ile Cys Glu Gln Ile Pro Ser Pro Thr  
 115 120 125  
 Leu Glu Ser Thr Pro Tyr Ser Leu Ser Thr Thr Thr Ile Leu Ala Asn  
 130 135 140  
 Gly Lys Ala Met Gln Gly Val Phe Glu Tyr Tyr Lys Ser Val Thr Phe  
 145 150 155 160  
 Val Ser Asn Cys Gly Ser His Pro Ser Thr Thr Ser Lys Gly Ser Pro  
 165 170 175  
 Ile Asn Thr Gln Tyr Val Phe  
 180

<210> SEQ ID NO 134  
 <211> LENGTH: 191  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL829-99-G3-c-myc-Aga2

<400> SEQUENCE: 134

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
 1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu

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	20		25		30										
Gly	Ser	Leu	Asp	Lys	Arg	Ala	Lys	Glu	Leu	Arg	Cys	Gln	Cys	Ile	Lys
	35						40					45			
Thr	Tyr	Ser	Lys	Pro	Phe	His	Pro	Lys	Phe	Ile	Lys	Glu	Leu	Arg	Val
	50					55					60				
Ile	Glu	Ser	Gly	Pro	His	Cys	Ala	Asn	Thr	Glu	Ile	Ile	Val	Lys	Leu
65					70					75					80
Ser	Asp	Gly	Arg	Glu	Leu	Cys	Leu	Asp	Pro	Lys	Glu	Asn	Trp	Val	Gln
				85					90					95	
Arg	Val	Val	Glu	Lys	Phe	Leu	Lys	Arg	Ala	Glu	Asn	Ser	Gly	Gly	Gly
			100					105					110		
Glu	Gln	Lys	Leu	Ile	Ser	Glu	Glu	Asp	Leu	Gln	Glu	Leu	Thr	Thr	Ile
		115					120					125			
Cys	Glu	Gln	Ile	Pro	Ser	Pro	Thr	Leu	Glu	Ser	Thr	Pro	Tyr	Ser	Leu
	130					135					140				
Ser	Thr	Thr	Thr	Ile	Leu	Ala	Asn	Gly	Lys	Ala	Met	Gln	Gly	Val	Phe
145					150					155					160
Glu	Tyr	Tyr	Lys	Ser	Val	Thr	Phe	Val	Ser	Asn	Cys	Gly	Ser	His	Pro
			165						170					175	
Ser	Thr	Thr	Ser	Lys	Gly	Ser	Pro	Ile	Asn	Thr	Gln	Tyr	Val	Phe	
			180						185				190		

<210> SEQ ID NO 135  
 <211> LENGTH: 223  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL923-115-G3-c-myc-Aga2

<400> SEQUENCE: 135

Met	Lys	Val	Leu	Ile	Val	Leu	Leu	Ala	Ile	Phe	Ala	Ala	Leu	Pro	Leu
1				5					10					15	
Ala	Leu	Ala	Gln	Pro	Val	Ile	Ser	Thr	Thr	Val	Gly	Ser	Ala	Ala	Glu
			20					25					30		
Gly	Ser	Leu	Asp	Lys	Arg	Thr	Pro	Val	Val	Arg	Lys	Gly	Arg	Cys	Ser
		35					40					45			
Cys	Ile	Ser	Thr	Asn	Gln	Gly	Thr	Ile	His	Leu	Gln	Ser	Leu	Lys	Asp
	50					55					60				
Leu	Lys	Gln	Phe	Ala	Pro	Ser	Pro	Ser	Cys	Glu	Lys	Ile	Glu	Ile	Ile
65					70					75					80
Ala	Thr	Leu	Lys	Asn	Gly	Val	Gln	Thr	Cys	Leu	Asn	Pro	Asp	Ser	Ala
				85					90					95	
Asp	Val	Lys	Glu	Leu	Ile	Lys	Lys	Trp	Glu	Lys	Gln	Val	Ser	Gln	Lys
			100					105					110		
Lys	Lys	Gln	Lys	Asn	Gly	Lys	Lys	His	Gln	Lys	Lys	Lys	Val	Leu	Lys
		115					120						125		
Val	Arg	Lys	Ser	Gln	Arg	Ser	Arg	Gln	Lys	Lys	Thr	Thr	Gly	Gly	Gly
	130					135					140				
Glu	Gln	Lys	Leu	Ile	Ser	Glu	Glu	Asp	Leu	Gln	Glu	Leu	Thr	Thr	Ile
145					150					155					160
Cys	Glu	Gln	Ile	Pro	Ser	Pro	Thr	Leu	Glu	Ser	Thr	Pro	Tyr	Ser	Leu
			165						170					175	
Ser	Thr	Thr	Thr	Ile	Leu	Ala	Asn	Gly	Lys	Ala	Met	Gln	Gly	Val	Phe

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180	185	190
Glu Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro		
195	200	205
Ser Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe		
210	215	220

<210> SEQ ID NO 136  
 <211> LENGTH: 197  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL1022-98-G3-c-myc-Aga2

<400> SEQUENCE: 136

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu		
1	5	10
Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu		
20	25	30
Gly Ser Leu Asp Lys Arg Val Pro Leu Ser Arg Thr Val Arg Cys Thr		
35	40	45
Cys Ile Ser Ile Ser Asn Gln Pro Val Asn Pro Arg Ser Leu Glu Lys		
50	55	60
Leu Glu Ile Ile Pro Ala Ser Gln Phe Cys Pro Arg Val Glu Ile Ile		
65	70	75
Ala Thr Met Lys Lys Lys Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser		
85	90	95
Lys Ala Ile Lys Asn Leu Leu Lys Ala Val Ser Lys Glu Arg Ser Lys		
100	105	110
Arg Ser Pro Gly Gly Gly Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu		
115	120	125
Gln Glu Leu Thr Thr Ile Cys Glu Gln Ile Pro Ser Pro Thr Leu Glu		
130	135	140
Ser Thr Pro Tyr Ser Leu Ser Thr Thr Thr Ile Leu Ala Asn Gly Lys		
145	150	155
Ala Met Gln Gly Val Phe Glu Tyr Tyr Lys Ser Val Thr Phe Val Ser		
165	170	175
Asn Cys Gly Ser His Pro Ser Thr Thr Ser Lys Gly Ser Pro Ile Asn		
180	185	190
Thr Gln Tyr Val Phe		
195		

<210> SEQ ID NO 137  
 <211> LENGTH: 193  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-hCXCL1122-94-G3-c-myc-Aga2

<400> SEQUENCE: 137

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu		
1	5	10
Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu		
20	25	30
Gly Ser Leu Asp Lys Arg Phe Pro Met Phe Lys Arg Gly Arg Cys Leu		
35	40	45

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Cys Ile Gly Pro Gly Val Lys Ala Val Lys Val Ala Asp Ile Glu Lys  
 50 55 60  
 Ala Ser Ile Met Tyr Pro Ser Asn Asn Cys Asp Lys Ile Glu Val Ile  
 65 70 75 80  
 Ile Thr Leu Lys Glu Asn Lys Gly Gln Arg Cys Leu Asn Pro Lys Ser  
 85 90 95  
 Lys Gln Ala Arg Leu Ile Ile Lys Lys Val Glu Arg Lys Asn Phe Gly  
 100 105 110  
 Gly Gly Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr  
 115 120 125  
 Thr Ile Cys Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr  
 130 135 140  
 Ser Leu Ser Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly  
 145 150 155 160  
 Val Phe Glu Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser  
 165 170 175  
 His Pro Ser Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val  
 180 185 190

Phe

<210> SEQ ID NO 138  
 <211> LENGTH: 189  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mCXCL128-96-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 138

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
 1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
 20 25 30  
 Gly Ser Leu Asp Lys Arg Ala Asn Glu Leu Arg Cys Gln Cys Leu Gln  
 35 40 45  
 Thr Met Ala Gly Ile His Leu Lys Asn Ile Gln Ser Leu Lys Val Leu  
 50 55 60  
 Pro Ser Gly Pro His Cys Thr Gln Thr Glu Val Ile Ala Thr Leu Lys  
 65 70 75 80  
 Asn Gly Arg Glu Ala Cys Leu Asp Pro Glu Ala Pro Leu Val Gln Lys  
 85 90 95  
 Ile Val Gln Lys Met Leu Lys Gly Val Pro Lys Gly Gly Gly Glu Gln  
 100 105 110  
 Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys Glu  
 115 120 125  
 Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser Thr  
 130 135 140  
 Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu Tyr  
 145 150 155 160  
 Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser Thr  
 165 170 175  
 Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
 180 185



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<210> SEQ ID NO 139  
 <211> LENGTH: 190  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mCXCL231-100-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 139

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
 1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
 20 25 30  
 Gly Ser Leu Asp Lys Arg Ala Ser Glu Leu Arg Cys Gln Cys Leu Lys  
 35 40 45  
 Thr Leu Pro Arg Val Asp Phe Lys Asn Ile Gln Ser Leu Ser Val Thr  
 50 55 60  
 Pro Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys  
 65 70 75 80  
 Gly Gly Gln Lys Val Cys Leu Asp Pro Glu Ala Pro Leu Val Gln Lys  
 85 90 95  
 Ile Ile Gln Lys Ile Leu Asn Lys Gly Lys Ala Asn Gly Gly Gly Glu  
 100 105 110  
 Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys  
 115 120 125  
 Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser  
 130 135 140  
 Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu  
 145 150 155 160  
 Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser  
 165 170 175  
 Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
 180 185 190

<210> SEQ ID NO 140  
 <211> LENGTH: 190  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mCXCL331-100-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 140

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
 1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
 20 25 30  
 Gly Ser Leu Asp Lys Arg Ala Ser Glu Leu Arg Cys Gln Cys Leu Asn  
 35 40 45  
 Thr Leu Pro Arg Val Asp Phe Glu Thr Ile Gln Ser Leu Thr Val Thr  
 50 55 60  
 Pro Pro Gly Pro His Cys Thr Gln Thr Glu Val Ile Ala Thr Leu Lys  
 65 70 75 80  
 Asp Gly Gln Glu Val Cys Leu Asn Pro Gln Gly Pro Arg Leu Gln Ile  
 85 90 95  
 Ile Ile Lys Lys Ile Leu Lys Ser Gly Lys Ser Ser Gly Gly Gly Glu  
 100 105 110

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Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys  
115 120 125

Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser  
130 135 140

Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu  
145 150 155 160

Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser  
165 170 175

Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
180 185 190

<210> SEQ ID NO 141

<211> LENGTH: 196

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: LS-mCXCL430-105-G3-c-myc-Aga2

<400> SEQUENCE: 141

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
1 5 10 15

Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
20 25 30

Gly Ser Leu Asp Lys Arg Val Thr Ser Ala Gly Pro Glu Glu Ser Asp  
35 40 45

Gly Asp Leu Ser Cys Val Cys Val Lys Thr Ile Ser Ser Gly Ile His  
50 55 60

Leu Lys His Ile Thr Ser Leu Glu Val Ile Lys Ala Gly Arg His Cys  
65 70 75 80

Ala Val Pro Gln Leu Ile Ala Thr Leu Lys Asn Gly Arg Lys Ile Cys  
85 90 95

Leu Asp Arg Gln Ala Pro Leu Tyr Lys Lys Val Ile Lys Lys Ile Leu  
100 105 110

Glu Ser Gly Gly Gly Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln  
115 120 125

Glu Leu Thr Thr Ile Cys Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser  
130 135 140

Thr Pro Tyr Ser Leu Ser Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala  
145 150 155 160

Met Gln Gly Val Phe Glu Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn  
165 170 175

Cys Gly Ser His Pro Ser Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr  
180 185 190

Gln Tyr Val Phe  
195

<210> SEQ ID NO 142

<211> LENGTH: 191

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: LS-mCXCL548-118-G3-c-myc-Aga2

<400> SEQUENCE: 142

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
1 5 10 15

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Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
 20 25 30

Gly Ser Leu Asp Lys Arg Ala Thr Glu Leu Arg Cys Val Cys Leu Thr  
 35 40 45

Val Thr Pro Lys Ile Asn Pro Lys Leu Ile Ala Asn Leu Glu Val Ile  
 50 55 60

Pro Ala Gly Pro Gln Cys Pro Thr Val Glu Val Ile Ala Lys Leu Lys  
 65 70 75 80

Asn Gln Lys Glu Val Cys Leu Asp Pro Glu Ala Pro Val Ile Lys Lys  
 85 90 95

Ile Ile Gln Lys Ile Leu Gly Ser Asp Lys Lys Lys Ala Gly Gly Gly  
 100 105 110

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile  
 115 120 125

Cys Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu  
 130 135 140

Ser Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe  
 145 150 155 160

Glu Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro  
 165 170 175

Ser Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
 180 185 190

&lt;210&gt; SEQ ID NO 143

&lt;211&gt; LENGTH: 186

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-mCXCL748-113-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 143

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
 1 5 10 15

Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
 20 25 30

Gly Ser Leu Asp Lys Arg Ile Glu Leu Arg Cys Arg Cys Thr Asn Thr  
 35 40 45

Ile Ser Gly Ile Pro Phe Asn Ser Ile Ser Leu Val Asn Val Tyr Arg  
 50 55 60

Pro Gly Val His Cys Ala Asp Val Glu Val Ile Ala Thr Leu Lys Asn  
 65 70 75 80

Gly Gln Lys Thr Cys Leu Asp Pro Asn Ala Pro Gly Val Lys Arg Ile  
 85 90 95

Val Met Lys Ile Leu Glu Gly Tyr Gly Gly Gly Glu Gln Lys Leu Ile  
 100 105 110

Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys Glu Gln Ile Pro  
 115 120 125

Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser Thr Thr Thr Ile  
 130 135 140

Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu Tyr Tyr Lys Ser  
 145 150 155 160

Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser Thr Thr Ser Lys  
 165 170 175

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Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe  
180 185

<210> SEQ ID NO 144  
 <211> LENGTH: 225  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mCXCL922-126-G3-c-myc-Aga2

<400> SEQUENCE: 144

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
20 25 30  
 Gly Ser Leu Asp Lys Arg Thr Leu Val Ile Arg Asn Ala Arg Cys Ser  
35 40 45  
 Cys Ile Ser Thr Ser Arg Gly Thr Ile His Tyr Lys Ser Leu Lys Asp  
50 55 60  
 Leu Lys Gln Phe Ala Pro Ser Pro Asn Cys Asn Lys Thr Glu Ile Ile  
65 70 75 80  
 Ala Thr Leu Lys Asn Gly Asp Gln Thr Cys Leu Asp Pro Asp Ser Ala  
85 90 95  
 Asn Val Lys Lys Leu Met Lys Glu Trp Glu Lys Lys Ile Ser Gln Lys  
100 105 110  
 Lys Lys Gln Lys Arg Gly Lys Lys His Gln Lys Asn Met Lys Asn Arg  
115 120 125  
 Lys Pro Lys Thr Pro Gln Ser Arg Arg Arg Ser Arg Lys Thr Thr Gly  
130 135 140  
 Gly Gly Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr  
145 150 155 160  
 Thr Ile Cys Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr  
165 170 175  
 Ser Leu Ser Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly  
180 185 190  
 Val Phe Glu Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser  
195 200 205  
 His Pro Ser Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val  
210 215 220  
 Phe  
225

<210> SEQ ID NO 145  
 <211> LENGTH: 197  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: LS-mCXCL1022-98-G3-c-myc-Aga2

<400> SEQUENCE: 145

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu  
1 5 10 15  
 Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu  
20 25 30  
 Gly Ser Leu Asp Lys Arg Ile Pro Leu Ala Arg Thr Val Arg Cys Asn

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35	40	45																	
Cys	Ile	His	Ile	Asp	Asp	Gly	Pro	Val	Arg	Met	Arg	Ala	Ile	Gly	Lys				
50						55					60								
Leu	Glu	Ile	Ile	Pro	Ala	Ser	Leu	Ser	Cys	Pro	Arg	Val	Glu	Ile	Ile				
65					70					75					80				
Ala	Thr	Met	Lys	Lys	Asn	Asp	Glu	Gln	Arg	Cys	Leu	Asn	Pro	Glu	Ser				
				85					90					95					
Lys	Thr	Ile	Lys	Asn	Leu	Met	Lys	Ala	Phe	Ser	Gln	Lys	Arg	Ser	Lys				
			100					105					110						
Arg	Ala	Pro	Gly	Gly	Gly	Glu	Gln	Lys	Leu	Ile	Ser	Glu	Glu	Asp	Leu				
			115				120					125							
Gln	Glu	Leu	Thr	Thr	Ile	Cys	Glu	Gln	Ile	Pro	Ser	Pro	Thr	Leu	Glu				
	130					135						140							
Ser	Thr	Pro	Tyr	Ser	Leu	Ser	Thr	Thr	Thr	Ile	Leu	Ala	Asn	Gly	Lys				
145					150					155					160				
Ala	Met	Gln	Gly	Val	Phe	Glu	Tyr	Tyr	Lys	Ser	Val	Thr	Phe	Val	Ser				
				165					170					175					
Asn	Cys	Gly	Ser	His	Pro	Ser	Thr	Thr	Ser	Lys	Gly	Ser	Pro	Ile	Asn				
			180					185					190						
Thr	Gln	Tyr	Val	Phe															
			195																

&lt;210&gt; SEQ ID NO 146

&lt;211&gt; LENGTH: 199

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: LS-mCXCL1122-100-G3-c-myc-Aga2

&lt;400&gt; SEQUENCE: 146

Met	Lys	Val	Leu	Ile	Val	Leu	Leu	Ala	Ile	Phe	Ala	Ala	Leu	Pro	Leu				
1				5					10					15					
Ala	Leu	Ala	Gln	Pro	Val	Ile	Ser	Thr	Thr	Val	Gly	Ser	Ala	Ala	Glu				
			20					25					30						
Gly	Ser	Leu	Asp	Lys	Arg	Phe	Leu	Met	Phe	Lys	Gln	Gly	Arg	Cys	Leu				
		35					40					45							
Cys	Ile	Gly	Pro	Gly	Met	Lys	Ala	Val	Lys	Met	Ala	Glu	Ile	Glu	Lys				
	50					55					60								
Ala	Ser	Val	Ile	Tyr	Pro	Ser	Asn	Gly	Cys	Asp	Lys	Val	Glu	Val	Ile				
65					70					75					80				
Val	Thr	Met	Lys	Ala	His	Lys	Arg	Gln	Arg	Cys	Leu	Asp	Pro	Arg	Ser				
				85					90					95					
Lys	Gln	Ala	Arg	Leu	Ile	Met	Gln	Ala	Ile	Glu	Lys	Lys	Asn	Phe	Leu				
			100					105					110						
Arg	Arg	Gln	Asn	Met	Gly	Gly	Glu	Gln	Lys	Leu	Ile	Ser	Glu	Glu					
			115					120					125						
Asp	Leu	Gln	Glu	Leu	Thr	Thr	Ile	Cys	Glu	Gln	Ile	Pro	Ser	Pro	Thr				
	130						135					140							
Leu	Glu	Ser	Thr	Pro	Tyr	Ser	Leu	Ser	Thr	Thr	Thr	Ile	Leu	Ala	Asn				
145					150						155				160				
Gly	Lys	Ala	Met	Gln	Gly	Val	Phe	Glu	Tyr	Tyr	Lys	Ser	Val	Thr	Phe				
				165					170					175					
Val	Ser	Asn	Cys	Gly	Ser	His	Pro	Ser	Thr	Thr	Ser	Lys	Gly	Ser	Pro				

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180	185	190	
Ile Asn Thr Gln Tyr Val Phe			
195			
<210> SEQ ID NO 147			
<211> LENGTH: 573			
<212> TYPE: DNA			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic: pCHA-LS-hCXCL1-G3-c-myc-Aga2			
<400> SEQUENCE: 147			
atgaaggttt tgattgtctt gttggctatc ttcgctgctt tgccattggc cttagctcaa			60
ccggttattt ctactaccgt cggttccgct gcagaaggct ctttgacaa gagagccacc			120
gagctgagat gccagtgcct gcagaccctg cagggcatcc accccaagaa catccagagc			180
gtgaacgtga agtcccctgg cccccactgc gccagaccg aagtgatcgc caccctgaag			240
aacggccgga aggctgcct gaaccccgcc agccccatcg tgaagaaaat catcgagaag			300
atgctgaaca gcgacaagag caacggcgga ggcaacaaa agcttatctc cgaagaagac			360
ttgcaggaac tgacaactat atgcgagcaa atccccctcac caactttaga atcgacgccg			420
tactctttgt caacgactac tattttggcc aacgggaagg caatgcaagg agttttttaa			480
tattacaaat cagtaacggt tgctcagtaat tgcggttctc acccctcaac aactagcaaa			540
ggcagcccca taaacacaca gtatgttttt taa			573

<210> SEQ ID NO 148			
<211> LENGTH: 190			
<212> TYPE: PRT			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic: LS-hCXCL1-G3-c-myc-Aga2			
<400> SEQUENCE: 148			
Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu			
1	5	10	15
Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu			
20	25	30	
Gly Ser Leu Asp Lys Arg Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln			
35	40	45	
Thr Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys			
50	55	60	
Ser Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys			
65	70	75	80
Asn Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys			
85	90	95	
Ile Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn Gly Gly Gly Glu			
100	105	110	
Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln Glu Leu Thr Thr Ile Cys			
115	120	125	
Glu Gln Ile Pro Ser Pro Thr Leu Glu Ser Thr Pro Tyr Ser Leu Ser			
130	135	140	
Thr Thr Thr Ile Leu Ala Asn Gly Lys Ala Met Gln Gly Val Phe Glu			
145	150	155	160
Tyr Tyr Lys Ser Val Thr Phe Val Ser Asn Cys Gly Ser His Pro Ser			

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	165	170	175	
Thr Thr Ser Lys Gly Ser Pro Ile Asn Thr Gln Tyr Val Phe				
	180	185	190	
<p>&lt;210&gt; SEQ ID NO 149                  &lt;211&gt; LENGTH: 2556                  &lt;212&gt; TYPE: DNA                  &lt;213&gt; ORGANISM: Artificial Sequence                  &lt;220&gt; FEATURE:                  &lt;223&gt; OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)                  CK138</p>				
<p>&lt;400&gt; SEQUENCE: 149</p>				
atggaagcac acaagagtga gatcgcccat cggataaatg atttgggaga acaacatttc				60
aaaggcctag tcctgattgc cttttccag tatctccaga aatgctcata cgatgagcat				120
gccaaattag tgcaggaagt aacagacttt gcaaagcgt gtgttgccga tgagtctgcc				180
gccaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac				240
ctccgtgaaa actatggtga actggctgac tgctgtacaa aacaagagcc cgaaagaaac				300
gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag				360
gctgaggcca tgtgcacctc ctttaaggaa aaccaacca cctttatggg aactatttg				420
catgaagttg ccagaagaca tccttatttc tatgcccag aacttcttta ctatgctgag				480
cagtacaatg agattctgac ccagtgtgtg gcagaggctg acaaggaaag ctgcctgacc				540
ccgaagcttg atggtgtgaa ggagaaagca ttggtctcat ctgtccgtca gagaatgaag				600
tgctccagta tgcagaagtt tggagagaga gcttttaaag catgggcagt agctcgtctg				660
agccagacat tcccacatgc tgactttgca gaaatcacca aattggcaac agacctgacc				720
aaagtcaaca aggagtgtg ccatggtgac ctgctggaat ggcagatga cagggcggaa				780
cttgccaagt acatgtgtga aaaccaggcg actatctcca gcaaactgca gacttgtgctc				840
gataaaccac tgttgaagaa agcccactgt cttagttagg tggagcatga caccatgcct				900
gctgatctgc ctgccattgc tgetgatttt gttgaggacc aggaagtgtg caagaactat				960
gctgaggcca aggatgtctt cctgggcacg ttcttgtatg aatattcaag aagacaccct				1020
gattactctg tatccctggt gctgagactt gctaagaaat atgaagccac tctggaaaag				1080
tgetgcgctg aagccaatcc tcccgcacgc tacggcacag tgettgctga atttcagcct				1140
cttgtagaag agcctaagaa cttggtcaaa accaactgtg atctttacga gaagcttggg				1200
gaatatggat tccaaaatgc cattctagtt cgctacaccc agaaagcacc tcagggtgca				1260
accccaactc tcgtggaggc tgaagaaac cttaggaagag tgggcaccaa gtgtgtgaca				1320
cttctgaag atcagagact gccttgtgtg gaagactatc tgtctgcaat cctgaaccgt				1380
gtgtgtctgc tgcattgaga gaccccagtg agtgagcatg ttaccaagtg ctgtagtgga				1440
tccctggtgg aaaggcggcc atgcttctct gctctgacag ttgatgaaac atatgtcccc				1500
aaagagttta aagctgagac cttcaccttc cactctgata tctgcacact tccagagaag				1560
gagaagcaga ttaagaaaca aacggctctt gctgagctgg tgaagcacia gcccaaggct				1620
acagcggagc aactgaagac tgcattggat gactttgcac agttcctgga tacatgttgc				1680
aaggctgctg acaaggacac ctgcttctcg actgagggtc caaacctgtg cactagatgc				1740
aaagacgctc tagccgtggt aggaggctct ggtggaggcg gtagcggagg cggagggtcg				1800

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gctatccaga tgacccggtc cccgagctcc ctgtccgct ctgtgggcca tagggtcacc 1860
atcacctgcc gtgccagtca gtaccacgac ggttctgcag cctggatca acagaaacca 1920
ggaaaagctc cgaagcttct gatttacggc gcacctacc tctactctgg agtcccttcc 1980
cgcttctctg gtagccgttc cgggacggat ttcactctga ccatcagcag tctgcagccg 2040
gaagacttcc caacttatta ctgtcagcaa tcttcttatt ctctgatcac gttcggacag 2100
ggtaccaagg tggagatcaa aggtactact gccgctagtg gtagtagtgg tggcagtagc 2160
agtggtgccg aggttcagct ggtggagtct gacggtgccc tgggtgcagcc agggggctca 2220
ctccgtttgt cctgtgcagc ttctggcttc aacctctctt actacggtat gactgggtg 2280
cgtcaggccc cgggtaaggc cctggaatgg gttgcataca ttgcttetta cctggctac 2340
acttcttatg ccgatagcgt caaggccgt ttcactataa gcgcagacac atccaaaaac 2400
acagcctacc tacaatgaa cagcttaaga gctgaggaca ctgccgtcta ctattgtgct 2460
cgctctggtt acagttactc tccgtattat tcttggttct ctgctggtat gaactactgg 2520
ggtcaaggag ccctggtcac cgtctcctcg tgatag 2556

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<210> SEQ ID NO 150
<211> LENGTH: 2530
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)
      CK157

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<400> SEQUENCE: 150
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caaagccta gtcctgattg ccttttccca gtatctccag aaatgctcat acgatgagca 120
tgccaaatta gtgcaggaag taacagactt tgcaaaagcg tgtgttgccg atgagtctgc 180
cgccaaactg gacaaatccc ttcacactct ttttggagat aagttgtgtg ccattccaaa 240
cctccgtgaa aactatgggtg aactggctga ctgctgtaca aaacaagagc ccgaaagaaa 300
cgaatgtttc ctgcaacaca aagatgacaa cccagccta ccaccatttg aaaggccaga 360
ggctgaggcc atgtgcacct cctttaagga aaaccaacc acctttatgg gacactattt 420
gcatgaagtt gccagaagac atccttattt ctatgoccca gaacttcttt actatgctga 480
gcagtacaat gagattctga cccagtgttg tgcagaggct gacaaggaaa gctgcctgac 540
cccgaagctt gatgggtgta aggagaaagc attggtctca tctgtccgtc agagaatgaa 600
gtgctccagt atgcagaagt ttggagagag agcttttaaa gcatgggagc tagctcgtct 660
gagccagaca ttccccaatg ctgactttgc agaaatcacc aaattggcaa cagacctgac 720
caaagtcaac aaggagtgtc gccatgggtg cctgctggaa tgcgcagatg acagggccga 780
acttgccaag tacatgtgtg aaaaccaggc gactatctcc agcaaactgc agacttgctg 840
cgataaacca ctgttgaaga aagcccactg tcttagtgag gtggagcatg acaccatgcc 900
tgctgatctg cctgccattg ctgctgattt tgttggaggc caggaagtgt gcaagaacta 960
tgctgaggcc aaggatgtct tctggggcac gttcttctat gaatattcaa gaagacacct 1020
tgattactct gtatccctgt tctgagact tgctaagaaa tatgaagcca ctctggaaaa 1080
gtgctgcgct gaagccaatc ctcccgcag ctacggcaca gtgcttgctg aatttcagcc 1140
tcttgtagaa gagcctaaga acttgggtcaa aaccaactgt gatctttacg agaagcttgg 1200

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agaatatgga ttccaaaatg ccattctagt tcgctacacc cagaaagcac ctcaggtgtc 1260
aaccccaact ctcgtggagg ctgcaagaaa cctaggaaga gtgggcacca agtgtgtgac 1320
acttcctgaa gatcagagac tgccttgtgt ggaagactat ctgtctgcaa tcctgaaccg 1380
tgtgtgtctg ctgcatgaga agacccagcagt gaggtagcat gttaccaagt gctgtagtgg 1440
atccctgggtg gaaaggcggc catgcttctc tgctctgaca gttgatgaaa catatgtccc 1500
caaagagttt aaagctgaga ccttcacctt ccaactctgat atctgcacac ttccagagaa 1560
ggagaagcag attaagaaac aaacggctct tgctgagctg gtgaagcaca agcccaaggc 1620
tacagcggag caactgaaga ctgtcatgga tgactttgca cagttcctgg atacatgttg 1680
caaggctgct gacaaggaca cctgcttctc gactgagggt ccaaaccttg tcactagatg 1740
caaagacgcc ttagccgggtg gaggaggctc tgggtggagg ggtagcggag gcggagggtc 1800
ggatatccag atgaccagc ccccgagctc cctgtccgcc tctgtgggcg atagggtcac 1860
catcacctgc cgtgccagtc agtcttacgg tgggtgtagc tggatatcaac agaaaccagg 1920
aaaagccccg aagcttctga tttactctgc atcctacctc tactctggag tcccttctcg 1980
cttctctggt agccgttccg ggacggattt cactctgacc atcagcagtc tgcagccgga 2040
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cgaggtggag atcaaaggta ctactgccgc tagtggtagt agtgggtggca gtagcagtgg 2160
tgccgaggtt cagctggtgg agtctggcgg tggcctggtg cagccagggg gctcactccg 2220
tttgcctgtg gcagcttctg gctccaacc ctaactactac ggtggtacgc actgggtgcg 2280
tcaggccccg ggtgaggagc tggaatgggt tgcctctatt ggttcttacc ctggctacac 2340
tgactatgcc gatagcgtca agggccggtt cactataagc gcagacacat ccaaaaacac 2400
agcctaccta caaatgaaca gcttaagagc tgaggacact gccgtctatt attgtgctcg 2460
ccattactac tggtagcatg ctactgacta ctgggggtcaa ggaaccctgg tcaccgtctc 2520
ctcgtgatag 2530

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&lt;210&gt; SEQ ID NO 151

&lt;211&gt; LENGTH: 2550

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK129

&lt;400&gt; SEQUENCE: 151

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atggaagcac acaagagtga gatcgcccat cgggtataatg atttgggaga acaacatttc 60
aaaggcctag tcctgattgc cttttcccag tatctccaga aatgctcata cgatgagcat 120
gccaaattag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc 180
gccaaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac 240
ctccgtgaaa actatggtga actggctgac tgctgtacaa aacaagagcc cgaagaaaac 300
gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag 360
gctgaggcca tgtgcacctc ctttaaggaa aaccacaacca cctttatggg aactatattg 420
catgaagtgt ccagaagaca tccttatttc tatgcccag aacttcttta ctatgctgag 480
cagtacaatg agattctgac ccagtggtgt gcagaggctg acaaggaaag ctgcctgacc 540

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ccgaagcttg atggtgtgaa ggagaaagca ttggtctcat ctgtccgtca gagaatgaag 600
tgctccagta tgcagaagtt tggagagaga gcttttaaag catgggcagt agctcgtctg 660
agccagacat tcccacatgc tgactttgca gaaatcacca aattggcaac agacctgacc 720
aaagtcaaca aggagtgtgt ccatggtgac ctgctggaat ggcgagatga cagggcgaa 780
cttgccaagt acatgtgtga aaaccaggcg actatctcca gcaaactgca gacttgtctg 840
gataaaccac tgttgaagaa agcccactgt cttagtggag tggagcatga caccatgcct 900
gctgatctgc ctgccattgc tgctgatttt gttgaggacc aggaagtgtg caagaactat 960
gctgaggcca aggatgtctt cctgggcacg ttcttgtatg aatattcaag aagacaccct 1020
gattactctg tatecctggt gctgagactt gctaagaaat atgaagccac tctggaaaag 1080
tgctgcgctg aagccaatcc tcccgcacgc tacggcacag tgcttctgta atttcagcct 1140
ctttagaag agcctaagaa cttggtcaaa accaactgtg atctttacga gaagcttgg 1200
gaatatggat tccaaaatgc cattctagtt cgctacaccc agaaagcacc tcaggtgtca 1260
acccaactc tcgtggaggc tgcaagaaac ctaggaagag tgggcaccaa gtgttgata 1320
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gtgtgtctgc tgcagagaa gaccccagtg agtgagcatg ttaccaagtg ctgtagtgg 1440
tccttgggtg aaaggcggcc atgcttctct gctctgacag ttgatgaaac atatgtccc 1500
aaagagtta aagctgagac cttcaccttc cactctgata tctgcacact tccagagaag 1560
gagaagcaga ttaagaaaca aacggctctt gctgagctgg tgaagcaca gcccaggct 1620
acagcggagc aactgaagac tgcctatgat gactttgcac agttcctgga tacatgttg 1680
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gctagcgata tccagatgac ccagtcoccg agcccctgt ccgcctctgt gggogatagg 1860
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ccagaaaag ctcogaagct tctgatttac ggtgcatccc ttctctactc tggagtccct 1980
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ggtaccaagg tggagatoga aggtactact gccgctagtg gtagtagtgg tggcagtag 2160
agtgtgccc aggttcagct ggtggagtct gccggtggcc tgggtcagcc aggggctca 2220
ctccgtttat cctgtgcagc ttctggcttc aacatctctt cttacggctc tatgcactgg 2280
gtgcgtcagg ccccggttaa gggcctggaa tgggttgcac ctatttacc ttactctagc 2340
tctacttact atgccgatag cgtcaagggc cgtttcacta taagcgcaga cacatccaaa 2400
aacacagcct acctacaat gaacagctta agagctgagg aactgcccgt ctattattgt 2460
gctcgtggtt acggtccgtg gtacgcttac tcttactctg ctttggacta ctggggtcaa 2520
ggaaccctgg tcaccgtctc ctctgatag 2550

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&lt;210&gt; SEQ ID NO 152

&lt;211&gt; LENGTH: 2556

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK138-ds1 (VL100Q>C / VH44G>C)

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&lt;400&gt; SEQUENCE: 152

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atggaagcac acaagagtga gatcgcccat cggataatg atttgggaga acaacatttc      60
aaaggcctag tcctgattgc cttttcccag tatctccaga aatgctcata cgatgagcat      120
gccaaattag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc      180
gccaaactgt acaaatcoct tcacactctt tttggagata agttgtgtgc cattccaaac      240
ctccgtgaaa actatggtga actggctgac tgctgtacaa aacaagagcc cgaagaagaac      300
gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag      360
gctgaggcca tgtgcacctc ctttaaggaa aaccaacca cctttatggg aactattttg      420
catgaagtgt ccagaagaca tccttatttc tatgccccag aacttcttta ctatgctgag      480
cagtacaatg agattctgac ccagtgttgt gcagaggctg acaaggaaag ctgcctgacc      540
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tgctccagta tgcagaagtt tggagagaga gcttttaaag catgggcagt agctcgtctg      660
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aaagtcaaca aggagtgtgt ccatggtgac ctgctggaat gcgcagatga cagggcggaa      780
cttgccaagt acatgtgtga aaaccaggcg actatctcca gcaaactgca gacttctgctc      840
gataaaccac tgttgaagaa agcccactgt cttagtgagg tggagcatga caccatgcct      900
gctgatctgc ctgccattgc tgctgatttt gttgaggacc aggaagtgtg caagaactat      960
gctgaggcca aggatgtcct cctgggcacg ttcttgtatg aatattcaag aagacaccct     1020
gattactctg tatccctggt gctgagactt gctaagaaat atgaagccac tctggaaaag     1080
tgctgcgctg aagccaatcc tcccgcacgc tacggcacag tgcttctgga atttcagcct     1140
ctttagaag agcctaagaa cttggtcaaa accaactgtg atctttacga gaagcttgga     1200
gaatatggat tccaaaatgc cattctagtt cgctacaccc agaaagcacc tcaggtgtca     1260
acccaactc tcgtggaggc tgcaagaaac ctaggaagag tgggcacca gtgttgtaaca     1320
cttctgaag atcagagact gccttgtgtg gaagactatc tgtctgcaat cctgaaccgt     1380
gtgtgtctgc tgcattgaga gaccccagtg agtgagcatg ttaccaagtg ctgtagtgga     1440
tccttgggtg aaaggcggcc atgcttctct gctctgacag ttgatgaaac atatgtcccc     1500
aaagagttta aagctgagac cttcaccttc cactctgata tctgcacact tccagagaag     1560
gagaagcaga ttaagaaaca aacggctcct gctgagctgg tgaagcaca gcccaaggct     1620
acagcggagc aactgaagac tgtcatggat gactttgcac agttcctgga tacatgttgc     1680
aaggctgctg acaaggacac ctgcttctcg actgagggtc caaaccttgt cactagatgc     1740
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gctatccaga tgacccggtc cccgagctcc ctgtccgctc ctgtgggcca tagggtcacc     1860
atcacctgcc gtgccagtca gtaccacgac ggttctgcag cctggtatca acagaaacca     1920
ggaaaagctc cgaagcttct gatttacggt gcatcctacc tctactctgg agtcccttc     1980
cgcttctctg gtaccggttc cgggacggat ttcactctga ccatcagcag tctgcagccg     2040
gaagacttgc caacttatta ctgtcagcaa tcttcttatt ctctgatcac gttcggatgc     2100
ggtaccaagg tggagatcaa aggtactact gccgctagtg gtagtagtgg tggcagtagc     2160
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ctccgtttgt cctgtgcagc ttctggcttc aacctctctt actacggat gcactgggtg	2280
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acttcttatg ccgatagcgt caagggccgt ttcactataa gcgcagacac atccaaaaac	2400
acagcctacc tacaatgaa cagcttaaga gctgaggaca ctgccgtcta ctattgtgct	2460
cgctctggtt acagttactc tccgtattat tcttggttct ctgctggtat gaactactgg	2520
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&lt;210&gt; SEQ ID NO 153

&lt;211&gt; LENGTH: 2562

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK138-ds2 (VL43A>C / VH105Q>C)

&lt;400&gt; SEQUENCE: 153

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gccaaattag tgcaggaagt aacagacttt gcaaagcgt gtgttgccga tgagtctgcc	180
gccaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac	240
ctccgtgaaa actatggtga actggctgac tgctgtacaa aacaagagcc cgaagaagaa	300
gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag	360
gctgaggcca tgtgcacctc ctttaaggaa aaccaacca ctttatggg aactatattg	420
catgaagtgt ccagaagaca tccttatttc tatgccccag aacttcttta ctatgctgag	480
cagtacaatg agattctgac ccagtgtgtg gcagaggctg acaaggaaag ctgctgacc	540
ccgaagcttg atggtgtgaa ggagaaagca ttggtctcat ctgtccgtca gagaatgaag	600
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aaagtcaaca aggagtgtg ccatggtgac ctgctggaat gcgcagatga cagggcggaa	780
cttgccaagt acatgtgtga aaaccaggcg actatctcca gcaaactgca gacttctgctc	840
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gctgatctgc ctgccattgc tgctgatttt gttgaggacc aggaagtgtg caagaactat	960
gctgaggcca aggatgtcct cctgggcacg ttcttgtatg aatattcaag aagacaccct	1020
gattactctg tatccctggt gctgagactt gctaagaaat atgaagccac tctggaaaag	1080
tgctgctgctg aagccaatcc tcccgcacgc tacggcacag tgcttctgta atttcagcct	1140
ctttagaag agcctaagaa cttggtcaaa accaactgtg atctttacga gaagcttgg	1200
gaatatggat tccaaaatgc cattctagtt cgctacaccc agaaagcacc tcaggtgtca	1260
acccaactc tcgtggaggc tgcaagaaac ctaggaagag tgggcaccaa gtgtgtgaca	1320
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gtgtgtctgc tgcagagaa gaccccagtg agtgagcatg ttaccaagtg ctgtagtgg	1440
tcccctggtg aaaggcggcc atgctctctc gctctgacag ttgatgaaac atatgcccc	1500
aaagagtta aagctgagac cttcaccttc cactctgata tctgcacact tccagagaag	1560

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gagaagcaga ttaagaaaca aacggctctt gctgagctgg tgaagcacia gcccaaggct 1620
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tgtgctcgtc ctggttacag ttactctccg tattattctt ggttctctgc tggatatgac 2520
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&lt;210&gt; SEQ ID NO 154

&lt;211&gt; LENGTH: 2529

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK157-ds1 (VL100Q>C / VH44E>C)

&lt;400&gt; SEQUENCE: 154

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aaaggcctag tcctgattgc ctttcccag tatctccaga aatgctcata cgatgagcat 120
gccaaattag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc 180
gccaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac 240
ctccgtgaaa actatggtga actggctgac tgctgtacaa aacaagagcc cgaagaagaa 300
gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag 360
gctgaggcca tgtgcacctc ctttaaggaa aaccaacca ctttatggg aactatttg 420
catgaagtty ccagaagaca tccttatttc tatgccccag aacttcttta ctatgctgag 480
cagtacaatg agattctgac ccagtgttgt gcagaggctg acaaggaaag ctgctgacc 540
ccgaagcttg atggtgtgaa ggagaaagca ttggtctcat ctgtccgtca gagaatgaag 600
tgctccagta tgcagaagtt tgagagagaga gcttttaaag catgggcagt agctcgtctg 660
agccagacat tccccaatgc tgactttgca gaaatcacca aattggcaac agacctgacc 720
aaagtcaaca aggagtgtg ccatggtgac ctgctggaat gcgcagatga cagggcggaa 780
cttgccaagt acatgtgtga aaaccaggcg actatctcca gcaaaactgca gacttgtctg 840
gataaaccac tgttgaagaa agcccactgt cttagttagg tggagcatga caccatgcct 900
gctgatctgc ctgccattgc tgctgatttt gttgaggacc aggaagtgtg caagaactat 960

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gctgaggcca aggatgtcct cctgggcacg ttcttgatg aatattcaag aagacaccct 1020
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tgctgcgctg aagccaatcc tcccgcatgc tacggcacag tgcttgctga atttcagcct 1140
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gaggtggaga tcaaaggtag tactgcccct agtggtagta gtggtggcag tagcagtgg 2160
gccgaggttc agctggtgga gctggtggt gccctggtgc agccaggggg ctcactccgt 2220
ttgtcctgtg cagcttctgg ctccaacccc tactactacg gtggtacgca ctgggtgct 2280
caggccccgg gtgagtgcct ggaatgggtt gcatctattg gttcttacc tggctacact 2340
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gcctacctac aaatgaacag cttaagagct gaggacactg ccgtctatta ttgtgctgc 2460
cattactact ggtacgatgc tactgactac tggggtcaag gaaccctggt cacogtctcc 2520
tcgtgatag 2529

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&lt;210&gt; SEQ ID NO 155

&lt;211&gt; LENGTH: 2529

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK157-ds2 (VL43A>C / VH105Q>C)

&lt;400&gt; SEQUENCE: 155

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gccaatttag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc 180
gccaactgtg acaaatccct tcacactctt ttggagata agttgtgtgc cattccaac 240
ctccgtgaaa actatggtga actggtgac tgctgtacaa aacaagacc cgaagaagaac 300

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catgaagtgt	ccagaagaca	tccttatttc	tatgcccag	aacttcttta	ctatgctgag	480
cagtacaatg	agattctgac	ccagtgttgt	gcagaggctg	acaaggaaag	ctgectgacc	540
ccgaagcttg	atggtgtgaa	ggagaaagca	ttggtctcat	ctgtccgtca	gagaatgaa	600
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agccagacat	tccccaatgc	tgactttgca	gaaatcacca	aattggcaac	agacctgacc	720
aaagtcaaca	aggagtgtctg	ccatggtgac	ctgctggaat	gcgagatga	cagggcggaa	780
cttgccaagt	acatgtgtga	aaaccaggcg	actatctcca	gcaaactgca	gacttgctgc	840
gataaaccac	tgttgaagaa	agcccactgt	cttagtgagg	tggagcatga	caccatgcct	900
gctgatctgc	ctgccattgc	tgctgatttt	gttgaggacc	aggaagtgtg	caagaactat	960
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gaatatggat	tccaaaatgc	cattctagtt	cgctacaccc	agaaagcacc	tcagggtgca	1260
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aaatgccca	agcttctgat	ttactctgca	tcctacctct	actctggagt	cccttctcgc	1980
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gcctacctac	aaatgaacag	cttaagagct	gaggacactg	ccgtctatta	ttgtgctcgc	2460
cattactact	ggtacgatgc	tactgactac	tggggttgcg	gaacctggg	caccgtctcc	2520
tcgtgatag						2529

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<210> SEQ ID NO 156  
<211> LENGTH: 2121  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)-VL CK157

<400> SEQUENCE: 156

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gccaatttag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc	180
gccaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac	240
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gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag	360
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gacttcgcaa cttattactg tcagcaacca tctcatctga tcacgttcgg acaggggtacc	2100
gaggtggaga tcaaatgata g	2121
<210> SEQ ID NO 157	
<211> LENGTH: 2169	
<212> TYPE: DNA	
<213> ORGANISM: Artificial Sequence	
<220> FEATURE:	
<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)-VH CK157	
<400> SEQUENCE: 157	
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gccaaattag tgcaggaagt aacagacttt gcaaagcgt gtgttgccga tgagtctgcc	180
gccaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac	240
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gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag	360
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cagtacaatg agattctgac ccagtgtgtg gcagaggctg acaaggaaaag ctgcctgacc	540
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gccgaggttc agctggtgga gtctggcggg ggccctggtgc agccaggggg ctcactccgt	1860
ttgtcctgtg cagcttctgg ctccaacccc tactactacg gtggtacgca ctgggtgcgt	1920
caggccccgg gtgaggagct ggaatggggt gcatctattg gttcttacc tggctacact	1980
gactatgccc atagcgtcaa gggccgtttc actataagcg cagacacatc caaaaacaca	2040
gctacacctac aaatgaacag cttaagagct gaggacactg ccgtctatta ttgtgctcgc	2100
cattactact ggtacgatgc tactgactac tggggccaag gaacctggt caccgtctcc	2160
tcgtgatag	2169

&lt;210&gt; SEQ ID NO 158

&lt;211&gt; LENGTH: 2544

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK129-ds1 (VL100Q>C / VH44G>C)

&lt;400&gt; SEQUENCE: 158

atggaagcac acaagagtg gatcgcccat cggataaatg atttgggaga acaacatttc	60
aaaggcctag tcctgattgc cttttcccag tatctccaga aatgctcata cgatgagcat	120
gccaaattag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc	180
gccaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac	240
ctccgtgaaa actatggtga actggctgac tgctgtacaa aacaagagcc cgaaagaaac	300
gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag	360
gctgaggcca tgtgcacctc ctttaaggaa aacccaacca cctttatggg aactatttg	420
catgaagttg ccagaagaca tccttatttc tatgcccag aacttcttta ctatgctgag	480
cagtacaatg agattctgac ccagtggtgt gcagaggctg acaaggaaag ctgcctgacc	540
ccgaagcttg atggtgtgaa ggagaaagca ttggtctcat ctgtccgtca gagaatgaag	600
tgctccagta tgcagaagtt tggagagaga gcttttaaag catgggcagt agctcgtctg	660
agccagacat tcccacatgc tgactttgca gaaatcacca aattggcaac agacctgacc	720
aaagtcaaca aggagtgtg ccatggtgac ctgctggaat gcgcagatga cagggcggaa	780
cttgccaagt acatgtgtga aaaccaggcg actatctcca gcaaactgca gacttctgctc	840
gataaaccac tgttgaagaa agcccactgt cttagtgagg tggagcatga caccatgcct	900
gctgatctgc ctgccattgc tgetgatttt gttgaggacc aggaagtgtg caagaactat	960
gctgaggcca aggatgtctt cctgggcacg ttcttgtatg aatattcaag aagacaccct	1020
gattactctg tatccctggt gctgagactt gctaagaaat atgaagccac tctggaaaag	1080
tgetgcgctg aagccaatcc tcccgcacg tacggcacag tgcttctgca atttcagcct	1140
cttgtagaag agcctaagaa cttggtcaaa accaactgtg atctttacga gaagcttggg	1200
gaatatggat tccaaaatgc cattctagtt cgctacacct agaagcacc tcaggtgtca	1260
acccaactc tcgtggaggc tgcaagaaac ctaggaagag tgggcaccaa gtgtgttaca	1320
cttctgaag atcagagact gccttgtgtg gaagactatc tgtctgcaat cctgaaccgt	1380
gtgtgtctgc tgcagagaa gaccccagtg agtgagcatg ttaccaagtg ctgtagtgga	1440
tccctggtgg aaaggcggcc atgcttctct gctctgacag ttgatgaaac atatgtcccc	1500
aaagagttta aagctgagac cttcacctc cactctgata tctgcacact tccagagaag	1560

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gagaagcaga ttaagaaaca aacggctctt gctgagctgg tgaagcacia gcecaaggct 1620
acagcggagc aactgaagac tgcatggat gactttgcac agttcctgga tacatgttgc 1680
aaggctgctg acaaggacac ctgcttctcg actgagggtc caaaccttgt cactagatgc 1740
aaagacgctc tagccggtgg aggaggctct ggtggaggcg gtagcggagg cggagggtcg 1800
gatatccaga tgacccagtc cccgagcccc ctgtccgctt ctgtgggcca tagggtcacc 1860
atcacctgcc gtgccagtca gtacgggtgt tacgtagcct ggatcaaca gaaaccagga 1920
aaagtccega agcttctgat ttacgggtgca tcccttctct actctggagt ccttctctgc 1980
ttctctggtg gccgttccgg gacggatttc actctgacca tcagcagtct gcagccggaa 2040
gacttcgcaa cttattactg tcagcagggt catgctctga tcacggtcgg atgcggtacc 2100
aaggtggaga tcgaaggtac tactgcccct agtggtagta gtggtggcag tagcagtggt 2160
gccgaggttc agctggtgga gtctggcggg gccctggtgc agccaggggg ctcaactcgt 2220
ttatcctgtg cagcttctgg cttcaacatc tcttcttacg gttctatgca ctgggtgcgt 2280
caggccccgg gtaagtgcct ggaatgggtt gcactatatt acccttactc tagctctact 2340
tactatgccc atagcgtcaa gggcccgttc actataagcg cagacacatc caaaaacaca 2400
gcctacctac aaatgaacag cttaagagct gaggacactg ccgtctatta ttgtgctcgt 2460
ggttacggtc cgtggtacgc ttactcttac ttcgctttgg actactgggg tcaaggaacc 2520
ctggtcacgc tctcctcgtg atag 2544

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&lt;210&gt; SEQ ID NO 159

&lt;211&gt; LENGTH: 2544

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK129-ds2 (VL43A>C / VH105Q>C)

&lt;400&gt; SEQUENCE: 159

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atggaagcac acaagagtga gatcgcccat cgggtataatg atttgggaga acaacatttc 60
aaaggcctag tcctgattgc cttttcccag tatctccaga aatgctcata cgatgagcat 120
gccccaaatag tgcaggaagt aacagacttt gcaaagacgt gtgttgccga tgagtctgcc 180
gccaactgtg acaaatccct tcacactctt tttggagata agttgtgtgc cattccaaac 240
ctccgtgaaa actatggtga actggctgac tgctgtacaa aacaagagcc cgaagaaac 300
gaatgtttcc tgcaacacaa agatgacaac cccagcctac caccatttga aaggccagag 360
gctgaggcca tgtgcacctc ctttaaggaa aacccaacca cctttatggg acactatttg 420
catgaagttg ccagaagaca tccttatttc tatgcccag aacttcttta ctatgctgag 480
cagtacaatg agattctgac ccagtgttgt gcagaggctg acaaggaaaag ctgcctgacc 540
ccgaagcttg atggtgtgaa ggagaaagca ttggtctcat ctgtccgtca gagaatgaag 600
tgctccagta tgcagaagtt tggagagaga gcttttaaag catgggcagt agctcgtctg 660
agccagacat tccccaatgc tgactttgca gaaatcacca aattggcaac agacctgacc 720
aaagtcaaca aggagtgtg ccatggtgac ctgctggaat gcgcagatga cagggcggaa 780
cttgccaagt acatgtgtga aaaccaggcg actatctcca gaaaactgca gacttctctg 840
gataaaccac tgttgaagaa agcccactgt cttagtggag tggagcatga caccatgcct 900

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gctgatctgc ctgccattgc tgctgatttt gttgaggacc aggaagtgtg caagaactat 960
gctgaggcca aggatgtcct cctgggcacg ttcttgatg aatattcaag aagacaccct 1020
gattactctg tatecctggt gctgagactt gctaagaaat atgaagccac tctggaaaag 1080
tgctgcgctg aagccaatcc tcccgcacgc tacggcacag tgcttgctga atttcagcct 1140
ctttagaag agcctaagaa cttggtcaaa accaactgtg atctttacga gaagcttgga 1200
gaatatggat tccaaaatgc cattctagtt cgctacaccc agaaagcacc tcaggtgtca 1260
accccaactc tcgtggagge tgcaagaaac ctaggaagag tgggcaccaa gtgttgta 1320
cttctgaag atcagagact gccttggtg gaagactatc tgtctgcaat cctgaaccgt 1380
gtgtgtctgc tgcacagaa gacccacgtg agtgagcatg ttaccaagtg ctgtagtgga 1440
tccctggtgg aaaggcggcc atgcttctct gctctgacag ttgatgaaac atatgtcccc 1500
aaagagtta aagctgagac cttcaccttc cactctgata tctgcacact tccagagaag 1560
gagaagcaga ttaagaaaca aacggtctct gctgagctgg tgaagcaca gcccaggct 1620
acagcggagc aactgaagac tgcatggat gactttgcac agttcctgga tacatgttgc 1680
aaggctgctg acaaggacac ctgcttctcg actgagggtc caaacctgt cactagatgc 1740
aaagacgct tagccggtg aggaggctct ggtggaggcg gtagcggagg cggagggtcg 1800
gatatccaga tgacccagtc cccgagcccc ctgtccgcct ctgtggcgga tagggtcacc 1860
atcacctgcc gtgccagtc gtacggtggt tacgtagcct ggtatcaaca gaaaccagga 1920
aaatgccga agcttctgat ttacggtgca tcccttctct actctggagt cccttctcgc 1980
ttctctggtg gccgttccgg gacggatttc actctgacca tcagcagtct gcagccgga 2040
gacttcgcaa cttattactg tcagcgaggt catgctctga tcacggtcgg acagggtacc 2100
aaggtggaga tcgaaggtac tactgocgct agtggtagta gtggtggcag tagcagtggt 2160
gccgaggttc agctggtgga gtctggcggg gccctggtgc agccaggggg ctcactccgt 2220
ttatcctgty cagcttctgg cttcaacatc tcttcttacg gttctatgca ctgggtgcgt 2280
caggccccgg gtaagggcct ggaatgggtt gcactatatt acccttactc tagctctact 2340
tactatgccc atagcgtcaa gggccgtttc actataagcg cagacacatc caaaaacaca 2400
gcctacctac aaatgaacag cttaagagct gaggacactg ccgtctatta ttgtgetcgt 2460
ggttacggtc cgtggtaocg ttactcttac ttcgctttgg actactgggg ttgcggaacc 2520
ctggtcaccc tctcctcgtg atag 2544

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<210> SEQ ID NO 160
<211> LENGTH: 851
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)
        CK138

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<400> SEQUENCE: 160

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Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu
1             5             10             15
Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln
                20             25             30
Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp
35             40             45

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Phe	Ala	Lys	Thr	Cys	Val	Ala	Asp	Glu	Ser	Ala	Ala	Asn	Cys	Asp	Lys	50	55	60	
Ser	Leu	His	Thr	Leu	Phe	Gly	Asp	Lys	Leu	Cys	Ala	Ile	Pro	Asn	Leu	65	70	75	80
Arg	Glu	Asn	Tyr	Gly	Glu	Leu	Ala	Asp	Cys	Cys	Thr	Lys	Gln	Glu	Pro	85	90	95	
Glu	Arg	Asn	Glu	Cys	Phe	Leu	Gln	His	Lys	Asp	Asp	Asn	Pro	Ser	Leu	100	105	110	
Pro	Pro	Phe	Glu	Arg	Pro	Glu	Ala	Glu	Ala	Met	Cys	Thr	Ser	Phe	Lys	115	120	125	
Glu	Asn	Pro	Thr	Thr	Phe	Met	Gly	His	Tyr	Leu	His	Glu	Val	Ala	Arg	130	135	140	
Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu	Tyr	Tyr	Ala	Glu	Gln	145	150	155	160
Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala	Glu	Ala	Asp	Lys	Glu	Ser	165	170	175	
Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu	Lys	Ala	Leu	Val	Ser	180	185	190	
Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu	195	200	205	
Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro	210	215	220	
Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys	225	230	235	240
Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp	245	250	255	
Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser	260	265	270	
Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His	275	280	285	
Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala	290	295	300	
Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala	305	310	315	320
Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg	325	330	335	
Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys	340	345	350	
Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala	355	360	365	
Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro	370	375	380	
Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu	385	390	395	400
Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro	405	410	415	
Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg	420	425	430	
Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys	435	440	445	
Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His				

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450					455					460					
Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser
465					470					475					480
Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr
				485					490					495	
Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp
			500					505					510		
Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala
		515					520					525			
Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu
530					535					540					
Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys
545					550					555					560
Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val
				565					570					575	
Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
			580					585					590		
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ala	Ser	Ala	Ile	Gln	Met	Thr	Arg	Ser
		595					600					605			
Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys
610					615					620					
Arg	Ala	Ser	Gln	Tyr	His	Asp	Gly	Ser	Ala	Ala	Trp	Tyr	Gln	Gln	Lys
625					630					635					640
Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Gly	Ala	Ser	Tyr	Leu	Tyr
				645					650					655	
Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Arg	Ser	Gly	Thr	Asp	Phe
			660					665					670		
Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr
		675					680					685			
Cys	Gln	Gln	Ser	Ser	Tyr	Ser	Leu	Ile	Thr	Phe	Gly	Gln	Gly	Thr	Lys
690					695					700					
Val	Glu	Ile	Lys	Gly	Thr	Thr	Ala	Ala	Ser	Gly	Ser	Ser	Gly	Gly	Ser
705					710					715					720
Ser	Ser	Gly	Ala	Glu	Val	Gln	Leu	Val	Glu	Ser	Asp	Gly	Gly	Leu	Val
				725					730					735	
Gln	Pro	Gly	Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Asn
				740					745				750		
Leu	Ser	Tyr	Tyr	Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly
		755					760					765			
Leu	Glu	Trp	Val	Ala	Tyr	Ile	Ala	Ser	Tyr	Pro	Gly	Tyr	Thr	Ser	Tyr
770					775					780					
Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Ala	Asp	Thr	Ser	Lys
785					790					795					800
Asn	Thr	Ala	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala
				805					810					815	
Val	Tyr	Tyr	Cys	Ala	Arg	Ser	Gly	Tyr	Ser	Tyr	Ser	Pro	Tyr	Tyr	Ser
			820						825				830		
Trp	Phe	Ser	Ala	Gly	Met	Asn	Tyr	Trp	Gly	Gln	Gly	Ala	Leu	Val	Thr
			835						840				845		
Val	Ser	Ser													
850															

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<210> SEQ ID NO 161  
 <211> LENGTH: 842  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
 CK157

<400> SEQUENCE: 161

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
 1 5 10 15  
 Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
 20 25 30  
 Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp  
 35 40 45  
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys  
 50 55 60  
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu  
 65 70 75 80  
 Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro  
 85 90 95  
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu  
 100 105 110  
 Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
 115 120 125  
 Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
 130 135 140  
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln  
 145 150 155 160  
 Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser  
 165 170 175  
 Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser  
 180 185 190  
 Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu  
 195 200 205  
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro  
 210 215 220  
 Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys  
 225 230 235 240  
 Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp  
 245 250 255  
 Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser  
 260 265 270  
 Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His  
 275 280 285  
 Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala  
 290 295 300  
 Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala  
 305 310 315 320  
 Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg  
 325 330 335  
 Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys

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340					345					350					
Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala
	355						360					365			
Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro
	370					375					380				
Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu
	385					390					395				400
Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro
				405					410					415	
Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg
			420					425					430		
Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys
		435					440						445		
Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His
	450					455					460				
Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser
	465					470					475				480
Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr
			485						490					495	
Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp
			500					505						510	
Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala
		515					520						525		
Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu
	530					535					540				
Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys
	545					550					555				560
Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val
			565						570					575	
Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
			580					585						590	
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ala	Ser	Asp	Ile	Gln	Met	Thr	Gln	Ser
		595					600					605			
Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys
	610					615					620				
Arg	Ala	Ser	Gln	Ser	Tyr	Gly	Gly	Val	Ala	Trp	Tyr	Gln	Gln	Lys	Pro
	625					630					635				640
Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Ser	Ala	Ser	Tyr	Leu	Tyr	Ser
			645						650					655	
Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Arg	Ser	Gly	Thr	Asp	Phe	Thr
		660							665				670		
Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
		675					680						685		
Gln	Gln	Pro	Ser	His	Leu	Ile	Thr	Phe	Gly	Gln	Gly	Thr	Glu	Val	Glu
	690					695					700				
Ile	Lys	Gly	Thr	Thr	Ala	Ala	Ser	Gly	Ser	Ser	Gly	Gly	Ser	Ser	Ser
	705					710					715				720
Gly	Ala	Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro
			725						730					735	
Gly	Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Ser	Asn	Pro	Tyr
			740					745					750		



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Tyr Tyr Gly Gly Thr His Trp Val Arg Gln Ala Pro Gly Glu Glu Leu  
755 760 765

Glu Trp Val Ala Ser Ile Gly Ser Tyr Pro Gly Tyr Thr Asp Tyr Ala  
770 775 780

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn  
785 790 795 800

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val  
805 810 815

Tyr Tyr Cys Ala Arg His Tyr Tyr Trp Tyr Asp Ala Thr Asp Tyr Trp  
820 825 830

Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
835 840

<210> SEQ ID NO 162  
<211> LENGTH: 847  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK129

<400> SEQUENCE: 162

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
1 5 10 15

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
20 25 30

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp  
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys  
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu  
65 70 75 80

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro  
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu  
100 105 110

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
115 120 125

Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln  
145 150 155 160

Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser  
165 170 175

Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser  
180 185 190

Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu  
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro  
210 215 220

Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys  
225 230 235 240

Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp

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			245					250				255			
Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser
			260					265					270		
Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His
		275					280					285			
Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala
	290					295					300				
Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala
305					310					315					320
Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg
			325						330					335	
Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys
			340					345					350		
Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala
		355					360					365			
Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro
370						375					380				
Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu
385					390					395					400
Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro
				405					410						415
Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg
			420					425					430		
Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys
		435					440					445			
Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His
	450					455					460				
Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser
465					470					475					480
Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr
			485						490						495
Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp
			500					505					510		
Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala
		515					520					525			
Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu
530						535						540			
Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys
545				550							555				560
Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val
			565						570						575
Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
			580					585						590	
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ala	Ser	Asp	Ile	Gln	Met	Thr	Gln	Ser
		595					600					605			
Pro	Ser	Pro	Leu	Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys
	610					615						620			
Arg	Ala	Ser	Gln	Tyr	Gly	Gly	Tyr	Val	Ala	Trp	Tyr	Gln	Gln	Lys	Pro
625					630					635					640
Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Gly	Ala	Ser	Leu	Leu	Tyr	Ser
			645						650						655

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Gly Val Pro Ser Arg Phe Ser Gly Gly Arg Ser Gly Thr Asp Phe Thr  
                   660                                  665                                  670  
 Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys  
                   675                                  680                                  685  
 Gln Arg Gly His Ala Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Glu  
                   690                                  695                                  700  
 Ile Glu Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser  
                   705                                  710                                  715                                  720  
 Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro  
                                   725                                  730                                  735  
 Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser  
                                   740                                  745                                  750  
 Ser Tyr Gly Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu  
                   755                                  760                                  765  
 Glu Trp Val Ala Ser Ile Tyr Pro Tyr Ser Ser Ser Thr Tyr Tyr Ala  
                   770                                  775                                  780  
 Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn  
                   785                                  790                                  795                                  800  
 Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val  
                                   805                                  810                                  815  
 Tyr Tyr Cys Ala Arg Gly Tyr Gly Pro Trp Tyr Ala Tyr Ser Tyr Phe  
                   820                                  825                                  830  
 Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
                   835                                  840                                  845

&lt;210&gt; SEQ ID NO 163

&lt;211&gt; LENGTH: 851

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

 <223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
 CK138-ds1 (VL100Q>C / VH44G>C)

&lt;400&gt; SEQUENCE: 163

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
 1                  5                                  10                                  15  
 Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
                   20                                  25                                  30  
 Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp  
                   35                                  40                                  45  
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys  
                   50                                  55                                  60  
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu  
                   65                                  70                                  75                                  80  
 Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro  
                   85                                  90                                  95  
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu  
                   100                                  105                                  110  
 Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
                   115                                  120                                  125  
 Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
                   130                                  135                                  140  
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln

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145	150	155	160
Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser	165	170	175
Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser	180	185	190
Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu	195	200	205
Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro	210	215	220
Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys	225	230	235
Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp	245	250	255
Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser	260	265	270
Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His	275	280	285
Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala	290	295	300
Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala	305	310	315
Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg	325	330	335
Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys	340	345	350
Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala	355	360	365
Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro	370	375	380
Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu	385	390	395
Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro	405	410	415
Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg	420	425	430
Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys	435	440	445
Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His	450	455	460
Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser	465	470	475
Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr	485	490	495
Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp	500	505	510
Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala	515	520	525
Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu	530	535	540
Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys	545	550	555
			560

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Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val  
565 570 575

Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser Gly Gly Gly  
580 585 590

Gly Ser Gly Gly Gly Gly Ser Ala Ser Ala Ile Gln Met Thr Arg Ser  
595 600 605

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys  
610 615 620

Arg Ala Ser Gln Tyr His Asp Gly Ser Ala Ala Trp Tyr Gln Gln Lys  
625 630 635 640

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Ala Ser Tyr Leu Tyr  
645 650 655

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe  
660 665 670

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr  
675 680 685

Cys Gln Gln Ser Ser Tyr Ser Leu Ile Thr Phe Gly Cys Gly Thr Lys  
690 695 700

Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser  
705 710 715 720

Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Asp Gly Gly Leu Val  
725 730 735

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn  
740 745 750

Leu Ser Tyr Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Cys  
755 760 765

Leu Glu Trp Val Ala Tyr Ile Ala Ser Tyr Pro Gly Tyr Thr Ser Tyr  
770 775 780

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys  
785 790 795 800

Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala  
805 810 815

Val Tyr Tyr Cys Ala Arg Ser Gly Tyr Ser Tyr Ser Pro Tyr Tyr Ser  
820 825 830

Trp Phe Ser Ala Gly Met Asn Tyr Trp Gly Gln Gly Ala Leu Val Thr  
835 840 845

Val Ser Ser  
850

&lt;210&gt; SEQ ID NO 164

&lt;211&gt; LENGTH: 851

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK138-ds2 (VL43A>C / VH105Q>C)

&lt;400&gt; SEQUENCE: 164

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
1 5 10 15

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
20 25 30

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp



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Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His  
 450 455 460  
 Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser  
 465 470 475 480  
 Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr  
 485 490 495  
 Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp  
 500 505 510  
 Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala  
 515 520 525  
 Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu  
 530 535 540  
 Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys  
 545 550 555 560  
 Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val  
 565 570 575  
 Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser Gly Gly Gly  
 580 585 590  
 Gly Ser Gly Gly Gly Gly Ser Ala Ser Ala Ile Gln Met Thr Arg Ser  
 595 600 605  
 Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys  
 610 615 620  
 Arg Ala Ser Gln Tyr His Asp Gly Ser Ala Ala Trp Tyr Gln Gln Lys  
 625 630 635 640  
 Pro Gly Lys Cys Pro Lys Leu Leu Ile Tyr Gly Ala Ser Tyr Leu Tyr  
 645 650 655  
 Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe  
 660 665 670  
 Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr  
 675 680 685  
 Cys Gln Gln Ser Ser Tyr Ser Leu Ile Thr Phe Gly Gln Gly Thr Lys  
 690 695 700  
 Val Glu Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser  
 705 710 715 720  
 Ser Ser Gly Ala Glu Val Gln Leu Val Glu Ser Asp Gly Gly Leu Val  
 725 730 735  
 Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn  
 740 745 750  
 Leu Ser Tyr Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly  
 755 760 765  
 Leu Glu Trp Val Ala Tyr Ile Ala Ser Tyr Pro Gly Tyr Thr Ser Tyr  
 770 775 780  
 Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys  
 785 790 795 800  
 Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala  
 805 810 815  
 Val Tyr Tyr Cys Ala Arg Ser Gly Tyr Ser Tyr Ser Pro Tyr Tyr Ser  
 820 825 830  
 Trp Phe Ser Ala Gly Met Asn Tyr Trp Gly Cys Gly Ala Leu Val Thr  
 835 840 845

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 Val Ser Ser  
 850

<210> SEQ ID NO 165  
 <211> LENGTH: 842  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
 CK157-ds1 (VL100Q>C / VH44E>C)

&lt;400&gt; SEQUENCE: 165

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
 1 5 10 15  
 Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
 20 25 30  
 Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp  
 35 40 45  
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys  
 50 55 60  
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu  
 65 70 75 80  
 Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro  
 85 90 95  
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu  
 100 105 110  
 Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
 115 120 125  
 Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
 130 135 140  
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln  
 145 150 155 160  
 Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser  
 165 170 175  
 Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser  
 180 185 190  
 Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu  
 195 200 205  
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro  
 210 215 220  
 Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys  
 225 230 235 240  
 Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp  
 245 250 255  
 Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser  
 260 265 270  
 Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His  
 275 280 285  
 Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala  
 290 295 300  
 Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala  
 305 310 315 320  
 Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg  
 325 330 335



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Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys  
340 345 350  
Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala  
355 360 365  
Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro  
370 375 380  
Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu  
385 390 395 400  
Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro  
405 410 415  
Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg  
420 425 430  
Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys  
435 440 445  
Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His  
450 455 460  
Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser  
465 470 475 480  
Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr  
485 490 495  
Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp  
500 505 510  
Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala  
515 520 525  
Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu  
530 535 540  
Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys  
545 550 555 560  
Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val  
565 570 575  
Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser Gly Gly Gly  
580 585 590  
Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp Ile Gln Met Thr Gln Ser  
595 600 605  
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys  
610 615 620  
Arg Ala Ser Gln Ser Tyr Gly Gly Val Ala Trp Tyr Gln Gln Lys Pro  
625 630 635 640  
Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Leu Tyr Ser  
645 650 655  
Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr  
660 665 670  
Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys  
675 680 685  
Gln Gln Pro Ser His Leu Ile Thr Phe Gly Cys Gly Thr Glu Val Glu  
690 695 700  
Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser  
705 710 715 720  
Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro  
725 730 735

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Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Asn Pro Tyr  
740 745 750

Tyr Tyr Gly Gly Thr His Trp Val Arg Gln Ala Pro Gly Glu Cys Leu  
755 760 765

Glu Trp Val Ala Ser Ile Gly Ser Tyr Pro Gly Tyr Thr Asp Tyr Ala  
770 775 780

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn  
785 790 795 800

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val  
805 810 815

Tyr Tyr Cys Ala Arg His Tyr Tyr Trp Tyr Asp Ala Thr Asp Tyr Trp  
820 825 830

Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
835 840

<210> SEQ ID NO 166  
<211> LENGTH: 842  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK157-ds2 (VL43A>C / VH105Q>C)

<400> SEQUENCE: 166

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
1 5 10 15

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
20 25 30

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp  
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys  
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu  
65 70 75 80

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro  
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu  
100 105 110

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
115 120 125

Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln  
145 150 155 160

Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser  
165 170 175

Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser  
180 185 190

Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu  
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro  
210 215 220

Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys  
225 230 235 240

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Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp  
245 250 255

Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser  
260 265 270

Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His  
275 280 285

Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala  
290 295 300

Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala  
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg  
325 330 335

Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys  
340 345 350

Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala  
355 360 365

Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro  
370 375 380

Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu  
385 390 395 400

Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro  
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg  
420 425 430

Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys  
435 440 445

Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His  
450 455 460

Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser  
465 470 475 480

Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr  
485 490 495

Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp  
500 505 510

Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala  
515 520 525

Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu  
530 535 540

Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys  
545 550 555 560

Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val  
565 570 575

Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser Gly Gly Gly  
580 585 590

Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp Ile Gln Met Thr Gln Ser  
595 600 605

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys  
610 615 620

Arg Ala Ser Gln Ser Tyr Gly Gly Val Ala Trp Tyr Gln Gln Lys Pro  
625 630 635 640

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Gly Lys Cys Pro Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Leu Tyr Ser  
 645 650 655  
 Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr  
 660 665 670  
 Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys  
 675 680 685  
 Gln Gln Pro Ser His Leu Ile Thr Phe Gly Gln Gly Thr Glu Val Glu  
 690 695 700  
 Ile Lys Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser  
 705 710 715 720  
 Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro  
 725 730 735  
 Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Asn Pro Tyr  
 740 745 750  
 Tyr Tyr Gly Gly Thr His Trp Val Arg Gln Ala Pro Gly Glu Glu Leu  
 755 760 765  
 Glu Trp Val Ala Ser Ile Gly Ser Tyr Pro Gly Tyr Thr Asp Tyr Ala  
 770 775 780  
 Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn  
 785 790 795 800  
 Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val  
 805 810 815  
 Tyr Tyr Cys Ala Arg His Tyr Tyr Trp Tyr Asp Ala Thr Asp Tyr Trp  
 820 825 830  
 Gly Cys Gly Thr Leu Val Thr Val Ser Ser  
 835 840

&lt;210&gt; SEQ ID NO 167

&lt;211&gt; LENGTH: 706

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)-VL CK157

&lt;400&gt; SEQUENCE: 167

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
 1 5 10 15  
 Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
 20 25 30  
 Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp  
 35 40 45  
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys  
 50 55 60  
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu  
 65 70 75 80  
 Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro  
 85 90 95  
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu  
 100 105 110  
 Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
 115 120 125  
 Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
 130 135 140

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Arg	His	Pro	Tyr	Phe	Tyr	Ala	Pro	Glu	Leu	Leu	Tyr	Tyr	Ala	Glu	Gln
145					150					155					160
Tyr	Asn	Glu	Ile	Leu	Thr	Gln	Cys	Cys	Ala	Glu	Ala	Asp	Lys	Glu	Ser
			165						170					175	
Cys	Leu	Thr	Pro	Lys	Leu	Asp	Gly	Val	Lys	Glu	Lys	Ala	Leu	Val	Ser
			180					185					190		
Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu
		195					200					205			
Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro
	210					215					220				
Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys
225					230					235					240
Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp
				245					250					255	
Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser
			260					265					270		
Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His
		275					280					285			
Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala
	290					295					300				
Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala
305					310					315					320
Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg
				325					330					335	
Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys
			340					345					350		
Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala
		355					360					365			
Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro
	370					375					380				
Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu
385					390					395					400
Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro
				405					410					415	
Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg
			420					425					430		
Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys
		435					440					445			
Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His
	450					455					460				
Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser
465					470					475					480
Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr
				485					490					495	
Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp
			500					505					510		
Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala
		515					520					525			
Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu
	530					535					540				
Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys

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545              550              555              560
Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val
      565              570              575
Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser Gly Gly Gly
      580              585              590
Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp Ile Gln Met Thr Gln Ser
      595              600              605
Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
      610              615              620
Arg Ala Ser Gln Ser Tyr Gly Gly Val Ala Trp Tyr Gln Gln Lys Pro
      625              630              635              640
Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Leu Tyr Ser
      645              650              655
Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr
      660              665              670
Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
      675              680              685
Gln Gln Pro Ser His Leu Ile Thr Phe Gly Gln Gly Thr Glu Val Glu
      690              695              700
Ile Lys
705

<210> SEQ ID NO 168
<211> LENGTH: 722
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)-VH CK157

<400> SEQUENCE: 168
Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu
 1              5              10              15
Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln
 20              25              30
Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp
 35              40              45
Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys
 50              55              60
Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu
 65              70              75              80
Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro
 85              90              95
Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu
 100             105             110
Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys
 115             120             125
Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg
 130             135             140
Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln
 145             150             155             160
Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser
 165             170             175
Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser

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	180						185						190				
Ser	Val	Arg	Gln	Arg	Met	Lys	Cys	Ser	Ser	Met	Gln	Lys	Phe	Gly	Glu		
	195						200						205				
Arg	Ala	Phe	Lys	Ala	Trp	Ala	Val	Ala	Arg	Leu	Ser	Gln	Thr	Phe	Pro		
	210						215					220					
Asn	Ala	Asp	Phe	Ala	Glu	Ile	Thr	Lys	Leu	Ala	Thr	Asp	Leu	Thr	Lys		
	225				230						235				240		
Val	Asn	Lys	Glu	Cys	Cys	His	Gly	Asp	Leu	Leu	Glu	Cys	Ala	Asp	Asp		
				245					250						255		
Arg	Ala	Glu	Leu	Ala	Lys	Tyr	Met	Cys	Glu	Asn	Gln	Ala	Thr	Ile	Ser		
			260					265						270			
Ser	Lys	Leu	Gln	Thr	Cys	Cys	Asp	Lys	Pro	Leu	Leu	Lys	Lys	Ala	His		
		275					280						285				
Cys	Leu	Ser	Glu	Val	Glu	His	Asp	Thr	Met	Pro	Ala	Asp	Leu	Pro	Ala		
	290						295				300						
Ile	Ala	Ala	Asp	Phe	Val	Glu	Asp	Gln	Glu	Val	Cys	Lys	Asn	Tyr	Ala		
	305					310					315				320		
Glu	Ala	Lys	Asp	Val	Phe	Leu	Gly	Thr	Phe	Leu	Tyr	Glu	Tyr	Ser	Arg		
				325					330						335		
Arg	His	Pro	Asp	Tyr	Ser	Val	Ser	Leu	Leu	Leu	Arg	Leu	Ala	Lys	Lys		
			340					345							350		
Tyr	Glu	Ala	Thr	Leu	Glu	Lys	Cys	Cys	Ala	Glu	Ala	Asn	Pro	Pro	Ala		
		355					360						365				
Cys	Tyr	Gly	Thr	Val	Leu	Ala	Glu	Phe	Gln	Pro	Leu	Val	Glu	Glu	Pro		
	370						375						380				
Lys	Asn	Leu	Val	Lys	Thr	Asn	Cys	Asp	Leu	Tyr	Glu	Lys	Leu	Gly	Glu		
	385					390					395				400		
Tyr	Gly	Phe	Gln	Asn	Ala	Ile	Leu	Val	Arg	Tyr	Thr	Gln	Lys	Ala	Pro		
				405					410						415		
Gln	Val	Ser	Thr	Pro	Thr	Leu	Val	Glu	Ala	Ala	Arg	Asn	Leu	Gly	Arg		
			420						425					430			
Val	Gly	Thr	Lys	Cys	Cys	Thr	Leu	Pro	Glu	Asp	Gln	Arg	Leu	Pro	Cys		
		435					440						445				
Val	Glu	Asp	Tyr	Leu	Ser	Ala	Ile	Leu	Asn	Arg	Val	Cys	Leu	Leu	His		
	450					455						460					
Glu	Lys	Thr	Pro	Val	Ser	Glu	His	Val	Thr	Lys	Cys	Cys	Ser	Gly	Ser		
	465					470				475					480		
Leu	Val	Glu	Arg	Arg	Pro	Cys	Phe	Ser	Ala	Leu	Thr	Val	Asp	Glu	Thr		
				485					490						495		
Tyr	Val	Pro	Lys	Glu	Phe	Lys	Ala	Glu	Thr	Phe	Thr	Phe	His	Ser	Asp		
		500						505						510			
Ile	Cys	Thr	Leu	Pro	Glu	Lys	Glu	Lys	Gln	Ile	Lys	Lys	Gln	Thr	Ala		
		515					520						525				
Leu	Ala	Glu	Leu	Val	Lys	His	Lys	Pro	Lys	Ala	Thr	Ala	Glu	Gln	Leu		
	530					535						540					
Lys	Thr	Val	Met	Asp	Asp	Phe	Ala	Gln	Phe	Leu	Asp	Thr	Cys	Cys	Lys		
	545				550					555					560		
Ala	Ala	Asp	Lys	Asp	Thr	Cys	Phe	Ser	Thr	Glu	Gly	Pro	Asn	Leu	Val		
				565					570						575		
Thr	Arg	Cys	Lys	Asp	Ala	Leu	Ala	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly		
			580					585						590			

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Gly Ser Gly Gly Gly Gly Ser Ala Ser Ala Glu Val Gln Leu Val Glu  
595 600 605

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys  
610 615 620

Ala Ala Ser Gly Ser Asn Pro Tyr Tyr Tyr Gly Gly Thr His Trp Val  
625 630 635 640

Arg Gln Ala Pro Gly Glu Glu Leu Glu Trp Val Ala Ser Ile Gly Ser  
645 650 655

Tyr Pro Gly Tyr Thr Asp Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr  
660 665 670

Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser  
675 680 685

Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg His Tyr Tyr  
690 695 700

Trp Tyr Asp Ala Thr Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val  
705 710 715 720

Ser Ser

<210> SEQ ID NO 169  
 <211> LENGTH: 847  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
 CK129-ds1 (VL100Q>C / VH44G>C)

<400> SEQUENCE: 169

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
1 5 10 15

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
20 25 30

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp  
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys  
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu  
65 70 75 80

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro  
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu  
100 105 110

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
115 120 125

Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln  
145 150 155 160

Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser  
165 170 175

Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser  
180 185 190

Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu  
195 200 205



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Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro  
 210 215 220  
 Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys  
 225 230 235 240  
 Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp  
 245 250 255  
 Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser  
 260 265 270  
 Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His  
 275 280 285  
 Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala  
 290 295 300  
 Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala  
 305 310 315 320  
 Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg  
 325 330 335  
 Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys  
 340 345 350  
 Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala  
 355 360 365  
 Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro  
 370 375 380  
 Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu  
 385 390 395 400  
 Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro  
 405 410 415  
 Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg  
 420 425 430  
 Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys  
 435 440 445  
 Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His  
 450 455 460  
 Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser  
 465 470 475 480  
 Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr  
 485 490 495  
 Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp  
 500 505 510  
 Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala  
 515 520 525  
 Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu  
 530 535 540  
 Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys  
 545 550 555 560  
 Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val  
 565 570 575  
 Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser Gly Gly Gly  
 580 585 590  
 Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp Ile Gln Met Thr Gln Ser  
 595 600 605

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Pro Ser Pro Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
 610                               615                620

Arg Ala Ser Gln Tyr Gly Gly Tyr Val Ala Trp Tyr Gln Gln Lys Pro
 625                               630                635                640

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Ala Ser Leu Leu Tyr Ser
 645                               650                655

Gly Val Pro Ser Arg Phe Ser Gly Gly Arg Ser Gly Thr Asp Phe Thr
 660                               665                670

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
 675                               680                685

Gln Arg Gly His Ala Leu Ile Thr Phe Gly Cys Gly Thr Lys Val Glu
 690                               695                700

Ile Glu Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser
 705                               710                715                720

Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
 725                               730                735

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser
 740                               745                750

Ser Tyr Gly Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Cys Leu
 755                               760                765

Glu Trp Val Ala Ser Ile Tyr Pro Tyr Ser Ser Ser Thr Tyr Tyr Ala
 770                               775                780

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn
 785                               790                795                800

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 805                               810                815

Tyr Tyr Cys Ala Arg Gly Tyr Gly Pro Trp Tyr Ala Tyr Ser Tyr Phe
 820                               825                830

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 835                               840                845

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&lt;210&gt; SEQ ID NO 170

&lt;211&gt; LENGTH: 847

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

<223> OTHER INFORMATION: Synthetic: mouse SA-(Gly4Ser)3-scFv (VL-VH)  
CK129-ds2 (VL43A>C / VH105Q>C)

&lt;400&gt; SEQUENCE: 170

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Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu
 1           5           10           15

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln
 20           25           30

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp
 35           40           45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys
 50           55           60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu
 65           70           75           80

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro
 85           90           95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu
 100          105          110

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Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
           115  120  125

Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
   130  135  140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln  
 145  150  155  160

Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser  
   165  170  175

Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser  
   180  185  190

Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu  
   195  200  205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro  
   210  215  220

Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys  
 225  230  235  240

Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp  
   245  250  255

Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser  
   260  265  270

Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His  
   275  280  285

Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala  
   290  295  300

Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala  
 305  310  315  320

Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg  
   325  330  335

Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys  
   340  345  350

Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala  
   355  360  365

Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro  
   370  375  380

Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu  
 385  390  395  400

Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro  
   405  410  415

Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg  
   420  425  430

Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys  
   435  440  445

Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His  
   450  455  460

Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser  
 465  470  475  480

Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr  
   485  490  495

Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp  
   500  505  510

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Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala  
 515 520 525

Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu  
 530 535 540

Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys  
 545 550 555 560

Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val  
 565 570 575

Thr Arg Cys Lys Asp Ala Leu Ala Gly Gly Gly Gly Ser Gly Gly Gly  
 580 585 590

Gly Ser Gly Gly Gly Gly Ser Ala Ser Asp Ile Gln Met Thr Gln Ser  
 595 600 605

Pro Ser Pro Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys  
 610 615 620

Arg Ala Ser Gln Tyr Gly Gly Tyr Val Ala Trp Tyr Gln Gln Lys Pro  
 625 630 635 640

Gly Lys Cys Pro Lys Leu Leu Ile Tyr Gly Ala Ser Leu Leu Tyr Ser  
 645 650 655

Gly Val Pro Ser Arg Phe Ser Gly Gly Arg Ser Gly Thr Asp Phe Thr  
 660 665 670

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys  
 675 680 685

Gln Arg Gly His Ala Leu Ile Thr Phe Gly Gln Gly Thr Lys Val Glu  
 690 695 700

Ile Glu Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser  
 705 710 715 720

Gly Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro  
 725 730 735

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Ser  
 740 745 750

Ser Tyr Gly Ser Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu  
 755 760 765

Glu Trp Val Ala Ser Ile Tyr Pro Tyr Ser Ser Ser Thr Tyr Tyr Ala  
 770 775 780

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn  
 785 790 795 800

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val  
 805 810 815

Tyr Tyr Cys Ala Arg Gly Tyr Gly Pro Trp Tyr Ala Tyr Ser Tyr Phe  
 820 825 830

Ala Leu Asp Tyr Trp Gly Cys Gly Thr Leu Val Thr Val Ser Ser  
 835 840 845

<210> SEQ ID NO 171  
 <211> LENGTH: 585  
 <212> TYPE: PRT  
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 171

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu  
 1 5 10 15

Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln  
 20 25 30

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Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu  
           35                                  40                                  45  
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys  
           50                                  55                                  60  
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu  
   65                                  70                                  75                                  80  
 Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro  
                                   85                                  90                                  95  
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu  
                                   100                                  105                                  110  
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His  
                                   115                                  120                                  125  
 Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg  
                                   130                                  135                                  140  
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg  
   145                                  150                                  155                                  160  
 Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala  
                                   165                                  170                                  175  
 Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser  
                                   180                                  185                                  190  
 Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu  
                                   195                                  200                                  205  
 Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro  
                                   210                                  215                                  220  
 Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys  
   225                                  230                                  235                                  240  
 Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp  
                                   245                                  250                                  255  
 Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser  
                                   260                                  265                                  270  
 Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His  
                                   275                                  280                                  285  
 Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser  
                                   290                                  295                                  300  
 Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala  
   305                                  310                                  315                                  320  
 Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg  
                                   325                                  330                                  335  
 Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr  
                                   340                                  345                                  350  
 Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu  
                                   355                                  360                                  365  
 Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro  
                                   370                                  375                                  380  
 Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu  
   385                                  390                                  395                                  400  
 Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro  
                                   405                                  410                                  415  
 Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys  
                                   420                                  425                                  430

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Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
    435                               440                               445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
    450                               455                               460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465                               470                               475                               480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
    485                               490                               495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
    500                               505                               510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
    515                               520                               525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
    530                               535                               540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545                               550                               555                               560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
    565                               570                               575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
    580                               585
    
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<210> SEQ ID NO 172
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
    
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<400> SEQUENCE: 172

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
 1      5      10      15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
 20     25     30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
 35     40     45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50     55     60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
 65     70     75     80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
 85     90     95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100    105    110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115    120    125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130    135    140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145    150    155    160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165    170    175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180    185    190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195    200    205
    
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Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly  
 210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu  
 225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr  
 245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn  
 260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe  
 275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn  
 290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr  
 305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
 325 330

&lt;210&gt; SEQ ID NO 173

&lt;211&gt; LENGTH: 584

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 173

Glu Ala His Lys Ser Glu Ile Ala His Arg Tyr Asn Asp Leu Gly Glu  
 1 5 10 15

Gln His Phe Lys Gly Leu Val Leu Ile Ala Phe Ser Gln Tyr Leu Gln  
 20 25 30

Lys Cys Ser Tyr Asp Glu His Ala Lys Leu Val Gln Glu Val Thr Asp  
 35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Ala Asn Cys Asp Lys  
 50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Ala Ile Pro Asn Leu  
 65 70 75 80

Arg Glu Asn Tyr Gly Glu Leu Ala Asp Cys Cys Thr Lys Gln Glu Pro  
 85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Ser Leu  
 100 105 110

Pro Pro Phe Glu Arg Pro Glu Ala Glu Ala Met Cys Thr Ser Phe Lys  
 115 120 125

Glu Asn Pro Thr Thr Phe Met Gly His Tyr Leu His Glu Val Ala Arg  
 130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Tyr Tyr Ala Glu Gln  
 145 150 155 160

Tyr Asn Glu Ile Leu Thr Gln Cys Cys Ala Glu Ala Asp Lys Glu Ser  
 165 170 175

Cys Leu Thr Pro Lys Leu Asp Gly Val Lys Glu Lys Ala Leu Val Ser  
 180 185 190

Ser Val Arg Gln Arg Met Lys Cys Ser Ser Met Gln Lys Phe Gly Glu  
 195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Thr Phe Pro  
 210 215 220

Asn Ala Asp Phe Ala Glu Ile Thr Lys Leu Ala Thr Asp Leu Thr Lys

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225	230	235	240
Val Asn Lys Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp 245			255
Arg Ala Glu Leu Ala Lys Tyr Met Cys Glu Asn Gln Ala Thr Ile Ser 260		265	270
Ser Lys Leu Gln Thr Cys Cys Asp Lys Pro Leu Leu Lys Lys Ala His 275		280	285
Cys Leu Ser Glu Val Glu His Asp Thr Met Pro Ala Asp Leu Pro Ala 290		295	300
Ile Ala Ala Asp Phe Val Glu Asp Gln Glu Val Cys Lys Asn Tyr Ala 305	310		315 320
Glu Ala Lys Asp Val Phe Leu Gly Thr Phe Leu Tyr Glu Tyr Ser Arg 325		330	335
Arg His Pro Asp Tyr Ser Val Ser Leu Leu Leu Arg Leu Ala Lys Lys 340		345	350
Tyr Glu Ala Thr Leu Glu Lys Cys Cys Ala Glu Ala Asn Pro Pro Ala 355		360	365
Cys Tyr Gly Thr Val Leu Ala Glu Phe Gln Pro Leu Val Glu Glu Pro 370		375	380
Lys Asn Leu Val Lys Thr Asn Cys Asp Leu Tyr Glu Lys Leu Gly Glu 385	390		395 400
Tyr Gly Phe Gln Asn Ala Ile Leu Val Arg Tyr Thr Gln Lys Ala Pro 405		410	415
Gln Val Ser Thr Pro Thr Leu Val Glu Ala Ala Arg Asn Leu Gly Arg 420		425	430
Val Gly Thr Lys Cys Cys Thr Leu Pro Glu Asp Gln Arg Leu Pro Cys 435		440	445
Val Glu Asp Tyr Leu Ser Ala Ile Leu Asn Arg Val Cys Leu Leu His 450		455	460
Glu Lys Thr Pro Val Ser Glu His Val Thr Lys Cys Cys Ser Gly Ser 465	470		475 480
Leu Val Glu Arg Arg Pro Cys Phe Ser Ala Leu Thr Val Asp Glu Thr 485		490	495
Tyr Val Pro Lys Glu Phe Lys Ala Glu Thr Phe Thr Phe His Ser Asp 500		505	510
Ile Cys Thr Leu Pro Glu Lys Glu Lys Gln Ile Lys Lys Gln Thr Ala 515		520	525
Leu Ala Glu Leu Val Lys His Lys Pro Lys Ala Thr Ala Glu Gln Leu 530		535	540
Lys Thr Val Met Asp Asp Phe Ala Gln Phe Leu Asp Thr Cys Cys Lys 545	550		555 560
Ala Ala Asp Lys Asp Thr Cys Phe Ser Thr Glu Gly Pro Asn Leu Val 565		570	575
Thr Arg Cys Lys Asp Ala Leu Ala 580			

&lt;210&gt; SEQ ID NO 174

&lt;211&gt; LENGTH: 232

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 174



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Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala  
 1 5 10 15  
 Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro  
 20 25 30  
 Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val  
 35 40 45  
 Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val  
 50 55 60  
 Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln  
 65 70 75 80  
 Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln  
 85 90 95  
 Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala  
 100 105 110  
 Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro  
 115 120 125  
 Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr  
 130 135 140  
 Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser  
 145 150 155 160  
 Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr  
 165 170 175  
 Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr  
 180 185 190  
 Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe  
 195 200 205  
 Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys  
 210 215 220  
 Ser Leu Ser Leu Ser Pro Gly Lys  
 225 230

&lt;210&gt; SEQ ID NO 175

&lt;211&gt; LENGTH: 197

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: HSA domain I

&lt;400&gt; SEQUENCE: 175

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu  
 1 5 10 15  
 Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln  
 20 25 30  
 Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu  
 35 40 45  
 Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys  
 50 55 60  
 Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu  
 65 70 75 80  
 Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro  
 85 90 95  
 Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu  
 100 105 110

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Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
   115                               120                               125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
   130                               135                               140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
   145                               150                               155                               160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
   165                               170                               175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
   180                               185                               190

Ser Ala Lys Gln Arg
   195

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<210> SEQ ID NO 176
<211> LENGTH: 197
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: HSA domain II

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<400> SEQUENCE: 176

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Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln
  1                               5                               10                               15

Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser
   20                               25                               30

Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr
   35                               40                               45

Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu
   50                               55                               60

Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln
   65                               70                               75                               80

Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu
   85                               90                               95

Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala
  100                               105                               110

Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys
  115                               120                               125

Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr
  130                               135                               140

Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg
  145                               150                               155                               160

Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala
  165                               170                               175

Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu
  180                               185                               190

Val Glu Glu Pro Gln
  195

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<210> SEQ ID NO 177
<211> LENGTH: 200
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: HSA domain III

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<400> SEQUENCE: 177

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Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr  
 1 5 10 15  
 Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln  
 20 25 30  
 Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val  
 35 40 45  
 Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala  
 50 55 60  
 Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu  
 65 70 75 80  
 Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu  
 85 90 95  
 Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr  
 100 105 110  
 Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile  
 115 120 125  
 Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu  
 130 135 140  
 Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys  
 145 150 155 160  
 Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala  
 165 170 175  
 Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala  
 180 185 190  
 Ala Ser Gln Ala Ala Leu Gly Leu  
 195 200

<210> SEQ ID NO 178  
 <211> LENGTH: 15  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: linker domain

<400> SEQUENCE: 178

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
 1 5 10 15

<210> SEQ ID NO 179  
 <211> LENGTH: 22  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: Secretary leader sequence

<400> SEQUENCE: 179

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp  
 1 5 10 15

Leu Pro Gly Ala Arg Cys  
 20

<210> SEQ ID NO 180  
 <211> LENGTH: 8  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: FLAG tag

-continued

&lt;400&gt; SEQUENCE: 180

Asp Tyr Lys Asp Asp Asp Asp Lys  
 1 5

&lt;210&gt; SEQ ID NO 181

&lt;211&gt; LENGTH: 6

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: Polyhistidine (6-His)

&lt;400&gt; SEQUENCE: 181

His His His His His His  
 1 5

&lt;210&gt; SEQ ID NO 182

&lt;211&gt; LENGTH: 9

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: Hemagglutinin

&lt;400&gt; SEQUENCE: 182

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala  
 1 5

&lt;210&gt; SEQ ID NO 183

&lt;211&gt; LENGTH: 51

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: linker

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: misc\_feature

&lt;222&gt; LOCATION: (2)..(51)

&lt;223&gt; OTHER INFORMATION: "Gly Gly Gly Gly Ser" is present at least once and may or may not repeat up to 10 times.

&lt;400&gt; SEQUENCE: 183

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
 1 5 10 15

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly  
 20 25 30

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly  
 35 40 45

Gly Gly Ser  
 50

&lt;210&gt; SEQ ID NO 184

&lt;211&gt; LENGTH: 16

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: linker

&lt;400&gt; SEQUENCE: 184

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
 1 5 10 15

&lt;210&gt; SEQ ID NO 185

&lt;211&gt; LENGTH: 21

&lt;212&gt; TYPE: PRT

-continued

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<213> ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: linker

&lt;400&gt; SEQUENCE: 185

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
 1 5 10 15

Gly Gly Gly Gly Ser  
 20

&lt;210&gt; SEQ ID NO 186

&lt;211&gt; LENGTH: 31

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: linker

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: misc\_feature

&lt;222&gt; LOCATION: (2)..(31)

&lt;223&gt; OTHER INFORMATION: "Gly Gly Gly Gly Ser" is present at least once and may or may not repeat up to 6 times.

&lt;400&gt; SEQUENCE: 186

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
 1 5 10 15

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
 20 25 30

&lt;210&gt; SEQ ID NO 187

&lt;211&gt; LENGTH: 24

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: linker

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: misc\_feature

&lt;222&gt; LOCATION: (1)..(24)

&lt;223&gt; OTHER INFORMATION: "Gly Gly Gly Ser" is present at least once and may or may not repeat up to 6 times.

&lt;400&gt; SEQUENCE: 187

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Ser  
 20

&lt;210&gt; SEQ ID NO 188

&lt;211&gt; LENGTH: 26

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Synthetic: Fc interlinker from human IgG1 CH2 residues 297-322

&lt;400&gt; SEQUENCE: 188

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp  
 1 5 10 15

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys  
 20 25

&lt;210&gt; SEQ ID NO 189

&lt;211&gt; LENGTH: 25

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

-continued

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<220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: HSA interlinker from the D3 domain  
 of human serum albumin

<400> SEQUENCE: 189

Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val  
 1 5 10 15

Ser Thr Pro Thr Leu Val Glu Val Ser  
 20 25

<210> SEQ ID NO 190  
 <211> LENGTH: 27  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: linker  
 <220> FEATURE:  
 <221> NAME/KEY: misc\_feature  
 <222> LOCATION: (2)..(26)  
 <223> OTHER INFORMATION: "Glu Ala Ala Ala Lys" is present at least  
 twice and may or may not repeat up to 5 times

<400> SEQUENCE: 190

Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys  
 1 5 10 15

Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala  
 20 25

<210> SEQ ID NO 191  
 <211> LENGTH: 50  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: alpha-helix forming linker

<400> SEQUENCE: 191

Leu Glu Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Glu Ala Ala  
 1 5 10 15

Ala Lys Glu Ala Ala Ala Lys Ala Leu Glu Ala Glu Ala Ala Ala Lys  
 20 25 30

Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala  
 35 40 45

Leu Glu  
 50

<210> SEQ ID NO 192  
 <211> LENGTH: 4  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: linker

<400> SEQUENCE: 192

Gly Gly Ser Gly  
 1

<210> SEQ ID NO 193  
 <211> LENGTH: 20  
 <212> TYPE: PRT  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Synthetic: linker  
 <220> FEATURE:

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-continued

<221> NAME/KEY: misc\_feature  
<222> LOCATION: (1)..(20)  
<223> OTHER INFORMATION: "Gly Gly Ser Gly" is present at least once  
and may or may not repeat up to 5 times

<400> SEQUENCE: 193

Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly  
1 5 10 15

Gly Gly Ser Gly  
20

<210> SEQ ID NO 194  
<211> LENGTH: 4  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: linker

<400> SEQUENCE: 194

Gly Ser Ala Thr  
1

<210> SEQ ID NO 195  
<211> LENGTH: 30  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: linker  
<220> FEATURE:  
<221> NAME/KEY: misc\_feature  
<222> LOCATION: (1)..(30)  
<223> OTHER INFORMATION: "Gly Gly Ser Gly Gly Ser" is present at least  
once and may or may not repeat up to 5 times

<400> SEQUENCE: 195

Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly  
1 5 10 15

Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser  
20 25 30

<210> SEQ ID NO 196  
<211> LENGTH: 15  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: linker

<400> SEQUENCE: 196

Gly Leu Asn Asp Ile Phe Glu Ala Gln Lys Ile Glu Trp His Glu  
1 5 10 15

<210> SEQ ID NO 197  
<211> LENGTH: 20  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: secretory leader peptide sequence

<400> SEQUENCE: 197

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro  
1 5 10 15

Gly Ala Arg Cys  
20

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<210> SEQ ID NO 198  
<211> LENGTH: 8  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: acid flexible linker

<400> SEQUENCE: 198

Ser Ser Gly Val Asp Leu Gly Thr  
1 5

<210> SEQ ID NO 199  
<211> LENGTH: 7  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: Tobacco Etch Virus proteolytic  
cleavage site  
<220> FEATURE:  
<221> NAME/KEY: misc\_feature  
<222> LOCATION: (7)..(7)  
<223> OTHER INFORMATION: Xaa is Ala or Val

<400> SEQUENCE: 199

Glu Asn Leu Tyr Phe Gln Xaa  
1 5

<210> SEQ ID NO 200  
<211> LENGTH: 10  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: linker

<400> SEQUENCE: 200

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
1 5 10

<210> SEQ ID NO 201  
<211> LENGTH: 5  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: five amino-acid flexible spacer

<400> SEQUENCE: 201

Gly Gly Gly Gly Ser  
1 5

<210> SEQ ID NO 202  
<211> LENGTH: 18  
<212> TYPE: PRT  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Synthetic: secretory leader sequence

<400> SEQUENCE: 202

Met Gln Leu Leu Arg Cys Phe Ser Ile Phe Ser Val Ile Ala Ser Val  
1 5 10 15

Leu Ala

<210> SEQ ID NO 203  
<211> LENGTH: 15  
<212> TYPE: PRT



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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: flexible linker

<400> SEQUENCE: 203

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
1 5 10 15

<210> SEQ ID NO 204

<211> LENGTH: 16

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: flexible linker

<400> SEQUENCE: 204

Gly Thr Thr Ala Ala Ser Gly Ser Ser Gly Gly Ser Ser Ser Gly Ala  
1 5 10 15

<210> SEQ ID NO 205

<211> LENGTH: 11

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: c-myc epitope tag

<400> SEQUENCE: 205

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Gln  
1 5 10

<210> SEQ ID NO 206

<211> LENGTH: 33

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: primer

<400> SEQUENCE: 206

ggaggcggta gcgaggcgg agggctcggct agc 33

<210> SEQ ID NO 207

<211> LENGTH: 31

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: primer

<400> SEQUENCE: 207

gtcctcttca gaaataagct tttgttcgga t 31

<210> SEQ ID NO 208

<211> LENGTH: 22

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic: secretory leader peptide sequence

<400> SEQUENCE: 208

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp  
1 5 10 15

Leu Pro Gly Ala Arg Cys  
20

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<210> SEQ ID NO 209
<211> LENGTH: 38
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic: secretory leader sequence

<400> SEQUENCE: 209

Met Lys Val Leu Ile Val Leu Leu Ala Ile Phe Ala Ala Leu Pro Leu
1           5           10          15

Ala Leu Ala Gln Pro Val Ile Ser Thr Thr Val Gly Ser Ala Ala Glu
                20          25          30

Gly Ser Leu Asp Lys Arg
          35

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1. A fusion protein, comprising a multispecific variable region operably coupled to a polymer, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines.

2. The fusion protein of claim 2, wherein the multispecific variable region is operably coupled to the C-terminus of the polymer.

3. The fusion protein of claim 2, wherein the multispecific variable region is operably coupled to the N-terminus of the polymer.

4. The fusion protein of any one of claims 1-3, wherein the multispecific variable region is operably coupled to the polymer via a linker.

5. The fusion protein of claim 4, wherein the linker is a Gly-Ser linker.

6. The fusion protein of any one of claims 1-5, wherein the polymer is a serum albumin moiety.

7. The fusion protein of any one of claims 1-5, wherein the polymer is an Fc domain.

8. The fusion protein of any one of claims 1-7, wherein the multispecific variable region is a scFv.

9. The fusion protein of any one of claims 1-8, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines selected from the group consisting of: human CXCL1 (Gro $\alpha$ ), human CXCL2 (Gro $\beta$ ), human CXCL3 (Groy), human CXCL5 (ENA-78), human CXCL6 (GCP-2), human CXCL7 (NAP-2), human CXCL8 (IL-8), murine CXCL1 (KC), murine CXCL2 (MIP-2), murine CXCL3 (DCIP-1), murine CXCL5 (LIX), and murine CXCL7 (NAP-2).

10. The fusion protein of claim 9, wherein the at least four ELR+ CXC chemokines are hCXCL1, hCXCL2, hCXCL3 and mCXCL1.

11. The fusion protein of any one of claims 1-9, wherein the multispecific variable region binds to at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, or at least twelve ELR+ CXC chemokines.

12. The fusion protein of claim 11, wherein the at least six chemokines are human CXCL1, human CXCL5, human CXCL8, murine CXCL1, murine CXCL2 and murine CXCL5.

13. The fusion protein of claim 11, wherein the at least eleven chemokines are human CXCL8, murine CXCL2, murine CXCL1, murine CXCL3, human CXCL7, human CXCL5, human CXCL1, murine CXCL5, human CXCL3, human CXCL2, and human CXCL6.

14. The fusion protein of any one of claims 1-9, wherein the multispecific variable region binds murine or human ELR+ CXC chemokines.

15. The fusion protein of any one of claims 1-9, wherein the multispecific variable region binds murine and human ELR+ CXC chemokines.

16. The fusion protein of any one of the preceding claims, wherein the multispecific variable region comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21.

17. The fusion protein of any one of the preceding claims, wherein the multispecific variable region comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

18. The fusion protein of any one of the preceding claims, wherein the multispecific variable region comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21, and wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

19. A fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises a heavy chain variable region and a light chain variable region comprising the amino acid sequences set forth in:

- (a) SEQ ID NOs: 1 and 2, respectively;
- (b) SEQ ID NOs: 11 and 12, respectively; or
- (c) SEQ ID NOs: 21 and 22, respectively.

20. A fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises a heavy chain variable region and light chain variable region comprising amino acid sequences having 90% identity to the amino acid sequences set forth in:

- (a) SEQ ID NOs: 1 and 2, respectively;
- (b) SEQ ID NOs: 11 and 12, respectively; or
- (c) SEQ ID NOs: 21 and 22, respectively.

21. A fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+

CXC chemokines, and wherein the multispecific variable region comprises heavy and light chain CDRs selected from the group consisting of:

- (a) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively;
- (b) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 15, 16 and 17, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 18, 19 and 20, respectively; and
- (c) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively.

**22.** A fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+ CXC chemokines, and wherein the multispecific variable region comprises heavy and light chain variable regions, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 11 and 21; and wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 12 and 22.

**23.** The fusion protein of any one of claims 1-22, wherein the fusion protein inhibits binding of ELR+ CXC chemokines to their cognate CXCR1 and CXCR2.

**24.** An isolated monoclonal antibody, or binding fragment thereof, that binds to at least four ELR+ CXC chemokines.

**25.** The isolated monoclonal antibody, or binding fragment thereof, of claim 24, wherein the at least four ELR+ CXC chemokines are selected from the group consisting of: human CXCL1 (Gro $\alpha$ ), human CXCL2 (Gro $\beta$ ), human CXCL3 (Gro $\gamma$ ), human CXCL5 (ENA-78), human CXCL6 (GCP-2), human CXCL7 (NAP-2), human CXCL8 (IL-8), murine CXCL1 (KC), murine CXCL2 (MIP-2), murine CXCL3 (DCIP-1), murine CXCL5 (LIX), and murine CXCL7 (NAP-2).

**26.** The isolated monoclonal antibody, or binding fragment thereof, of claim 25, wherein the at least four ELR+ CXC chemokines are hCXCL1, hCXCL2, hCXCL3 and mCXCL1

**27.** The isolated monoclonal antibody, or binding fragment thereof, of claim 24 or 25, wherein the antibody or binding fragment thereof binds to at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, or at least twelve ELR+ CXC chemokines.

**28.** The isolated monoclonal antibody, or binding fragment thereof, of claim 27, wherein the at least six chemokines are human CXCL1, human CXCL5, human CXCL8, murine CXCL1, murine CXCL2 and murine CXCL5.

**29.** The isolated monoclonal antibody, or binding fragment thereof, of claim 27, wherein the at least eleven chemokines are human CXCL8, murine CXCL2, murine CXCL1, murine CXCL3, human CXCL7, human CXCL5, human CXCL1, murine CXCL5, human CXCL3, human CXCL2, and human CXCL6.

**30.** The isolated monoclonal antibody, or binding fragment thereof, of any one of claims 24-25, wherein the antibody or binding fragment thereof binds murine or human ELR+ CXC chemokines.

**31.** The isolated monoclonal antibody, or binding fragment thereof, of any one of claims 24-25, wherein the

antibody or binding fragment thereof binds murine and human ELR+ CXC chemokines.

**32.** The isolated monoclonal antibody, or binding fragment thereof, of any one of claims 24-31, wherein the antibody is a single chain variable fragment (scFv).

**33.** The isolated monoclonal antibody, or binding fragment thereof, of any one of claims 24-32, wherein the antibody or binding fragment comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21.

**34.** The isolated monoclonal antibody, or binding fragment thereof, of any one of claims 24-33, wherein the antibody or binding fragment comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

**35.** The isolated monoclonal antibody, or binding fragment thereof, of any one of claims 24-32, wherein the antibody or binding fragment comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 1, 11 or 21, and wherein the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NOs: 2, 12 or 22.

**36.** An isolated monoclonal antibody, or binding fragment thereof, that binds to at least four ELR+ CXC chemokines, wherein the antibody or binding fragment comprises a heavy chain variable region and light chain variable region comprising the amino acid sequences set forth in:

- (a) SEQ ID NOs: 1 and 2, respectively;
- (b) SEQ ID NOs: 11 and 12, respectively; or
- (c) SEQ ID NOs: 21 and 22, respectively.

**37.** An isolated monoclonal antibody, or binding fragment thereof, that binds to at least four ELR+ CXC chemokines, wherein the antibody or binding fragment comprises a heavy chain variable region and light chain variable region comprising amino acid sequences having 90% identity to the amino acid sequences set forth in:

- (a) SEQ ID NOs: 1 and 2, respectively;
- (b) SEQ ID NOs: 11 and 12, respectively; or
- (c) SEQ ID NOs: 21 and 22, respectively.

**38.** An isolated monoclonal antibody, or binding fragment thereof, that binds to at least four ELR+ CXC chemokines, wherein the antibody or binding fragment comprises heavy and light chain CDRs selected from the group consisting of:

- (a) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively;
- (b) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 15, 16 and 17, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 18, 19 and 20, respectively; and
- (c) heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively.

**39.** An isolated monoclonal antibody, or binding fragment thereof, that binds to at least four ELR+ CXC chemokines, wherein the antibody or binding fragment comprises heavy and light chain variable regions, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 11 or 21; and

wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 12 or 22.

**40.** A method of treating an autoimmune disorder in a subject in need thereof, the method comprising administering an effective amount of the fusion protein of any one of claims **1-23**, or the isolated monoclonal antibody of any one of claims **24-39**.

**41.** The method of claim **40**, wherein the autoimmune disorder is rheumatoid arthritis.

**42.** A method of blocking neutrophil infiltration in a subject with an autoimmune disorder, the method comprising administering an effective amount of the fusion protein of any one of claims **1-23**, or the isolated monoclonal antibody of any one of claims **24-39**.

**43.** The method of claim **42**, wherein neutrophil infiltration of the synovial fluid of arthritic joints is blocked.

**44.** A method of preventing establishment of an autoimmune disorder in a subject, the method comprising administering an effective amount of the fusion protein of any one of claims **1-23**, or the isolated monoclonal antibody of any one of claims **24-39**.

**45.** A method of reversing inflammatory arthritis in a subject in need thereof, the method comprising administering an effective amount of the fusion protein of any one of claims **1-23**, or the isolated monoclonal antibody of any one of claims **24-39**.

**46.** A fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+CXC chemokines, and wherein the multispecific variable region comprises heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 5, 6 and 7, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 8, 9 and 10, respectively.

**47.** A fusion protein, comprising a multispecific variable region operably coupled to a serum albumin moiety, wherein the multispecific variable region binds to at least four ELR+CXC chemokines, and wherein the multispecific variable region comprises heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 25, 26 and 27, respectively, and light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NOs: 28, 29 and 30, respectively.

**48.** A fusion protein comprising an amino acid sequence selected from the group consisting of SEQ ID Nos: 95-105 and 160-170.

**49.** A fusion protein comprising an amino acid sequence having at least 90% identity to an amino acid sequence selected from the group consisting of SEQ ID Nos: 95-105 and 160-170.

\* \* \* \* \*