KDDF
Korea Drug Development Fund

Asset #12
Boston Children's Hospital

Novel Anti-PD1 Antibodies for Inhibiting T-cell Activity

Therapeutic Area	Immunology	**Indications**	Autoimmune Diseases(RA), Type1 DM
Modality	Monoclonal Antibody	**Development Stage**	Target Identification/Validation

Overview

Background

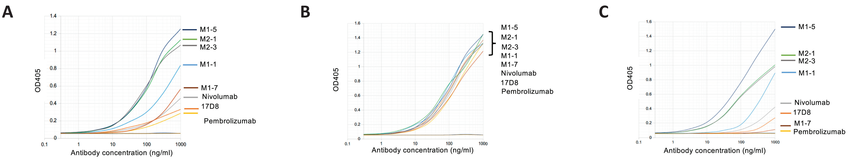
- PD1 (Programmed Death 1) is an immune checkpoint protein that negatively regulates immune system activity through its interaction with PD ligands. In cancer, inhibition of the PD1/PD ligand interaction by anti-PD1 antibodies has been harnessed as an effective therapeutic strategy to boost immune attack against tumors. On the other hand, stimulating the PD1 pathway by therapeutic antibodies could potentially suppress deleterious immune activities in autoimmune diseases, and there is currently a shortage of such PD1 agonist antibodies.

Technology Advantages

- Researchers at Boston Children's Hospital generated novel humanized anti-PD1 antibodies, using an in vivo mouse model of antibody diversification that harnesses the natural affinity maturation processes. Some of these new anti-PD1 antibodies can enhance, rather than inhibit, PD1 interaction with its ligand, PD-L1.
- These novel anti-PD1 antibodies were isolated from mouse models, where antibodies with poly-reactivities and unstable conformations are eliminated by quality control systems in vivo. Such antibodies may be more amenable to clinical application.

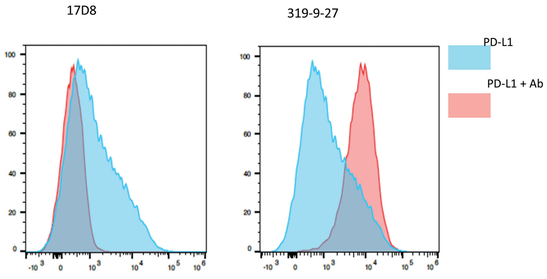
Key Data

Analysis of PD1-binding activities of the 17D8 variant antibodies



the comparison of PD1-binding activities of new anti-PD1 antibodies versus the original 17D8 antibody in different assays revealed epitope diversification of the prototype in both mouse models.
(A)ELISA analysis of PD1-binding activities of 17D8 antibody, nivolumab, pembrolizumab, and five new anti-PD1 antibodies isolated from mouse models 1 and 2. In this ELISA experiment, PD1 extracellular domain, without Fc fusion, was coated on the ELISA plate. (B) ELISA analysis of the same antibodies in C, but with PD1–Fc fusion as the coating antigen on ELISA plate. (C) ELISA analysis of the same antibodies in C, but with PD1 N-terminal–GST fusion protein as the coating antigen on ELISA plate.

The effects of anti-PD1 antibodies on PD1/ligand interaction.



Original anti-PD1 antibody (17D8) before diversification inhibited binding of PD-L1 to PD1 whereas the newly diversified anti-PD1 antibody (319-9-27) enhanced PD1/PD-L1 interaction.
FACS analysis of the effects of anti-PD1 antibodies on PD1/PD-L1 interaction. The x-axis of the plots represents the levels of PD-L1 binding to PD1 expressed on NS1 cell surface; the y-axis represents relative cell number, with the highest peak set at 100% (modal mode). The additions of PD-L1 and various anti-PD1 antibodies are indicated underneath the plots. In the plot "PD-L1," only PD-L1 was added to the binding reaction, as represented by the red histogram; the blue histograms show PD-L1 binding to PD1 in the presence of various antibodies.

IP Status & Publication(s)

Intellectual Property

Patent Number
PCT-US2021-041407 (2021.07.13)

Patent Family
PCT, EP

Publication(s)

- Tian, M. et al. (2021). An in vivo method for diversifying the functions of therapeutic antibodies. Proceedings of the National Academy of Sciences of the United States of America, 118(10).