276 ANTI-INTEGRIN αVβ6 ANTIBODIES

Asset Overview

Product Type	Antibody
Indication	Oncology
Current Stage	Lead discovery/optimization
Target (MoA)	IKK ALPHA Selective Compounds
Brief Description	A series of anti-αvβ6 antibodies has been generated through a loop grafting approach, which involved taking advantage of the A20FMDV2 peptide, which has high affinity and selectivity for αvβ6 was inserted into CEA Antibody. Therefore, the series of anti-αvβ6 antibodies includes antibodies engineered to be highly αvβ6-specific and an antibody which also cross-reacts with the CEA. Importantly, B6.2 was determined to be as structurally stable as the parent scFv, indicating that insertion of the A20FMDV2 peptide and the Y100bP mutation (removes CEA cross-reactivity) was not detrimental to the protein structure. The humanised variant B6.3 has been generated in diabody and full IgG formats, the diabody variant of which has a Kd of 2.78 nM (as measured by Biacore).
Organization	Cancer Research UK

Differentiation

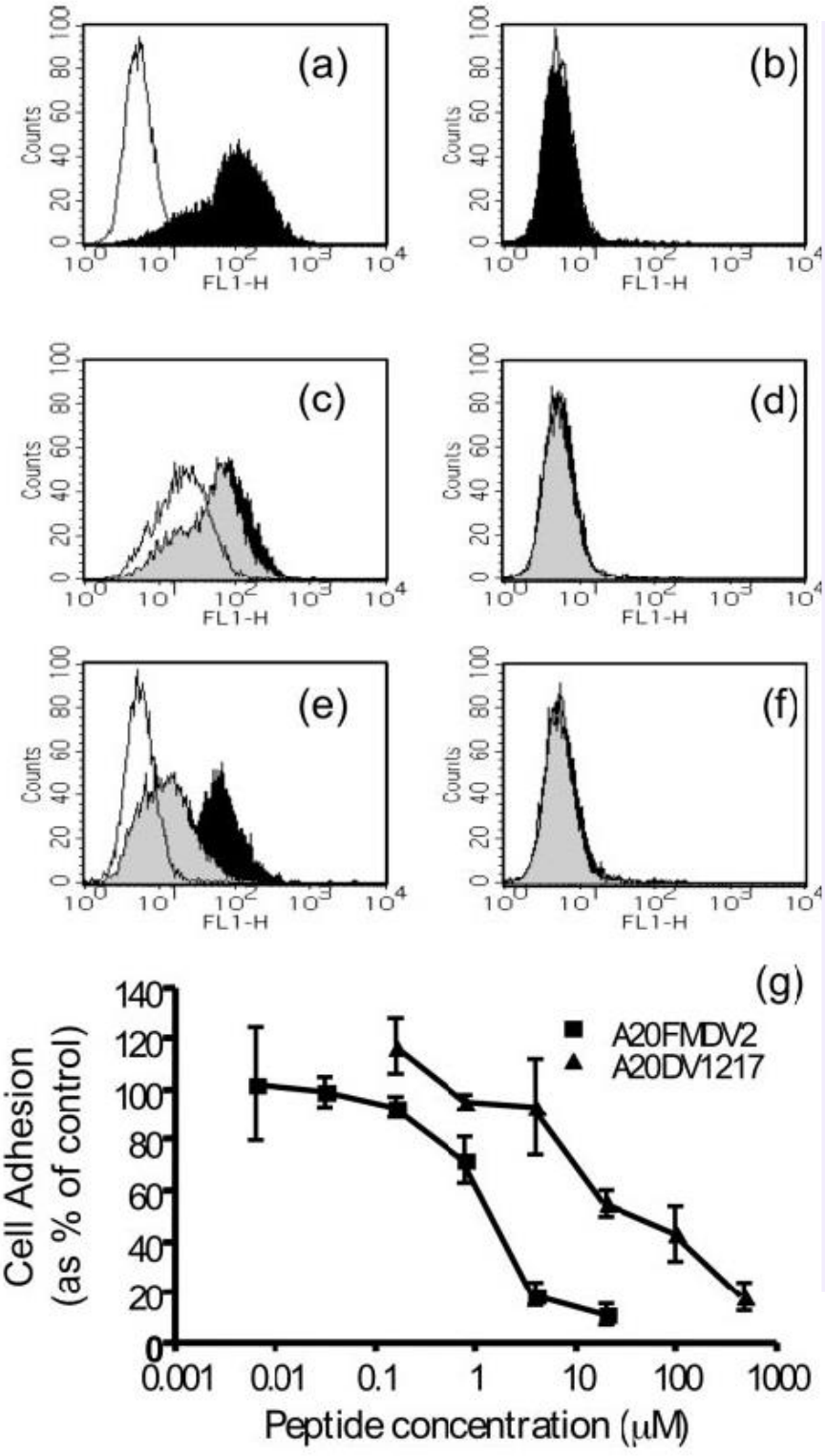
□ **Unmet Needs**

- For castrate reisistant prostate cancer, current therapies exert inadequate therapeutic benefit
- Of 1 in 8 men diagnosed with prostate cancer, 25 will die of metastatic disease. Despite the approval of four new agents (abiraterone, enzalutamide and provenge) that have been shown to prolong life for up to 3-9 months in advanced PC patients, it remains an incurable disease

□ **Innovations**

- A mutation that prevents IKK α activation slows down prostate cancer growth and inhibits metastasis in TRAMP mice
- Suppression of IKK α by siRNA delays the appearance of CRPC in the murine myc CaP allograft model of PC
- The amount of active nuclear IKK α in mouse and human prostate cancer correlates with metastatic progression
- Nuclear IKK α appears to provide a mechanism for hormone resistance in the development of CRPC
- Deletion of BAG 3 which is required for IKK α nuclear translocation delays development of castrate resistant disease

Key Data



The post-RGD helix is required to improve peptide affinity and potency. Flow cytometry was used to measure binding of biotinylated peptides to A375Pβ6puro (a, c, and e) or A375Pβ6puro (b, d, and f). a and b, unfilled histograms, IgG control; black solid histograms, 10D5 (mouse anti-avb6). c and d, e and f, A20DV1217 at 100 nM Radiolabeled ^{51}Cr-VB6 cells were added to 96-well plates coated with 50 μl (0.25 μg/ml) LAP in various concentrations of peptides A20FMDV2 or A20DV1217. Data shown are from one experiment using triplicate samples and are representative of three separate experiments with similar results.

Intellectual Property

Patent No.	US 8383593 B2
Application Date	2006.10.03
Status	Registered
Country	US, EP, JP, CA

Contact Information

Contact Person	Matthew Burney
Email	matthew.burney@cancer.org.uk
URL	http://commercial.cancerresearchuk.org/anti-integrin-%C9%91v%C3%9F6-antibodies