249 NOVEL TUMOR SELECTIVE INTERNALIZING ANTIBODIES

Asset Overview

Product Type	Antiboody
Indication	Oncology
Current Stage	PRECLINICAL
Target(MoA)	The new antibodies have the potential to guide immunotherapies with greater accuracy against mesothelioma or other cancers expressing the target antigen
Brief Description	Scientists at the University of California, San Francisco have developed a set of human monoclonal antibodies that specifically recognize a cell surface antigen highly expressed in mesothelioma and other cancers, as well as cancers that undergo epithelia to mesenchymal transition (EMT). The antigen is a hallmark specifically expressed by mesothelioma and all subtypes of mesothelioma but not by normal mesothelium. The new antibodies have the potential to guide immunotherapies with greater accuracy against mesothelioma or other cancers expressing the target antigen. Additionally, the novel antibodies are able to block tumor cell invasion, indicating application for inhibition of tumor function such as invasion or self-renewal. Furthermore, the inventors showed that the target antigen is preferentially expressed by tumor-associated blood vessels, thus exhibiting potential as an anti-angiogenic therapy. The antibodies and antigen have been evaluated in nude mice models using available devices and measurement methods. This technology can be rapidly incorporated into clinical trial.
Organization	University of California, San Francisco

Differentiation

□ **High specificity for tumor cells**

- Can be utilized in several ways including: antibody-drug conjugation, immune activation and cell based therapy
- Novel antibody compositions that are fully human, which confers minimum immunogenicity

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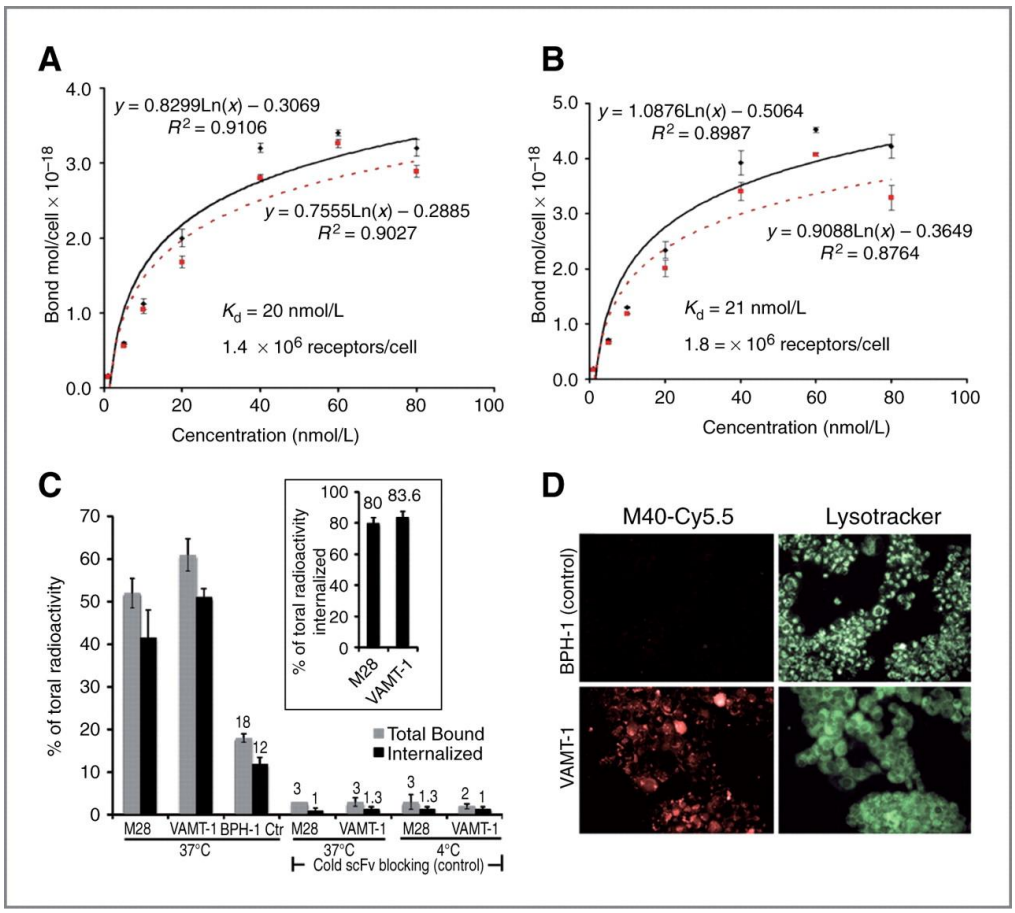
Key Data

In vitro characterization of ^{99m}Tc-M40



The binding affinity of 99mTc-M40 to the mesothelioma cells exhibited an apparent Kd of 20 to 21 nmol/L and the antigen density for M40 derived from the saturation cell binding assay was comparable on both tumor cells (Fig. 1A, 1B). M40 was rapidly internalized over the concentrations tested with about 68% to 92% of total cell-associated uptake, following 1 hour incubation at 37°C (Fig. 1C), whereas the binding and uptake in the control BPH-1 cells was much less (Fig. 1C). Specificity was further demonstrated by blocking of uptake/ internalization into both M28 and VAMT-1 (>95%) cells with a 10-fold excess of unlabeled M40 (Fig. 1C). As shown in Figure 1D, Cy5.5-M40 was rapidly internalized into mesothelioma cells within 1 hour after incubation at 37°C, whereas there was negligible uptake in the control (BPH-1) cells under identical conditions.

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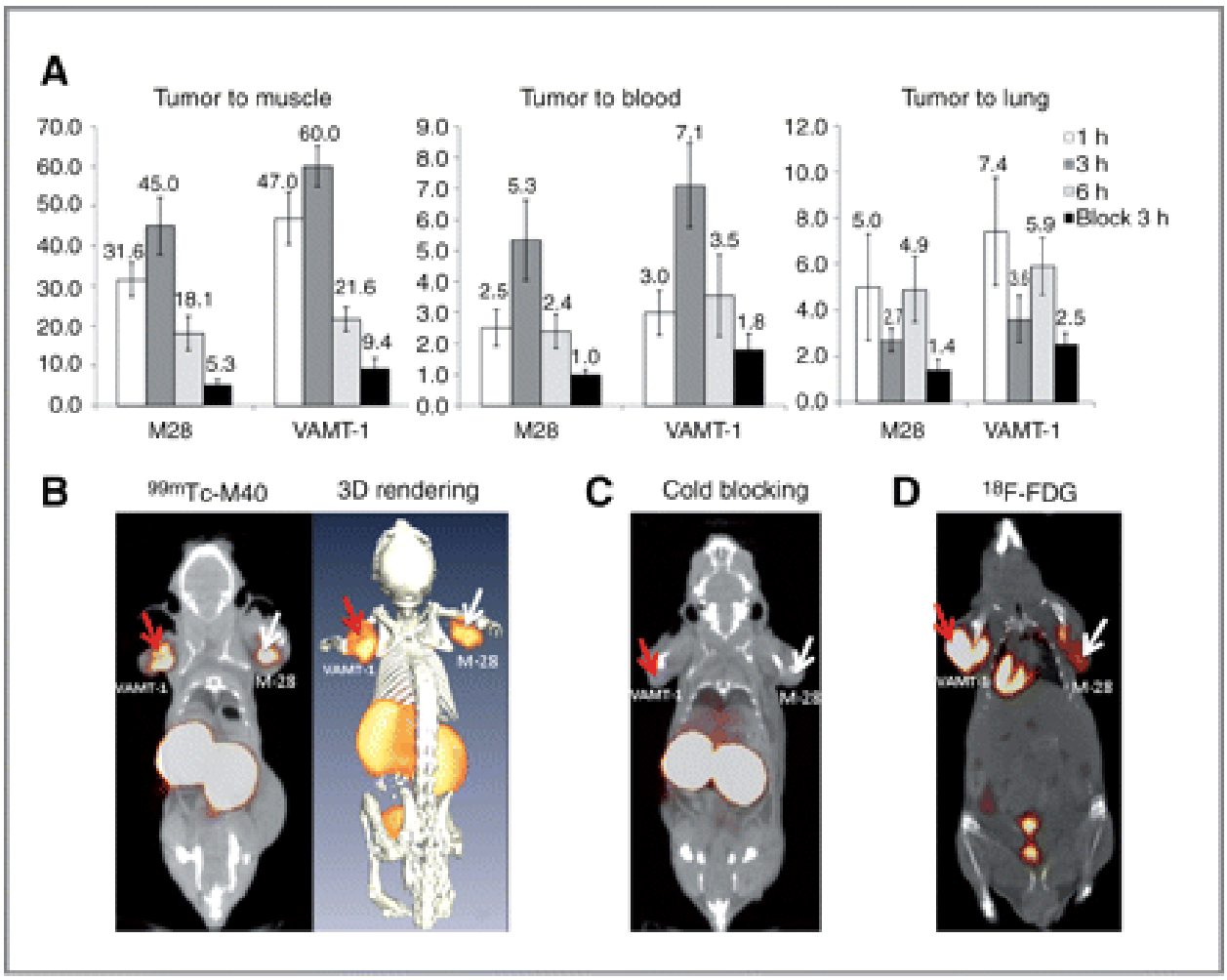

In vivo tumor targeting of 99mTc-M40. A, tumor to nontarget tissue ratios of 99mTc-M40. Tumor/muscle (left), tumor/blood (center), and tumor/lung (right) ratios in mice bearing both subtypes of mesothelioma tumors are shown at 1, 3, and 6 hours after injection and blocking study using the 10-fold excess unlabeled M40 1 hour before 99mTc-M40 (Block 3 hours). B, SPECT/CT fused coronal image of 99mTc-M40 imaged 3 hours after injection (left); 3D fused SPECT/CT coronal image (right). C, blocking control study. D, PET-CT fused coronal image of 18F-FDG imaged 1 hour after injection.

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Intellectual Property

Patent No.	
Application Date	
Status	
Country	

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