VAN ANDEL INSTITUTE

Business Development / Technology Transfer

Applications

- Amenable for imaging studies
- A potential method of delivering anti-cancer drugs to MET-expressing tumors

Benefits/Advantages

- High specificity
- Low toxicity
- Non-immunogenic in human patients

VARI IP-00067

Patent Status: Issued
U.S. 8,039,598

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Human MET Antibody Fragments

Human fragments of antibodies (Fab) and scFv fragments specific to the human MET extracellular domain, which are readily internalized upon receptor binding, can be potentially used for imaging or drug delivery.

Background

Aberrant growth and proliferation of cancer cells are often associated with the abnormal activity of specific proteins. One such protein is the cellular receptor known as MET, which plays an important role in tumor growth and metastasis. As such, increased MET is usually associated with aggressive tumors. The magnitude of MET expression can aid in predicting the aggressiveness of many MET-expressing cancer types. A common method of assessing the level of MET produced by cancer cells is immunohistochemistry; however, this method requires obtaining a sample of the tumor, which can be invasive and difficult.

Technology

Using an in-house generated human Fab library and subtractive bio-panning, researchers at Van Andel Research Institute (VARI) identified a specific Fab that reacts with the extracellular domain of human MET. To further increase its binding affinity for MET, the researchers used affinity maturation techniques to generate two new anti-MET fragments: scFv designated S1 and Fab designated Fab-Met-2. These two new fragments exhibit high affinity for MET and are able to be internalized once bound together.

These novel agents can potentially be used for radioimmunoscintography in humans, allowing for assessment of MET expression without obtaining a tumor sample. These fragments also can be used as a carrier for delivering chemotherapy and immunotherapy agents directly and specifically to MET-expressing cancer cells.

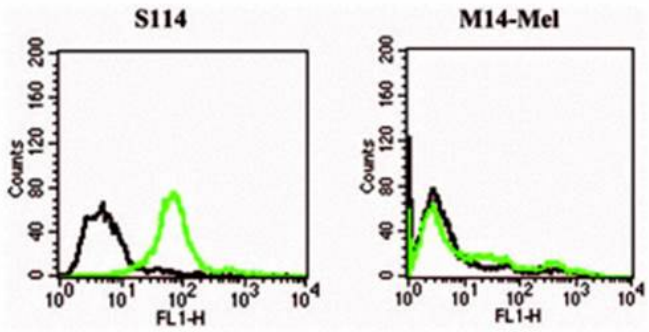

Figure 1: *The binding affinity of hFab-Met-1*. To confirm its specificity, hFab-Met-1 was analyzed for its ability to bind to MET receptors on cell membranes by FACS analysis. The surface staining of hFab-Met-1 (green trace) in S114 (MET+) but not in M14 (MET-) cells indicated that hFab-Met-1 binds Met in its native form. The black trace indicates staining with a secondary antibody only.

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Through biomedical research and science education Van Andel Institute is committed to improving the health and enhancing the lives of current and future generations.