Fully Human Antibodies and Fragments Recognizing c-Met

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SUMMARY

UCLA researchers in the Department of Molecular and Medical Pharmacology have developed several novel recognition sequences against the human oncogene c-MET. These unique sequences are the basic building blocks used to make intact human antibodies and antibody fragments that can be conjugated to various payloads endowing them with great therapeutic and diagnostic potential *in vitro* and *in vivo*.

BACKGROUND

The proto-oncogene c-MET (hepatocyte growth factor receptor, HGFR) is a membrane-bound tyrosine kinase receptor expressed on the surface of cells of epithelial origin. In normal cells, c-MET signaling is initiated in response to hepatocyte growth factor (HGF), and is responsible for wound healing and tissue regeneration. However, in the case of cancer, this pathway is abnormally activated leading to several biological processes known together as invasive growth. In fact, the c-MET pathway is one of the most frequently dysregulated pathways in human cancer. Aberrant c-MET signaling has been documented in most solid tumors and hematological malignancies, and is tightly associated with the resistance to various cancer therapies. Reflecting their critical roles in cancer development and progression, c-MET and HGF have become leading candidates for targeted cancer therapies and diagnostics. Several mouse c-MET antibodies are available for in vitro use, and a single humanized c-MET antibody is being evaluated for its therapeutic and diagnostic potential. However, there are currently no fully human c-Met antibodies being available for cancer therapeutics or diagnostics.

INNOVATION

Dr. Anna Wu and colleagues in UCLA's Department of Molecular and Medical Pharmacology have developed several novel human recognition sequences against the oncogene c-MET. These sequences are the basic building blocks used to synthesize c-MET-specific intact antibodies and antibody fragments (scFV, diabody, cys-diabody) with varying sizes and pharmacokinetics. The novel sequences recognize c-MET with high affinity (nanomolar/sub-nanomolar) and are less likely to induce a detrimental immune response in human patients since they are fully human (low immunogenicity). Intact antibodies or antibody fragments can be used alone as potential blocking agents or conjugated to a number of different payloads. Specifically, the formation of cys-diabody fragments allow for site-specific conjugation to various payloads (fluorophores, radioisotopes, nanoparticles or cytotoxic drugs) making them very convenient reagents for a number of in vitro and in vivo applications. Researchers have confirmed that the novel recognition sequences have nanomolar affinity for c-MET and are currently testing the utility of these antibody fragments in diagnostic applications.

APPLICATIONS

- Receptor antagonist
- *In vivo* imaging (immunoPET)
- Targeted drug delivery
- *In vitro* diagnosis
- Circulating tumor cell capture

ADVANTAGES

- Fully human (low immunogenicity)
- Nanomolar (or sub-nanomolar) affinity for c-MET
- c-MET recognition sequences can be reformatted to fit various size and pharmaco-kinetic requirements

CONTACT

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INVENTORS

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OTHER INFORMATION

KEYWORDS

Antibody, Diagnostics, Cancer, Oncology, Therapeutics, Chemotherapy

CATEGORIZED AS

- **Medical**
  - Diagnostics
  - Disease: Cancer
  - Imaging
  - Research Tools

RELATED CASES

2013-185-0

- Antibody (or antibody fragments) can be conjugated to various payloads

STATE OF DEVELOPMENT

- Validated nanomolar (or sub-nanomolar) specificity for human c-MET
- Formed into diabodies and cys-diabodies
- Currently testing diagnostic applications in vitro

RELATED MATERIALS

- IBC Antibody Engineering Conference Poster (2012) - [Abstract S7]
- Antibodies for molecular imaging of cancer. Cancer J. (2008)

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,407,503	09/10/2019	2013-185

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- A Novel Immuno-PET Tracer for Imaging of CD20
- A Novel Renilla-Derived Luciferase with Enhanced Activity and Stability
- System to Produce Biotinylated Proteins
- Humanized Antibodies to the Extracellular Domains of Human N-Cadherin

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