

ANTI-MESOTHELIN MONOCLONAL ANTIBODIES FOR THE TREATMENT OF CANCER

SUMMARY

The National Cancer Institute, Laboratory of Molecular Biology is seeking parties interested in collaborative research to further co-develop monoclonal antibodies for the treatment of mesothelin-expressing cancers.

REFERENCE NUMBER

E-236-2012

PRODUCT TYPE

- Therapeutics

KEYWORDS

- Therapeutic
- cancer
- monoclonal antibodies
- mesothelin
- diagnostic
- epitopes

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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DESCRIPTION OF TECHNOLOGY

The National Cancer Institute, [Laboratory of Molecular Biology](#) seeks parties interested in collaborative research to further co-develop monoclonal antibodies for the treatment of mesothelin-expressing cancers. The antibody was able to inhibit tumor growth in mouse xenograft models, and corresponding immunotoxins were able to inhibit tumor cell growth in vitro

Mesothelin is a cell surface protein that is highly expressed in aggressive cancers such as malignant mesothelioma, ovarian cancer, pancreatic cancer, lung cancer, breast cancer, cholangiocarcinoma, bile duct carcinoma and gastric cancer. This selective expression makes mesothelin an excellent candidate for targeted therapeutics such as monoclonal antibodies (mAbs) and corresponding chimeric molecules.

NCI Technology Transfer Center

<https://techtransfer.cancer.gov/pdf/e-236-2012.pdf>

Unfortunately, current anti-mesothelin mAb candidates have drawbacks, such as competition with a serum protein (MUC16/CA125) for binding to mesothelin, the formation of neutralizing antibodies because they are non-human antibodies, and the inability to trigger complement-dependent cytotoxicity (CDC).

In order to address this concern, NIH inventors generated two single domain human mAbs: SD1 and SD2. SD1 recognizes a unique epitope in region III of mesothelin which is not out-competed for binding by MUC16/CA125. SD1 was also capable of triggering CDC, as well as antibody-dependent cellular cytotoxicity (ADCC). Due to its human origin, SD1 is also less likely to elicit the formation of neutralizing antibodies when administered to patients. Each of these characteristics suggests SD1 may be an effective therapeutic agent. Indeed, SD1 was able to inhibit tumor growth in mouse xenograft models, and corresponding immunotoxins were able to inhibit tumor cell growth *in vitro*, supporting the use of SD1 as a therapeutic mAb.

Development Stage: Early Stage, *in vitro* data available, *in vivo* data available

Patent Status: U.S. Provisional Patent Application No. 61/706,396 filed 27 Sep 2012

POTENTIAL COMMERCIAL APPLICATIONS

- Therapeutic use in the treatment of mesothelin-expressing cancers as a stand-alone mAbs or as an mAb-drug conjugate (e.g., an immunotoxin)
- Diagnosis of mesothelin-expressing cancers
- Antibody-related research use, including immunoprecipitation, western blot analysis, immunohistochemistry, ELISA, etc.

COMPETITIVE ADVANTAGES

- Binding of a new epitope on mesothelin may improve therapeutic applications due to non-competition from serum proteins
- Human origin may significantly limit the formation of neutralizing antibodies, thereby increasing therapeutic potential of the mAb
- Ability to trigger both CDC and ADCC may elicit a more complete therapeutic response

INVENTOR(S)

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DEVELOPMENT STAGE

- Pre-clinical (in vivo)

PUBLICATIONS

1. Tang, Z., *et al.* *Mol Cancer Ther*, 2013 [PMID: [23371858](#)]
2. Hassan, R., *et al.* *Eur J Cancer*, 2008 [PMID: [17945478](#)]

PATENT STATUS

- U.S. Filed: 61/706,396 filed 27 Sep 2012

THERAPEUTIC AREA

- Cancer/Neoplasm