

## HIGH-AFFINITY RABBIT MONOCLONAL ANTIBODIES FOR CANCER TREATMENT

### SUMMARY

The National Cancer Institute, Laboratory of Molecular Biology seeks parties to co-develop monoclonal antibodies for the treatment of mesothelin-expressing cancers.

### REFERENCE NUMBER

E-198-2012

### PRODUCT TYPE

- Diagnostics
- Therapeutics

### KEYWORDS

- mesothelin
- epitope

### COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

### CONTACT

John D. Hewes  
NCI - National Cancer Institute  
240-276-5515

[John.Hewes@nih.gov](mailto:John.Hewes@nih.gov)

### DESCRIPTION OF TECHNOLOGY

Mesothelin is a cell surface protein that is highly expressed in aggressive cancers, such as malignant mesothelioma, ovarian cancer and pancreatic cancer, lung cancer, breast cancer, cholangiocarcinoma, bile duct carcinoma and gastric cancer. Because of this selective expression, mesothelin is an excellent candidate for targeted therapeutics, such as monoclonal antibodies (mAbs) and chimeric molecules. Current anti-mesothelin therapeutic mAb candidates bind to an epitope in Region I of mesothelin. Unfortunately, Region I contains the interaction site MUC16/CA125, a mesothelin-interacting protein that is present in the serum of patients with mesothelin-related cancers. Because the current therapeutic mAb candidates must compete with MUC16/CA125 for binding to mesothelin, they may not reach their full therapeutic potential due to interference.

NIH inventors generated several rabbit mAbs that recognize unique epitopes of mesothelin: (1) YP223, which recognizes region II; (2) YYP218, which recognizes region III; and (3) YP3 which recognizes a native conformation epitope of mesothelin. These mAbs bind to mesothelin with sub-nanomolar affinity and are

not out-competed for binding by the current anti-mesothelin therapeutic mAb candidates or MUC16/CA125. This strong binding affinity for an alternative binding site on mesothelin suggests that these mAbs are excellent therapeutic candidates.

### 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 new epitope on mesothelin may improve therapeutic applications due to non-competition from serum proteins
- High binding affinity (sub-nanomolar levels) also increases chances of binding and subsequent therapeutic activity

### INVENTOR(S)

[Mitchell Ho](#) (NCI)

### DEVELOPMENT STAGE

- Discovery (Lead Identification)

### PUBLICATIONS

- Hassan, R., *et al.* *Eur J Cancer*, 2008[PMID: [17945478](#)]

### PATENT STATUS

- **U.S. Issued:** U.S. Patent 9,409,992 (9 August 2016)

### THERAPEUTIC AREA

- Cancer/Neoplasm