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**Ho et al.**

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(54) **MESOTHELIN DOMAIN-SPECIFIC MONOCLONAL ANTIBODIES AND USE THEREOF**

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See application file for complete search history.

(71) Applicant: **The United States of America, as represented by the Secretary, Department of Health and Human Services, Washington, DC (US)**

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(72) Inventors: **Mitchell Ho, Urbana, MD (US); Ira H. Pastan, Potomac, MD (US); Yen T. Phung, Annandale, VA (US); Yifan Zhang, Haymarket, VA (US); Wei Gao, Rockville, MD (US); Raffit Hassan, Gaithersburg, MD (US)**

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(73) Assignee: **The United States of America, as represented by the Secretary, Department of Health and Human Services, Washington, DC (US)**

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(\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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*Primary Examiner* — Jessica H Roark  
(74) *Attorney, Agent, or Firm* — Klarquist Sparkman, LLP

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(57) **ABSTRACT**

Described herein is the use of rabbit hybridoma technology, along with a panel of truncated mesothelin domain fragments, to identify anti-mesothelin mAbs that bind specific regions of mesothelin. In one aspect of the present disclosure, the rabbit mAbs bind an epitope that is not part of Region I. In particular, the identified mAbs (YP187, YP223, YP218 and YP3) bind either Region II (391-486), Region III (487-581) or a native conformation of mesothelin with subnanomolar affinity. These antibodies do not compete for binding with the mesothelin-specific immunotoxin SS1P or mesothelin-specific antibody MORAb-009. In another aspect, disclosed is a high-affinity rabbit mAb that binds Region I of mesothelin (YP158). YP158 binds native mesothelin protein in cancer cells and tissues with high affinity and specificity.

(52) **U.S. Cl.**  
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**27 Claims, 15 Drawing Sheets**