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(54) Title: ORALLY DELIVERABLE AND ANTI-TOXIN ANTIBODIES AND METHODS FOR MAKING AND USING THEM

(57) Abstract: The invention provides antibodies with superior therapeutic efficacy and related methods of engineering such antibodies to increase their stability and resistance to proteases, e.g., in the digestive tract. Protease cleavage motifs are identified and subsequently modified to reduce or eliminate cleavage at that site. Methods of employing these orally deliverable antibodies as therapeutic compositions, particularly against gastrointestinal pathogens are also provided herein. In one aspect, the invention provides combinations of monoclonal antibodies, e.g., "synthetic polyclonals", that work synergistically to neutralize bacterial toxins, particularly enteric bacterial toxins such as Clostridium difficile toxin A.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/47100

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC: **A61K 39/395( 2006.01);C07K 16/00( 2006.01)**  
  
 USPC: **424/9.1,9.2,133.1;435/721;530/387.3**  
 According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**  
 Minimum documentation searched (classification system followed by classification symbols)  
 U.S. : 424/9.1, 9.2, 133.1; 435/721; 530/387.3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
 Sequence search of SEQ ID NOS: 1-6 in commercial protein sequence databases. See sequence search results in SCORE.

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 Please See Continuation Sheet

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,821,505 B2 (WARD) 23 November 2004 (23.11.2004) see abstract, Col. 2, line 30- Col. 6, line 60;	1, 2, 6-12, 14-21, 23-28, 31, 32, , 38, 39, 49, 51-60, 63-65, 70, 71, 75, 76, 79-86, 89-91, 95-99, 102-104, 108-111, 113, 114, 116-123, 125-130, 132, 140, 141, 146, 149, 151, 153-162, 164-167, 172, 173, 177, 181-185, 187 and 188

Further documents are listed in the continuation of Box C.  See patent family annex.

* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 19 December 2006 (19.12.2006)	Date of mailing of the international search report <b>08 JAN 2007</b>
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**INTERNATIONAL SEARCH REPORT**

International application No.

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Continuation of B. *FIELDS SEARCHED* Item 3:

Electronic databases searched: PubMed and WEST

Search terms: antibody and (catabolic or catabolism) and (protease site and protease cleavage site) and (enzymatic site or enzymatic cleavage site) and (intestine or intestinal) and (protease degradation)