

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
29 July 2004 (29.07.2004)

PCT

(10) International Publication Number  
WO 2004/063351 A3

- (51) International Patent Classification<sup>7</sup>: A61K 39/395, C07K 16/28
- (21) International Application Number: PCT/US2004/000643
- (22) International Filing Date: 9 January 2004 (09.01.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/439,498 9 January 2003 (09.01.2003) US  
60/456,041 19 March 2003 (19.03.2003) US  
60/514,549 23 October 2003 (23.10.2003) US
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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 31 March 2005
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IDENTIFICATION AND ENGINEERING OF ANTIBODIES WITH VARIANT Fc REGIONS AND METHODS OF USING SAME

(57) Abstract: The present invention relates to molecules, particularly polypeptides, more particularly immunoglobulins (e.g., antibodies), comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, which variant Fc region binds Fc $\gamma$ RIIIA and/or Fc $\gamma$ RIIA with a greater affinity, relative to a comparable molecule comprising the wild-type Fc region. The molecules of the invention are particularly useful in preventing, treating, or ameliorating one or more symptoms associated with a disease, disorder, or infection. The molecules of the invention are particularly useful for the treatment or prevention of a disease or disorder where an enhanced efficacy of effector cell function (e.g., ADCC) mediated by Fc $\gamma$ R is desired, e.g., cancer, infectious disease, and in enhancing the therapeutic efficacy of therapeutic antibodies the effect of which is mediated by ADCC.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/00643

<p>A. CLASSIFICATION OF SUBJECT MATTER</p> <p>IPC(7) : A61K 39/395 C07K 16/28</p> <p>US CL : 530/387.3, 388.22, 424/133.1, 143.1</p> <p>According to International Patent Classification (IPC) or to both national classification and IPC</p>												
<p>B. FIELDS SEARCHED</p> <p>Minimum documentation searched (classification system followed by classification symbols)</p> <p>U.S. : 530/387.3, 388.22, 424/133.1, 143.1</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)</p> <p>Please See Continuation Sheet</p>												
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>P,X</td> <td>US 2004/0002587 A1 (WATKINS et al) 01 January 2004 (01.01.2004), see pages 2, 21-22.</td> <td>1, 15, 40, 57-58, 60</td> </tr> <tr> <td>P,Y</td> <td>US 2004/0185045 A1 (KOENIG et al) 23 September 2004 (23.09.2004), see pages 3-8.</td> <td>165-173</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	P,X	US 2004/0002587 A1 (WATKINS et al) 01 January 2004 (01.01.2004), see pages 2, 21-22.	1, 15, 40, 57-58, 60	P,Y	US 2004/0185045 A1 (KOENIG et al) 23 September 2004 (23.09.2004), see pages 3-8.	165-173	
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C.      <input type="checkbox"/> See patent family annex.</p>												
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"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	
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<p>Date of the actual completion of the international search</p> <p>05 January 2005 (05.01.2005)</p>		<p>Date of mailing of the international search report</p> <p>02 FEB 2005</p>										
<p>Name and mailing address of the ISA/US</p> <p>Mail Stop PCT, Attn: ISA/US                  Commissioner for Patents                  P.O. Box 1450                  Alexandria, Virginia 22313-1450</p> <p>Facsimile No. (703)305-3230</p>		<p>Authorized officer <i>David J Blanchard</i></p> <p>David J Blanchard</p> <p>Telephone No. (571) 272-0827</p>										

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US04/00643

Continuation of B. FIELDS SEARCHED Item 3:

WEST, Medline, EMBASE, Cancerlit, CAPLUS, Biotechno, Biosis.

Search terms:Fc variant/mutant, Fc gammaRIIA, Fc gammaRIIB, CH2, CH3, autoimmune, infectious disease, cancer or tumor, Fc residues.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US04/00643

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

- 1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
- 2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
- 3.  Claims Nos.: 146-148  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

- 1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  - 2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  - 3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
  
  
  
  
  
  
  
  
  
  - 4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
- Remark on Protest**    The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.