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ning of each regular issue of the PCT Gazette.*

(54) Title: MODIFIED ANTI-TNF ALPHA ANTIBODY

(57) Abstract: The invention relates to the modification of antibodies reactive to human tumor necrosis factor alpha (TNF alpha) to result in anti-TNF alpha antibodies that are substantially non-immunogenic or less immunogenic than any non-modified parental antibody when used *in vivo*. The invention relates also to peptide molecules comprising T-cell epitopes of the V-regions of the parental antibody which are modified by amino acid alteration in order to reduce or eliminate said T-cell epitopes.



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INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/24 C07K16/46 C12N15/13 A61K39/395 C07K7/04

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)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, EMBASE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 92 16553 A (UNIV NEW YORK ;CENTOCOR INC (US)) 1 October 1992 (1992-10-01) page 10; examples 18-28 ---	2-31, 33-36
Y	US 2001/027249 A1 (DADDONA PETER ET AL) 4 October 2001 (2001-10-04) paragraph '0156! ---	2-31, 33-36
Y	WO 99 53038 A (GENENCOR INT) 21 October 1999 (1999-10-21) example 2 ---	2-31, 33-36
Y	EP 0 699 755 A (CENTRO IMMUNOLOGIA MOLECULAR) 6 March 1996 (1996-03-06) examples 1-6 --- -/--	2-31, 33-36

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
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- *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
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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 52976 A (BIOVATION LTD ;CARR FRANCIS J (GB)) 26 November 1998 (1998-11-26) page 27; examples 5,6 ----	2-31, 33-36
Y	WO 00 34317 A (ADAIR FIONA SUZANNE ;CARR FRANCIS JOSEPH (GB); HAMILTON ANITA ANNE) 15 June 2000 (2000-06-15) page 8 -page 9 ----	2-31, 33-36
P,Y	WO 02 12502 A (CENTOCOR INC) 14 February 2002 (2002-02-14) the whole document ----	2-31, 33-36
P,Y	WO 02 069232 A (MERCK PATENT GMBH ;CARTER GRAHAM (GB); JONES TIM (GB); CARR FRANCI) 6 September 2002 (2002-09-06) the whole document -----	2-31, 33-36

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/12566

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 1, 32
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:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1, 32

The scope of claim 1 is not clearly defined because the skilled person, in the possession of an antibody, is not able to determine whether said antibody has been modified in comparison to a possible parental antibody.

Present claim 32 relates to an extremely large number of possible peptides, especially because the wording "created from the primary sequence" includes the possibility of modifying the fragments. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the peptides. A meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been limited to the subject-matter defined by claim 33.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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