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(54) Title: HUMAN-ANTI-HUMAN CD3 BINDING MOLECULES

(57) Abstract: The present invention provides a method for the preparation of a human binding molecule, fragment or derivative thereof which specifically binds to the human CD3 complex. Furthermore, the invention provides a human binding molecules specifically binding to the human CD3 complex and means comprising said human binding molecules.



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INTERNATIONAL SEARCH REPORT

Intern: I Application No
PCT/EP2004/005684

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K16/28 A61K39/00

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, BIOSIS, WPI Data, EMBASE, MEDLINE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MALETZ KONSTANTIN ET AL: "Bispecific single-chain antibodies as effective tools for eliminating epithelial cancer cells from human stem cell preparations by redirected cell cytotoxicity" INTERNATIONAL JOURNAL OF CANCER, vol. 93, no. 3, 1 August 2001 (2001-08-01), pages 409-416, XP002301955 ISSN: 0020-7136 the whole document ----- -/--	1-20, 22-59

☒ 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
- "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)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

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- "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
- "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.
- "&" document member of the same patent family

Date of the actual completion of the international search

17 February 2005

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INTERNATIONAL SEARCH REPORT

Internat

Application No

PCT/EP2004/005684

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LOEFFLER ANJA ET AL: "A recombinant bispecific single-chain antibody, CD19 X CD3, induces rapid and high lymphoma-directed cytotoxicity by unstimulated T lymphocytes" BLOOD, vol. 95, no. 6, 15 March 2000 (2000-03-15), pages 2098-2103, XP002301956 ISSN: 0006-4971 the whole document -----	1-20, 22-59
X	GIL DIANA ET AL: "Recruitment of Nck by CD3epsilon reveals a ligand-induced conformational change essential for T cell receptor signaling and synapse formation" CELL, vol. 109, no. 7, 28 June 2002 (2002-06-28), pages 901-912, XP002301957 ISSN: 0092-8674 the whole document -----	1-20, 22-59
X	MASON D Y ET AL: "DETECTION OF T CELLS IN PARAFFIN WAX EMBEDDED TISSUE USING ANTIBODIES AGAINST A PEPTIDE SEQUENCE FROM THE CD3 ANTIGEN" JOURNAL OF CLINICAL PATHOLOGY (LONDON), vol. 42, no. 11, 1989, pages 1194-1200, XP009038551 ISSN: 0021-9746 the whole document -----	1-20, 22-59
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X	POPOV S ET AL: "A NOVEL AND EFFICIENT ROUTE FOR THE ISOLATION OF ANTIBODIES THAT RECOGNISE T CELL RECEPTOR VCHIS" MOLECULAR IMMUNOLOGY, ELMSFORD, NY, US, vol. 33, no. 6, April 1996 (1996-04), pages 493-502, XP001042150 ISSN: 0161-5890 the whole document -----	1-20, 22-59

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INTERNATIONAL SEARCH REPORT

Intern:

I Application No

PCT/EP2004/005684

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE EMBL EBI; Myosin-reactive immunoglobulin light variable 1 May 2000 (2000-05-01), WU: "Myosin-reactive immunoglobulin light variable region (fragment)" XP002318217 retrieved from EBI Database accession no. Q9UL77 abstract	1-20, 22-59
X	----- WO 93/11236 A (MEDICAL RESEARCH COUNCIL; CAMBRIDGE ANTIBODY TECHNOLOGY LIMITED) 10 June 1993 (1993-06-10) the whole document	1-20, 22-59
X	----- KREBS B ET AL: "RECOMBINANT HUMAN SINGLE CHAIN FV ANTIBODIES RECOGNIZING HUMAN INTERLEUKIN-6" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 273, no. 5, 30 January 1998 (1998-01-30), pages 2858-2865, XP002921461 ISSN: 0021-9258 the whole document	1-20, 22-59
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A	----- ALEGRE M L ET AL: "EFFECT OF A SINGLE AMINO ACID AA MUTATION IN THE FC PORTION OF A HUMANIZED OKT3 ON T CELL RESPONSES IN-VITRO" JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, vol. 2, no. 3, 1991, page 530, XP002318216 & 24TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF NEPHROLOGY (ASN), BALTIMORE, MARYLAND, USA, NOVEMBER ISSN: 1046-6673 the whole document	1-20, 22-59

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/005684

Box 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.: 21
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 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:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,
part additional fees are to be refunded.

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.:
1-20 (completely), 22-59 (partially)
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 II.2

Claims Nos.: 21

Present claim 21 relates to a compound identified by the screening methods of claims 1-20. The compound is according to the claim formulated as a pharmaceutical composition. The latter term has a technical meaning and it is for this reason that this Authority view this claim as a disideratum.

The claim covers all compoundshaving this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). Consequently, no search has been carried out for the claim.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20

Pertains to method claims for the preparation of a diverse number of human CD3 binding molecules. These molecules range from polypeptides in general to single anti-CD3 antibodies to antibodies with dual specificity .

2. claims: 22-59

Pertains to product claims for a diverse number of human CD3 binding molecules. These molecules range from single anti-CD3 antibodies to antibodies with dual specificity . The latter relates to 506 different sequences . Each of which being a distinct anti-body with dual specificity for CD3 and a further antigen.

INTERNATIONAL SEARCH REPORT

 Intern: II Application No
 PCT/EP2004/005684

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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