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With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
22 May 1998 (22.05.98)

(54) Title: ANTIBODIES AGAINST A COMPLEX OF CD4 AND A CHEMOKINE RECEPTOR DOMAIN, AND THEIR USE AGAINST HIV INFECTIONS

(57) Abstract

This invention is directed to monoclonal antibodies produced by using CD4-expressing T lymphocytes, such as peripheral blood mononuclear T cells, thymocytes, splenocytes and leukemia or lymphoma derived T cell line cells such as HPB-ALL or SUP-T as the immunogen in accordance with the protocols and screening procedures described. The monoclonal antibodies of the present invention are characterized by their ability to neutralize *in vitro* and *in vivo* primary isolates of Human Immunodeficiency Virus (HIV) and related immunodeficiency viruses. The antibodies are directed against a host cell antigen complex comprising CD4 protein in association with domains from chemokine receptors and have broad neutralizing activities against primary isolates from all clades of HIV type 1 (HIV-1) and primary isolates of HIV type 2 (HIV-2) and Simian Immunodeficiency Virus (SIV). The present invention is also directed to a method of selecting and producing such antibodies, hybridomas which secrete such antibodies, pharmaceutical compositions comprising such antibodies and methods for pre- and post-exposure prevention of immunodeficiency virus infection in primates, including humans, by such antibodies whose primary targets are CD4-expressing lymphocytes.

*(Referred to in PCT Gazette No. 14/1998, Section II)

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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 97/09449

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12P21/08 C07K16/28 C12N5/20 A61K39/395 C07K16/46
//C07K14/715,C07K16/10

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 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	M. SAMSON ET AL.: "Molecular cloning and functional expression of a new human CC-chemokine receptor gene." BIOCHEMISTRY, vol. 35, no. 11, 19 March 1996, USA, pages 3362-3367, XP002056369 cited in the application see abstract see figure 1 ---	1-62
A	EP 0 409 242 A (THE CALPIS FOOD INDUSTRY CO., LTD.) 23 January 1991 see the whole document ---	1-62
A	WO 94 15638 A (RAMOT UNIVERSITY AUTHORITY ETC.) 21 July 1994 see table II see claims ---	1-62
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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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

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Date of the actual completion of the international search
19 February 1998

Date of mailing of the international search report
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Authorized officer
Nooij, F

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inte: onal Application No
PCT/US 97/09449

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	H. DENG ET AL.: "Identification of a major co-receptor for primary isolates of HIV-1." NATURE, vol. 381, no. 6584, 20 June 1996, LONDON, GB, pages 661-666, XP002056370 cited in the application see page 662, right-hand column, line 26 - line 32 see figure 2B	1-62
P,A	A. TRKOLA ET AL.: "CD4-dependent, antibody-sensitive interactions between HIV-1 and its co-receptor CCR-5." NATURE, vol. 384, no. 6605, 14 November 1996, LONDON, GB, pages 184-187, XP002056371 see table 2	1-62
P,A	WO 96 41884 A (INSTITUT FRANCAIS DE RECHERCHE SCIENTIFIQUE ETC.) 27 December 1996 see examples see claims	1-62

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 97/09449

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. [X] Claims Nos.: 29-37
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 29-37 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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.:
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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte. onal Application No
PCT/US 97/09449

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 409242 A	23-01-91	JP 3053894 A	07-03-91
WO 9415638 A	21-07-94	AU 6080794 A	15-08-94
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