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*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: ANALYSIS OF HIV-1 CORECEPTOR USE IN THE CLINICAL CARE OF HIV-1-INFECTED PATIENTS

(57) Abstract: A change in viral tropism occurs in many HIV positive individuals over time and can be indicated by a shift in coreceptor use from CCR5 to CXCR4. The shift in coreceptor use to CXCR4 has been shown to correlate with increased disease progression. In patients undergoing HAART, the predominant populations of virus can be shifted back to CCR5- mediated entry after the CXCR4-specific strains have emerged. The present invention relates to a diagnostic method to monitor coreceptor use in the treatment of human immunodeficiency virus (HIV) infection. The present invention further relates to a diagnostic method applied to HIV-positive individuals undergoing HAART to monitor the suppression of CXCR4 specific strains. The diagnostic method can be used to assist in selecting antiretroviral therapy and to improve predictions of disease prognosis over time.



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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/29881

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/50 G01N33/569

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 G01N

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

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ESTE JA. ET AL.: "Shift of clinical human immunodeficiency virus type 1 isolates from X4 to R5 and prevention of emergence of the syncytium-inducing phenotype by blockade of CXCR4." J. VIROL., vol. 73, no. 7, July 1999 (1999-07), pages 5577-5585, XP002216448 page 5578, column 1 page 5582 -page 5584	1-17, 30-32
X	WO 99 14378 A (PAVLAKIS GN ET AL.) 25 March 1999 (1999-03-25) page 3, line 14 - line 26 page 5, line 12 - line 21 page 6, line 32 -page 7, line 10 claims 1,27,28	1-17, 30-32



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

"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

"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

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27.03.03

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/29881

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	PHILPOTT S. ET AL.: "Preferential suppression of CXCR4-specific strains of HIV-1 by antiviral therapy." J. CLIN. INVEST., vol. 107, no. 4, February 2001 (2001-02), pages 431-438, XP002216447 the whole document	1-17, 30-32
A	MOORE JP. ET AL.: "Co-receptors for HIV-1 entry." CURR. OPIN. IMMUNOL., vol. 9, 1997, pages 551-562, XP004313554 the whole document	
A	WODARZ D. ET AL.: "Defining CTL-induced pathology : implications for HIV." VIROLOGY, vol. 274, August 2000 (2000-08); pages 94-104, XP002216449 the whole document	
A	CALLAWAY DS. ET AL.: "Virus phenotype switching and disease progression in HIV-1 infection." PROC. R. SOC. LOND., vol. 266, 1999, pages 2523-2530, XP002216450 the whole document	
X	HOLTKAMP N. ET AL.: "Unexpected coreceptor usage of primary human immunodeficiency virus type 1 isolates from viremic patients under highly active antiretroviral therapy." J. INFECT. DIS., vol. 181, February 2000 (2000-02), pages 513-521, XP002231810 abstract page 517, column 1, paragraph 3 -column 2, last paragraph	20-29
X	CHAN S.Y. ET AL.: "V3 recombinants indicate a central role for CCR5 as a coreceptor in tissue infection by human immunodeficiency virus type 1." J. VIROL., vol. 73, no. 3, March 1999 (1999-03), pages 2350-2358, XP002231811 p. 2351-2352, paragraph 'Materials and Methods' abstract	33-53

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 01/29881

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 67429 A (UAB RESEARCH FOUNDATION) 29 December 1999 (1999-12-29) cited in the application claim 12; examples 3,4,7,10 ---	33-53
A	VERRIER F. ET AL.: "Role of the HIV type 1 glycoprotein 120 V3 loop in determining coreceptor usage." AIDS RES. HUM. RETROVIRUSES, vol. 15, no. 8, 1999, pages 731-743, XP002231812 the whole document ' ---	
P,A	WO 00 65356 A (BIO-TECH IMAGING, INC.) 2 November 2000 (2000-11-02) the whole document -----	

# INTERNATIONAL SEARCH REPORT

national application No.  
PCT/US 01/29881

## 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.: 1-17  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 18-19  
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.1

Although claims 1-17 can be considered as directed to a method of treatment of the human/animal body by surgery (due to the step of "obtaining a population of patient-derived acquired immunodeficiency virus"), the search has been carried out and based on the alleged effects of the compound/composition.

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## Continuation of Box I.1

Claims Nos.: 1-17

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

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## Continuation of Box I.2

Claims Nos.: 18-19

Present claims 18-19 relate to an extremely large number of possible products. In fact, the claims contain so many possible permutations and provisos that a lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has not been carried out for claims 18-19.

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

PCT/US 01/29881

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9914378	A	25-03-1999	AU 9495098 A WO 9914378 A2	05-04-1999 25-03-1999
WO 9967429	A	29-12-1999	AU 4827899 A EP 1088108 A1 WO 9967429 A1	10-01-2000 04-04-2001 29-12-1999
WO 0065356	A	02-11-2000	US 2002037498 A1 AU 4368800 A WO 0065356 A1	28-03-2002 10-11-2000 02-11-2000