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Declarations under Rule 4.17:

- as to the identity of the inventor (Rule 4.17(i)) for all designations
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- of inventorship (Rule 4.17(iv)) for US only

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

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29 December 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: INHIBITION OF HIV-1 REPLICATION BY DISRUPTION OF THE PROCESSING OF THE VIRAL CAPSID-SPACER PEPTIDE 1 PROTEIN

(57) Abstract: Inhibition of HIV-1 replication by disrupting the processing of the viral Gag capsid (CA) protein (p24) from the CA-spacer peptide 1 (SP1) protein precursor (p25) is disclosed. Amino acid sequences containing a mutation in the Gag p25 protein, with the mutation resulting in a decrease in the inhibition of processing of p25 to p24 by dimethylsuccinyl betulinic acid or dimethylsuccinyl betulin, polynucleotides encoding such mutated sequences and antibodies that selectively bind such mutated sequences are also included. Methods of inhibiting, inhibitory compounds and methods of discovering inhibitory compounds that target proteolytic processing of the HIV Gag protein are included. In one embodiment, such compounds inhibit the interaction of the HIV protease enzyme with Gag by binding to the Gag proteolytic cleavage site rather than to the protease enzyme. In another embodiment, viruses or recombinant proteins that contain mutations in the region of the Gag proteolytic cleavage site can be used in screening assays to identify compounds that target proteolytic processing.



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INTERNATIONAL SEARCH REPORT

International Application No. ~~11~~

PCT/US04/02393

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A01N 37/02, 37/06, 37/08, 37/10, 45/00; A61M 1/14; C12N 7/00; C12Q 1/70; G01N 33/53, 33/567
 US CL : 422/44; 435/5, 7.1, 7.2, 7.21, 7.24, 7.7, 7.9, 7.92, 235.1; 514/169, 530, 548, 557, 570, 572, 573

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)

U.S. : 422/44; 435/5, 7.1, 7.2, 7.21, 7.24, 7.7, 7.9, 7.92, 235.1; 514/169, 530, 548, 557, 570, 572, 573

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 practicable, search terms used)

West, Medline, Google Scholar

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Holz-Smith et al. "Role of Human Immunodeficiency Virus (HIV) Type 1 Envelope in the	1-8, 12, 13, and 17-22
---	Anti-HIV Activity of the Betulinic Acid Derivative IC9564" Antimicrobial Agents and	-----
Y	Chemotherapy, Vol. 45, No. 1 (January 2001), p. 60-66.	9-11, 14-16, and 23-41
X	Kashiwada et al. "3,28-Di-O-(dimethylsuccinyl)-betulin Isomers as Anti-HIV Agents"	1-8, 12, 13, and 17-22
---	Bioorganic & Medicinal Chemistry Letters 11 (2001) 183-185.	-----
Y		9-11, 14-16, and 23-41
X	Lee et al. "Recent advances in the discovery and development of plant-derived natural and	1-8, 12, 13, and 17-22
---	their analogs as anti-HIV agents" Pure Appl. Chem., Vol. 71, No. 6, (1999), pp. 1045-1051.	-----
Y		9-11, 14-16, and 23-41
Y	Fields. Fields Virology, 3rd edition, (Philadelphia, PA, Lippincott Williams & Wilkins, 1995), pp. 1882-1886. QR360.V5125.	1-41



Further documents are listed in the continuation of Box C.



See patent family 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 application or patent 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

28 September 2005 (28.09.2005)

Date of mailing of the international search report

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Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/02393

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.:
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:
Please See Continuation Sheet

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 additional fees, this Authority did not invite payment of any additional fees.
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.: 1-41
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 and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/02

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-22, drawn to a method of treating HIV infection by inhibiting processing of p25 to p24.

Group II, claims 23-28, drawn to a method for identifying compounds that inhibit HIV replication.

Group III, claims 29-34, drawn to a second method for identifying compounds that inhibit HIV replication.

Group IV, claim 35, drawn to a third method for identifying compounds that inhibit HIV replication.

Group V, claims 36-40, drawn to a fourth method for identifying compounds that inhibit HIV replication.

Group VI, claim 41, drawn to a fifth method for identifying compounds that inhibit HIV replication.

Group VII, claims 42-60, drawn to a polynucleotide encoding mutated p25, a vector, cell, virus, and method.

Group VIII, claims 61-63, 65, and 66, drawn to a polypeptide.

Group IX, claims 61, 64, and 66, drawn to a second polypeptide.

Group X, claims 67-69, drawn to an antibody that binds to SP1.

Group XI, claims 67 and 70, drawn to an antibody that binds to SEQ ID NOs 2 or 3 which includes the cleavage region (CA and SP1).

Group XII, claims 71 and 73, drawn to an antibody that binds SP1.

Group XIII, claims 72 and 73, drawn to an antibody that binds CA.

Group XIV, claims 74 and 75, drawn to a pharmaceutical composition comprising a compound that is not one of the enumerated compounds.

Group XV, claims 76-80, drawn to a pharmaceutical composition comprising a compound and further comprising an antiviral agent.

Group XVI, claim 81, drawn to a method of determining susceptibility to treatment.

The inventions listed as Groups I-XVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The technical feature of the claimed invention is a method of treating a patient by administering a compound that inhibits processing of gag. The specific compounds are