Title: PROTEIN-PROTEIN INTERACTIONS IN HUMAN IMMUNODEFICIENCY VIRUS

Abstract: The present invention relates to protein-protein interactions involved in AIDS. More specifically, the present invention relates to complexes of polypeptides or polynucleotides encoding the polypeptides, fragments of the polypeptides, antibodies to the complexes, selected Interacting Domains (SID®) which are identified due to the protein-protein interactions, methods for screening drugs of agents which modulate the interaction of proteins and pharmaceutical compositions that are capable of modulating the protein-protein interactions.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K/14/I6 C12N1S/10 C07K/16/00 A61K48/00 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 database consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, MEDLINE, SEQUENCE SEARCH, EMBASE, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<th>Category</th>
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<tr>
<td>Y</td>
<td>the whole document</td>
<td>1-4,6-26</td>
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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

**R** 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 novel or 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

**Z** document member of the same patent family

Date of the actual completion of the international search 10 July 2003

Date of mailing of the international search report 18.09.03

Name and mailing address of the ISA

European Patent Office, P.B. 5816 Patentbitsen 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, TX: 31 651 epo nl, Facs (+31-70) 340-3016

Authorized officer Pilat, D
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<td>Y</td>
<td>WO 00 66722 A (SHELIG LUC ; HYBRIDGENICS S A (FR); LEGRAND PIERRE (FR); RAJEAN JEAN CH) 9 November 2000 (2000-11-09) page 18, line 28 -page 21, line 18; claims</td>
<td>9-22</td>
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<td>Y</td>
<td>BENICHOU S ET AL: &quot;Use of the two-hybrid system to identify cellular partners of the HIV1 Nef protein.&quot; RESEARCH IN VIROLOGY, vol. 148, no. 1, 1997, pages 71-73, XP002247153 ISSN: 0923-2516 the whole document</td>
<td>1-4,6-26</td>
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Form PCT/ISA/210 (continuation of second sheet) (July 1999)
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<td>A</td>
<td>FIELDS S ET AL: &quot;THE TWO-HYBRID SYSTEM: AN ASSAY FOR PROTEIN-PROTEIN INTERACTIONS&quot; TRENDS IN GENETICS, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 10, no. 8, 1 August 1994 (1994-08-01), pages 286-292, XP000647708 ISSN: 0168-9525 abstract</td>
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<td>A</td>
<td>LEGRAIN P ET AL: &quot;Protein-protein interaction maps: a lead towards cellular functions&quot; TRENDS IN GENETICS, ELSEVIER, AMSTERDAM, NL, vol. 17, no. 6, 1 June 2001 (2001-06-01), pages 346-352, XP004249491 ISSN: 0168-9525</td>
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**INTERNATIONAL SEARCH REPORT**

**Box I**  Observations where certain claims were found unsearable (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.: 5 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:

- see additional 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 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.:

   1-26 partially

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: partially 1-26

A complex between HIV integrase and human VBPI, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of selected interaction domain (SID) or an interaction or a prey being human VBPI to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 38, 39, a SID polynucleotide SEQ ID N 15, 16, vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex. Use of siRNAs against human VBPI for the preparation of a medicament for treating HIV-1.

2. Claims: partially 1-26

A complex between HIV integrase and human TRN-SR, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of selected interaction domain (SID) or an interaction or a prey being human TRN-SR to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 40, a SID polynucleotide SEQ ID N 17, vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex. Use of siRNAs against human TRN-SR for the preparation of a medicament for treating HIV-1.

3. Claims: partially 1-26

A complex between HIV integrase and human RNUT1, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of selected interaction domain (SID) or an interaction or a prey being human RNUT1 to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 41, a SID polynucleotide SEQ ID N 18, vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex. Use of siRNAs against human RNUT1 for the preparation of a medicament for treating HIV-1.

4. Claims: partially 1-26

A complex between HIV integrase and human HBOA, a complex between two polynucleotides encoding said polypeptides, a
host cell containing a polynucleotide encoding one of said polypeptide, use of selected interaction domain (SID) or an interaction or a prey being human HBOA to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 42, 43, a SID polynucleotide SEQ ID N 19, 20 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex. Use of siRNAs against human HBOA for the preparation of a medicament for treating HIV-1.

5. Claims: partially 1-26

A complex between HIV integrase and human MCM7, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of selected interaction domain (SID) or an interaction or a prey being human MCM7 to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 44, a SID polynucleotide SEQ ID N 21, vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex. Use of siRNAs against human MCM7 for the preparation of a medicament for treating HIV-1.

6. Claims: partially 1-26

A complex between HIV integrase and human EIF3S3, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of selected interaction domain (SID) or an interaction or a prey being human EIF3S3 to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 45, 46 a SID polynucleotide SEQ ID N 22, 23 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex. Use of siRNAs against human EIF3S3 for the preparation of a medicament for treating HIV-1.

7. Claims: partially 1-26

A complex between HIV integrase and human PIASY, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of selected interaction domain (SID) or an interaction or a prey being human PIASY to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 47 a SID polynucleotide SEQ ID N 24 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors.
Antibodies specifically binding to said complex.

8. Claims: partially 1-26

A complex between HIV reverse transcriptase and a binding partner, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of selected interaction domain (SID) or an interaction or a prey being said binding partner to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 48, 49 a SID polynucleotide SEQ ID N 25, 26 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex.

9. Claims: partially 1-26

A complex between a HIV protease and a binding partner, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of a selected interaction domain (SID) or an interaction or a prey of said binding partner to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 50-53 a SID polynucleotide SEQ ID N 27-30 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex.

10. Claims: partially 1-26

A complex between a HIV gag polypeptide and a binding partner, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of a selected interaction domain (SID) or an interaction or a prey of said binding partner to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 54 a SID polynucleotide SEQ ID N 31 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex.

11. Claims: partially 1-26

A complex between a HIV gag polypeptide and a binding partner, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of a selected interaction domain (SID) or an interaction or a prey of said
binding partner to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 54, 55 a SID polynucleotide SEQ ID N 31, 32 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex.

12. Claims: partially 1-26

A complex between a HIV envelope protein and a binding partner, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of a selected interaction domain (SID) or an interaction or a prey of said binding partner to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 56, 57 a SID polynucleotide SEQ ID N 33, 34 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex.

13. Claims: partially 1-26

A complex between a HIV vpu and a binding partner, a complex between two polynucleotides encoding said polypeptides, a host cell containing a polynucleotide encoding one of said polypeptide, use of a selected interaction domain (SID) or an interaction or a prey of said binding partner to screen molecules that inhibit human immunodeficiency virus. A SID polypeptide comprising SEQ ID N 58–60 a SID polynucleotide SEQ ID N 35–37 vectors, fragments and variants thereof, compositions comprising the same and host cell containing said vectors. Antibodies specifically binding to said complex.
Continuation of Box I.2

Claims Nos.: 5

Present claims 5 relate to a compound defined by reference to a desirable characteristic or property, namely inhibiting human immunodeficiency virus obtained by the method of claim 4.

The claims cover all compounds having 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 only a very limited number of 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). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds as identified in table 2 column 4.

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.
<table>
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<td>US 6222024 B1</td>
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