The invention provides an isolated nucleic acid encoding a TRIM - cyclophilin A fusion sequence encoding a TRIMcyc fusion protein which is active as an anti-viral agent, and in particular an anti-HIV-1 agent. The invention provides for a nucleic acid encoding a polypeptide having both TRIM activity and cyclophilin activity. The invention provides for an isolated polynucleotide encoding a TRIM-cyclophilin fusion protein, or variants thereof retaining the TRIM and cyclophilin activities. The invention provides for compositions thereof, antibodies that specifically bind thereto, and vectors and host cells comprising the nucleic acid or polypeptide. In addition, the invention provides for methods for treating or preventing viral infection, or reducing viral load in a subject comprising administering the nucleic acid, polypeptide, vector, or composition to the subject in an amount effective to treat or prevent the viral infection. In some embodiments, the viral infection is HIV-1 infection, hepatitis C infection, pox virus infection, vaccinia virus infection, or HTLV infection.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
   IPC(8): C07H 21/02( 2006.01);A61K 39/00( 2006.01);C12N 5/00( 2006.01)
   USPC: 536/23.1;530/300;424/320.1
   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.: 536/23.1; 530/300; 424/320.1

   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)
   DB=PGPB,USPT,USOC,EPAB,JPAB,DWP,TDDB

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Strömlau M et al &quot;The cytoplasmic body component TRIM5 restricts HIV-1 infection in Old World monkeys&quot; Nature 427, 848-853 (26 February 2004)</td>
<td>1-44</td>
</tr>
</tbody>
</table>

☐ 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 involved in 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
13 April 2008 (13.04.2008)

Date of mailing of the international search report
29 APR 2008

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer
BO PENG
Telephone No. 271-272-0000
**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

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<table>
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<tr>
<td>1.</td>
<td>□ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.</td>
</tr>
<tr>
<td>2.</td>
<td>□ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.</td>
</tr>
<tr>
<td>3.</td>
<td>□ 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.:</td>
</tr>
</tbody>
</table>

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**

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<td>□</td>
<td>The additional search fees were accompanied by the applicant’s protest and, where applicable, the payment of a protest fee.</td>
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<tr>
<td>□</td>
<td>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.</td>
</tr>
<tr>
<td>□</td>
<td>No protest accompanied the payment of additional search fees.</td>
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</tbody>
</table>
BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group I, claim(s) 1-7, 11-14, 18-23, 25, 26, 28, 36-39, 41, 42 and 43, insofar as drawn to the special technical feature of an isolated nucleic acid molecule, vector, a host cell, comprising genes of TRIM-Cyp and variants, and the first method of using the product: a method of treating a subject suffering from a disease using a nucleic acid molecule of TRIM-Cyp and variants.

Group II, claim(s) 8-10, 25, 35, 38, 39, 42 and 43, insofar as drawn to the special technical feature of an isolated polypeptide of TRIM-Cyp and variants.

Group III, claim(s) 15-17, drawn to the special technical feature of a purified antibody that binds to TRIM50 and its variants.

Group IV, claim(s) 24, drawn to the special technical feature of a method for preparing a pharmaceutical composition comprising admixing polypeptides of TRIM50 and its variants.

Group V, claim(s) 26-36, 37 and 41, insofar as drawn to the special technical feature of a method of treating a subject suffering from a disease using a polypeptide of TRIM-Cyp and variants.

Group VI, claim(s) 28 and 37, insofar as drawn to the special technical feature of a method of preventing retroviral infection of a subject using a nucleic acid molecule of TRIM-Cyp and variants.

Group VII, claim(s) 28-36 and 37, insofar as drawn to the special technical feature of a method of preventing retroviral infection of a subject using a polypeptide of TRIM-Cyp and variants.

Group VIII, claim(s) 40, drawn to the special technical feature of a method of ex vivo gene therapy using a nucleic acid molecule of TRIM-Cyp and variants.

Group IX, claim(s) 44, drawn to the special technical feature of a method for reducing transposition events in a genome of a cell using nucleic acid molecule or protein of TRIM-Cyp and variants.