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60/995,708 26 September 2007 (26.09.2007) US(71) Applicant (for all designated States except US): **DANA-FARBER CANCER INSTITUTE, INC.** [US/US]; 44 Binney Street, Boston, Massachusetts 02115 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **REINHERZ, Ellis L.** [US/US]; 113 South Great Road, Lincoln, Massachusetts 01773 (US).(74) Agents: **MACPHAIL, Stuart** et al.; Fish & Richardson P.C., P.O. Box 1022, Minneapolis, Minnesota 55440-1022 (US).

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3 September 2009

(54) Title: REAGENTS FOR INDUCING AN IMMUNE RESPONSE

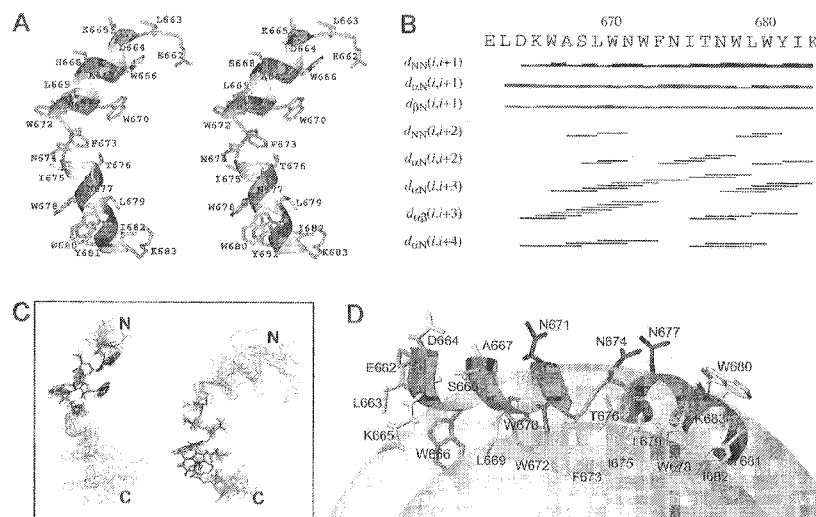


FIG. 1

(57) Abstract: The present disclosure relates to reagents (antigenic and/or immunogenic reagents) and kits that are useful in a variety of in vitro, in vivo, and ex vivo methods including, e.g., methods for inducing an immune response, or for generating an antibody, in a subject. The reagents described herein can be used in the treatment or prevention of HIV-1 infections. In addition, the disclosure provides methods and compositions useful for designing (or identifying) an agent that binds to a membrane proximal external region (MPER) of an HIV-1 gp160 polypeptide or an agent that inhibits the fusion of an HIV-1 particle to a cell.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/77916

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/00; A61K 9/16 (2009.01)

USPC - 530/324; 424/490

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(8) - A61K 38/00; A61K 9/16 (2009.01)

USPC - 530/324; 424/490

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 435/5, 435/69.1, 530/350, 424/283.1 - see keyword below

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST(USPT,PGPB,EPAB,JPAB); Medline, Google: HIV-1, gp160, membrane proximal external region (MPER), lipid, amino acid, nanoparticle, lipid bilayer, immune response, inducing, immunogen, surface, microorganism, container, composition, ingredient, label, mammal, instruction

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---	ZWICK. The membrane-proximal external region of HIV-1 gp41: a vaccine target worth exploring. AIDS 2005, 19:1725-1737; pg 1725, col 1, para 1, and col 2; pg 1726, col 2, last para, and Fig 1; pg 1727, col 2, para 2; pg 1728, Fig 2; pg 1729, col 2, mid and last para; pg 1730, col 2, last para; pg 1732, col 1, top para, and col 2, top and mid para; and pg 1733, col 1, top para	1-3, 51-53, 68-70, 85, 88
Y		48, 86-87
Y	US 2007/0014804 A1 (BURKHARD) 18 Jan 2007 (18.01.2007); para [0002], [0090], [0095]	48
Y	CN 1810830A (WANG et al.) 02 Aug 2006 (02.08.2006); Abstract and pg 10, SEQ ID NO: 2	86-87

☐ Further documents are listed in the continuation of Box C.

* 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 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

30 June 2009 (30.06.2009)

Date of mailing of the international search report

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Name and mailing address of the ISA/US

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Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/77916

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.: 4-47, 49-50, 54-67, 71, 76-83, 92-95
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:

Group I: claims 1-3, 48, 51-53, 68-70, 85-88, drawn to a reagent comprising:

- a particle encapsulated in lipid; and
- a polypeptide comprising a membrane proximal external region (MPER) of an HIV-1 gp160 polypeptide,
-- wherein at least one amino acid residue of the MPER is embedded in the lipid, and methods of using said reagent.

Group II, claims 72-75, drawn to a method comprising:

- providing a three-dimensional model of a composition comprising a membrane proximal external region (MPER) of an HIV-1 gp160 polypeptide and lipid; and
- performing computer fitting analysis to design an agent that interacts with the MPER.

*****Continued in extra 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 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.:
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.:
1-3, 48, 51-53, 68-70, 85-88

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.

***** SUPPLEMENTAL BOX *****

Continuation of: Box No III (unity of invention is lacking)

Group III, claim 84, drawn to a method comprising:

- generating a three dimensional model of a composition,
 - wherein the composition comprises lipid and a membrane proximal external region (MPER) of an HIV-1 gp160 polypeptide and
 - wherein at least one amino acid of the MPER is embedded in the lipid;
- employing the three-dimensional model to design or select a potential inhibitor of the binding of an HIV-1 particle to a cell; and
- synthesizing or obtaining the potential inhibitor.

Group IV: claims 89-91, drawn to a method comprising:

- providing a composition comprising lipid and an MPER of an HIV-I gp160 polypeptide,
 - wherein one or more amino acids of the MPER are embedded in the lipid;
- contacting the composition with a candidate agent; and
- detecting whether one or more amino acids of the MPER are extracted from the lipid.

The inventions listed as Groups I-IV 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:

Group I includes neither the inventive concept of employing the three-dimensional model to design or select a potential inhibitor of the binding of an HIV-1 particle to a cell, as required by Groups II and III, nor identifying an agent capable of extracting one or more amino acid residues of a MPER of an HIV gp160 polypeptide from lipid, as required by Group IV.

Groups II and III do not include the inventive concept of identifying an agent capable of extracting one or more amino acid residues of a MPER of an HIV gp160 polypeptide from lipid, as required by Group IV.

Group II do not include the inventive concept of synthesizing or obtaining the potential inhibitor, as required by Group III.

Groups I-IV share the technical feature of a polypeptide comprising a membrane proximal external region (MPER) of an HIV-I gp160 polypeptide, wherein at least one amino acid residue of the MPER is embedded in the lipid. However, this shared technical feature is obvious over the prior art. Specifically, a paper entitled "The membrane-proximal external region of HIV-1 gp41: a vaccine target worth exploring" by Zwick (AIDS 2005, 19:1725?1737) discloses that human monoclonal antibodies capable of neutralizing primary HIV-1 "recognize neighboring sites on the conserved membrane proximal external region (MPER) on gp41, defined roughly as residues 660 to 683 of HIV-1 gp160" (pg pg 1725, col 2). Zwick further explains that the MPER is not particularly antigenic on viral particles... If a subunit, or epitope-targeted vaccine approach is used, the MPER will most likely need to be constrained. The epitopes of 2F5, Z13 and 4E10, as well as potentially undiscovered neutralizing epitopes on the MPER, must also be presented so as to be accessible by the BCR, perhaps on a membrane surface or grafted into a protein, but in such a way as to limit the angle of approach of the antibodies to that which is permissible with respect to the cognate epitope on the virus (pg 1732, col 2). As the above MPER of an HIV-I gp160 polypeptide, having at least one amino acid residue embedded in the lipid, was obvious at the time of the invention, as evidenced by the teaching of Zwick, this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I-IV therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.