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Published:

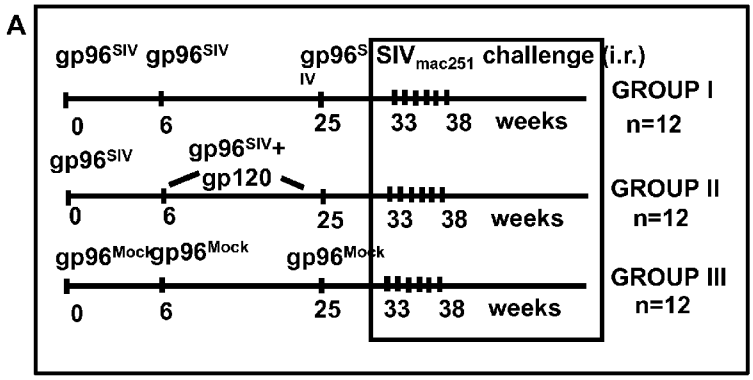
— *with international search report (Art. 21(3))*

[Continued on next page]

(54) **Title**: COMBINED CELL BASED GP96-IG-SIV/HIV, RECOMBINANT GP120 PROTEIN VACCINATION FOR PROTECTION FROM SIV/HIV

(57) **Abstract**: Compositions are provided comprising heat shock protein, immunoglobulins and retroviral antigens to induce systemic and mucosal immunity to infection from retroviruses such as Human Immunodeficiency Virus (HIV). Methods of treatment provided comprise administration of the compositions, which boost the immune systems response to the retroviral antigens or immunogens.

Figures 1A



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26 October 2012

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/26256

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/00 (2012.01)
USPC - 424/192.1, 278.1
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)
IPC(8) - A61K 39/00 (2012.01)
USPC - 424/192.1, 278.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 424/184.1

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWest (PGPB,USPT,USOC,EPAB,JPAB); PubMed (MEDLINE)
virus, vaccine, heat shock, chaperone, immunoglobulin, carrier

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 6,797,491 B2 (NEEFE et al.) 28 September 2004 (28.09.2004) col 1, ln 58 - col 2, ln 14; col 3, ln 29-46; col 4, ln 12-27; col 4, ln 28 - 67; col 5, ln 58 - grp94; col 6, ln 1-10; col 7, ln 57 - col 8 ln 15; col 12, ln 13-18; col 12, ln 48	1-7 --- 8-13
Y	US 2004/0052812 A1 (HOE et al.) 18 March 2004 (18.03.2004) para [0015], [0031], [0032], [0039]	8-13
A	US 2009/0148471 A1 (WU et al.) 11 June 2009 (11.06.2009)	1-13

☐ 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	Date of mailing of the international search report
18 July 2012 (18.07.2012)	03 AUG 2012
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: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/26256

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:
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 1-13, directed to a composition for generating viral antigen specific immune responses in vitro or in vivo, comprising a vaccine molecule having a first domain comprising at least one adjuvant or antigen carrier wherein the adjuvant or antigen carrier is a heat shock protein and an immunoglobulin, or nucleic acids encoding the heat shock protein and immunoglobulin, and, a second domain comprising at least one viral molecule.

- Please see extra sheet for continuation -

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.:
1-13

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.

Continuation of Box III: Lack of Unity of Invention

Group II: claims 14-25, directed to An isolated cell comprising a vector expressing a vaccine molecule having a first domain comprising at least one adjuvant or antigen carrier wherein the adjuvant or antigen carrier is a heat shock protein and an immunoglobulin, or nucleic acids encoding the heat shock protein and immunoglobulin, and, a second domain comprising at least one viral molecule.

Group III: claims 26-31, directed to a vaccine comprising a plurality of cells expressing an adjuvant comprising a heat shock protein (hsp) and immunoglobulin (Ig) and, one or more retroviral molecules wherein the one or more retroviral molecules comprise Gag, Tat, Rev, Nef, and gp160 or fragments thereof.

Group IV: claims 32-42, directed to a method of inducing an antigen-specific immune response against a virus in a subject, the method comprising: a) administering to the subject an adjuvant composition comprising a host cell expressing a secretable vaccine molecule having a first domain comprising at least one adjuvant or antigen carrier wherein the adjuvant or antigen carrier is a heat shock protein and an immunoglobulin, and a second domain comprising at least one viral molecule; b) administering a viral immunogen; and c) inducing an antigen-specific immune response against a virus in a subject.

Group V: claims 43-49, directed to a method of preventing or treating a retroviral infection in a subject comprising administering a therapeutically effective amount of a composition comprising: a host cell expressing a vaccine molecule having a first domain comprising at least one adjuvant or antigen carrier wherein the adjuvant or antigen carrier is a heat shock protein and an immunoglobulin, and, a second domain comprising at least one viral molecule; administering a viral immunogen; and, inducing an antigen-specific immune response against a virus in a subject.

The inventions listed as Groups I - V 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 special technical feature of the claims of Groups I-V are indicated above in the Group descriptions.

The only common technical element shared by all of the above groups is that they are related to a conjugate or fusion of a heat-shock protein adjuvant and a viral antigen. Groups II and III share the further common technical element of being related to cells expressing the fusion protein. Groups IV and V share the further common technical element of being related to method of preventing or treating an infection in a subject, comprising administering a composition comprising the hsp-adjuvant/viral protein conjugate or fusion or a vector encoding said fusion to a subject to produce an antigen-specific immune response. These common technical elements do not represent an improvement over the prior art of US 6,797,491 B2 to Neefe et al. (hereinafter 'Neefe') discloses a composition for generating viral antigen specific immune responses in vitro or in vivo (col 3, ln 29-46; col 4, ln 12-27), comprising a vaccine molecule (col 12, ln 13-18; composition administered intravenously or intramuscularly) having a first domain comprising at least one adjuvant or antigen carrier wherein the adjuvant or antigen carrier is a heat shock protein, or nucleic acids encoding the heat shock protein and immunoglobulin (col 1, ln 58 - col 2, ln 14; component (1) containing an HSP or immunostimulatory fragment thereof (col 7, ln 57 - col 8 ln 15 - the "third" protein can also be an immunoglobulin Fc domain); and a second domain comprising at least one viral molecule (col 1, ln 58 - col 2, ln 14; component (2) containing an HPV protein or antigenic fragment thereof). Neefe further discloses wherein said first domain and second domain may be joined by conjugation from nucleic acids or from protein conjugates (col 4, ln 12-67). Neefe further discloses wherein said conjugate composition, comprising two components, may further comprise a third component comprising an immunoglobulin Fc domain protein (col 7, ln 57 - col 8 ln 15). Neefe further discloses wherein said second domain may comprise at least one viral molecule (col 1, ln 58 - col 2, ln 14; component (2) containing an HPV protein or antigentic fragment thereof), and cells which recombinantly produce the heat shock proteins and viral antigen fusion molecules (col 6, ln 67 - col 7, ln 16). Neefe further discloses administration of the fusion protein or a vector encoding said protein to a subject (col 11, ln 25 - col 12, ln 18), to produce an antigen-specific immune response (the immune response elicited by the composition against the HPV antigen included in, for example, the fusion protein or protein conjugate; col 12, ln 19-45).

Therefore, the inventions of Groups I-V lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.