Title: RAPID, EFFICIENT PURIFICATION OF HSV-SPECIFIC T-LYMPHOCYTES AND HSV ANTIGENS IDENTIFIED VIA SAME

Abstract: Described is a method of identifying an immunologically active antigen of a virus that attacks skin, as well as a method of enriching a population of lymphocytes for T lymphocytes that are specific to a virus that attacks skin. Also provided are HSV antigens and epitopes that are useful for the prevention and treatment of HSV infection that have been identified via the methods of the invention. T-cells having specificity for antigens of the invention have demonstrated cytotoxic activity against cells loaded with virally-encoded peptide epitopes, and in many cases, against cells infected with HSV. The identification of immunogenic antigens responsible for T-cell specificity provides improved anti-viral therapeutic and prophylactic strategies. Compositions containing antigens or polynucleotides encoding antigens of the invention provide effectively targeted vaccines for prevention and treatment of HSV infection.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/68
US CL. : 435/6
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. : 435/6

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)
Please See Continuation Sheet

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>Y</td>
<td>WO 01/23414 A2 (UNIVERSITY OF WASHINGTON) 05 April 2001 (05.04.2001), see the claims 32-40.</td>
<td>1-6</td>
</tr>
<tr>
<td>Y</td>
<td>MARRIOTT et al. Rapid reconstitution of Epstein-Barr virus-specific T lymphocytes following allogeneic stem cell transplantation. Immunology. 15 October 2000, Vol. 96, No. 8, pages 2814-2821, see the entire document.</td>
<td>1-6</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories are listed of cited documents:
  * "T" 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" 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

Date of the actual completion of the international search 27 February 2004 (27.02.2004)
Date of mailing of the international search report 30 MAR 2004

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. (703)305-3230

Authorized officer
A R Salimi
Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)
<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>
</table>
### INTERNATIONAL SEARCH REPORT

**Box I  Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim 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. ☐ Claim 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:
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 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.: 1-6

**Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant’s protest.
- ☐ No protest accompanied the payment of additional search fees.
BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

The inventions listed as Groups I-VIII do not relate to a single 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 invention of Group I is known in the prior art as evidence by University of Washington (WO 01/23414 A2), wherein the reference teaches a general method of identifying immunogenic epitopes (see claims 32-40). The cited evidence prove that the technical feature of Group I does not make a contribution over the prior art. Thus, the claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the sequences listed confer different structure and presumably different immune response.

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, claim(s) 1-6, drawn to a method of identifying active antigen.

Group II, claim(s) 7-12, 33, 35, drawn to pharmaceutical composition comprising a herpes simplex virus (SEQ ID NO: 7), and method of use.

Group III, claim(s) 13-19, 34, 36, drawn to polynucleotide that encodes an amino acid sequence SEQ ID NO: 7, and method of use.

Group IV, claim(s) 20-23, drawn to genetically recombinant virus expressing SEQ ID NO: 7.

Group V, claim(s) 24-31, drawn to method of producing immune cells directed against HSV cells presenting SEQ ID NO: 7.

Group VI, claim(s) 32, drawn to method of enhancing proliferation of HSV specific T cells.

Group VII, claim(s) 37, drawn to method of treating or preventing an HSV infection.

Group VIII, claim(s) 38, drawn to method of enriching a population of T cells specific to a virus.

Groups II-VIII contain claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12 (Total Species 5)

The claims are deemed to correspond to the species listed above in the following manner:

Claims 7-12, 33, 35, 13-19, 34, 36, 20-23, and 24-31 are directed to sequences that are isolated and can be utilized in induction of immune response.
Continuation of B. FIELDS SEARCHED Item 3:
MEDLINE, DERWENT, IPA, EPA, NPL, CAPLUS

search terms: CTL, herpes?, HSV, CLA, pox virus, papillomavirus, skin