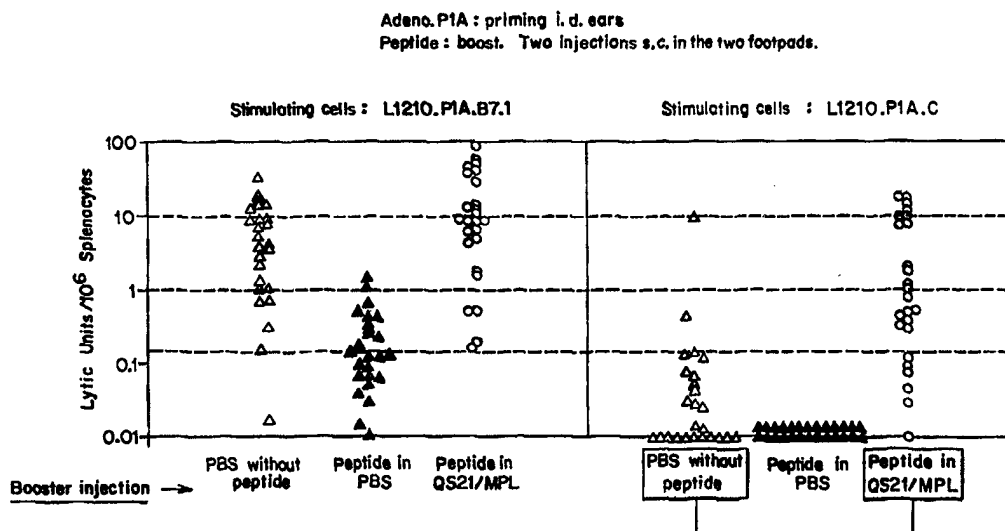




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>6</sup> : <b>C12N 15/12, A61K 48/00</b></p>	<p><b>A3</b></p>	<p>(11) International Publication Number: <b>WO 98/58956</b> (43) International Publication Date: 30 December 1998 (30.12.98)</p>
<p>(21) International Application Number: PCT/US98/12894 (22) International Filing Date: 19 June 1998 (19.06.98) (30) Priority Data: 08/880,979 23 June 1997 (23.06.97) US (71) Applicant: LUDWIG INSTITUTE FOR CANCER RESEARCH [CH/US]; 605 Third Avenue, New York, NY 10158 (US). (72) Inventors: WARNIER, Guy; Institute Ludwig pour la Recherche sur le Cancer, Avenue Hippocrate 74, UCL 7459, B-1200 Brussels (BE). UYTENHOVE, Catherine; Institute Ludwig pour la Recherche sur le Cancer, Avenue Hippocrate 74, UCL 7459, B-1200 Brussels (BE). BOON-FALLEUR, Thierry; Institute Ludwig pour la Recherche sur le Cancer, Avenue Hippocrate 74, UCL 7459, B-1200 Brussels (BE). (74) Agent: VAN AMSTERDAM, John, R.; Wolf, Greenfield &amp; Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).</p>		<p>(81) Designated States: AU, CA, CN, JP, KR, NZ, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). <b>Published</b> <i>With international search report.</i> (88) Date of publication of the international search report: 18 March 1999 (18.03.99)</p>

(54) Title: METHODS FOR INDUCING AN IMMUNE RESPONSE INVOLVING PRIME-BOOST PROTOCOLS



(57) Abstract

This invention relates to improved methods for modulating an immune response against an antigen using adenoviruses which express the antigen for priming immunization and antigen peptides for booster immunizations. Preferably the peptides are combined with QS21/MPL adjuvant. In particular, immunization methods for tumor antigens are provided. Kits for immunization are also provided.

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

<b>AL</b>	Albania	<b>ES</b>	Spain	<b>LS</b>	Lesotho	<b>SI</b>	Slovenia
<b>AM</b>	Armenia	<b>FI</b>	Finland	<b>LT</b>	Lithuania	<b>SK</b>	Slovakia
<b>AT</b>	Austria	<b>FR</b>	France	<b>LU</b>	Luxembourg	<b>SN</b>	Senegal
<b>AU</b>	Australia	<b>GA</b>	Gabon	<b>LV</b>	Latvia	<b>SZ</b>	Swaziland
<b>AZ</b>	Azerbaijan	<b>GB</b>	United Kingdom	<b>MC</b>	Monaco	<b>TD</b>	Chad
<b>BA</b>	Bosnia and Herzegovina	<b>GE</b>	Georgia	<b>MD</b>	Republic of Moldova	<b>TG</b>	Togo
<b>BB</b>	Barbados	<b>GH</b>	Ghana	<b>MG</b>	Madagascar	<b>TJ</b>	Tajikistan
<b>BE</b>	Belgium	<b>GN</b>	Guinea	<b>MK</b>	The former Yugoslav Republic of Macedonia	<b>TM</b>	Turkmenistan
<b>BF</b>	Burkina Faso	<b>GR</b>	Greece	<b>ML</b>	Mali	<b>TR</b>	Turkey
<b>BG</b>	Bulgaria	<b>HU</b>	Hungary	<b>MN</b>	Mongolia	<b>TT</b>	Trinidad and Tobago
<b>BJ</b>	Benin	<b>IE</b>	Ireland	<b>MR</b>	Mauritania	<b>UA</b>	Ukraine
<b>BR</b>	Brazil	<b>IL</b>	Israel	<b>MW</b>	Malawi	<b>UG</b>	Uganda
<b>BY</b>	Belarus	<b>IS</b>	Iceland	<b>MX</b>	Mexico	<b>US</b>	United States of America
<b>CA</b>	Canada	<b>IT</b>	Italy	<b>NE</b>	Niger	<b>UZ</b>	Uzbekistan
<b>CF</b>	Central African Republic	<b>JP</b>	Japan	<b>NL</b>	Netherlands	<b>VN</b>	Viet Nam
<b>CG</b>	Congo	<b>KE</b>	Kenya	<b>NO</b>	Norway	<b>YU</b>	Yugoslavia
<b>CH</b>	Switzerland	<b>KG</b>	Kyrgyzstan	<b>NZ</b>	New Zealand	<b>ZW</b>	Zimbabwe
<b>CI</b>	Côte d'Ivoire	<b>KP</b>	Democratic People's Republic of Korea	<b>PL</b>	Poland		
<b>CM</b>	Cameroon	<b>KR</b>	Republic of Korea	<b>PT</b>	Portugal		
<b>CN</b>	China	<b>KZ</b>	Kazakstan	<b>RO</b>	Romania		
<b>CU</b>	Cuba	<b>LC</b>	Saint Lucia	<b>RU</b>	Russian Federation		
<b>CZ</b>	Czech Republic	<b>LI</b>	Liechtenstein	<b>SD</b>	Sudan		
<b>DE</b>	Germany	<b>LK</b>	Sri Lanka	<b>SE</b>	Sweden		
<b>DK</b>	Denmark	<b>LR</b>	Liberia	<b>SG</b>	Singapore		
<b>EE</b>	Estonia						

## INTERNATIONAL SEARCH REPORT

International Application No

PC, JS 98/12894

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 6 C12N15/12 A61K48/00

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 6 A61K

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 practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WARNIER G ET AL: "Induction of a cytolytic T-cell response in mice with a recombinant adenovirus coding for tumor antigen P815A."            INTERNATIONAL JOURNAL OF CANCER, (1996 JUL 17) 67 (2) 303-10. JOURNAL CODE: GQU.            ISSN: 0020-7136., UNITED STATES, XP002079472            see the whole document            and note especially comments on page 307,            in paragraphs 3 and 6            ---            -/--</p>	1-14, 25-32

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

- \*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

2 October 1998

Date of mailing of the international search report

30 December 1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

SITCH, D

## INTERNATIONAL SEARCH REPORT

International Application No

PC./US 98/12894

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ZHAI Y ET AL: "Cloning and characterization of the genes encoding the murine homologues of the human melanoma antigens MART1 and gp100."            JOURNAL OF IMMUNOTHERAPY, (1997 JAN) 20 (1) 15-25. JOURNAL CODE: CUQ., UNITED STATES, XP002036182            see page 15            see abstract</p>	1-14, 25-32
A	<p>FRANCHINI ET AL: "Highly Attenuated HIV Type 2 Recombinant Poxviruses, but Not HIV-2 Recombinant Salmonella Vaccines, Induce Long-Lasting Protection in Rhesus Macaques"            AIDS RESEARCH AND HUMAN RETROVIRUSES, vol. 11, 1995, pages 909-920, XP002079473            see page 909            see abstract</p>	1-14, 25-32
A	<p>PIALOUX ET AL: "A Prime-Boost Approach to HIV Preventive Vaccine Using a Recombinant Canarypox Virus Expressing Glycoprotein 160 (MN) followed by a Recombinant Glycoprotein 160 (MN/LAI)"            AIDS RESEARCH AND HUMAN RETROVIRUSES, vol. 11, 1995, pages 373-381, XP002079474            see page 373            see abstract</p>	1-14, 25-32

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 12894

## Box I Observations where certain claims were found unsearchable (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:  
**Remark: Although claims 1-14 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
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 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 FURTHER INFORMATION 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.:

1,2,5-14,25-30 (all partially) 3,4,31,32 (all completely)

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1, 2, 5-14, 25-30 (all partially), 3, 4, 31, 32 (all completely)

A method for inducing an immune response in a mammal against an antigen comprising administering a virus containing a nucleic acid encoding the antigen or its precursor, and administering at least one booster dose comprising at least one peptide in an adjuvant, wherein the at least one peptide includes the antigen, and wherein the antigen is a tumour antigen; a kit for use in such a method.

2. Claims: 1, 2, 5-14, 25-30 (all partially)

A method for inducing an immune response in a mammal against an antigen comprising administering a virus containing a nucleic acid encoding the antigen or its precursor, and administering at least one booster dose comprising at least one peptide in an adjuvant, wherein the at least one peptide includes the antigen, and wherein the antigen is an antigen characteristic of a pathogen; a kit for use in such a method.

3. Claims: 15-24 (all completely)

A method for reducing an immune response in a mammal against an antigen comprising administering a virus containing a nucleic acid encoding the antigen or its precursor, and administering at least one booster dose comprising at least one peptide in a non-adjuvant carrier, wherein the at least one peptide includes the antigen.