



(51) International Patent Classification:

A61K 39/39 (2006.01) A61K 47/48 (2006.01)
A61K 38/08 (2006.01) A61K 47/42 (2006.01)

(21) International Application Number:

PCT/US2012/032708

(22) International Filing Date:

9 April 2012 (09.04.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/473,337 8 April 2011 (08.04.2011) US
61/602,668 24 February 2012 (24.02.2012) US

(71) Applicant (for all designated States except US): **H. LEE MOFFITT CANCER CENTER AND RESEARCH INSTITUTE, INC.** [US/US]; 12902 Magnolia Drive, Tampa, Florida 33612-9497 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **CELIS, Esteban** [US/US]; 17902 Arbor Greene Drive, Tampa, Florida 33647 (US).

(74) Agent: **LAWSON, Michele L.**; 180 Pine Avenue North, Oldsmar, Florida 34677 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available):

AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available):

ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

[Continued on next page]

(54) Title: METHOD OF DEVELOPING A VACCINE USING PEPTIDE-POLY IC COMPLEXES

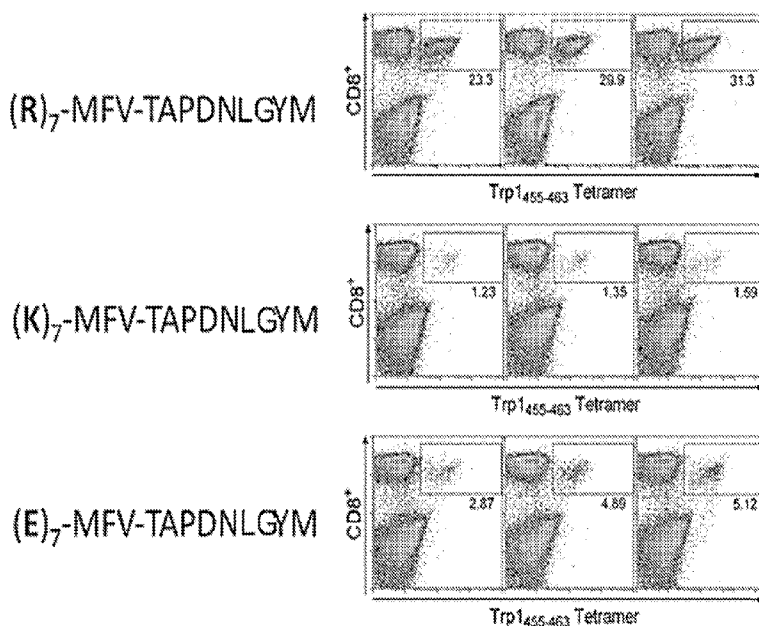


Figure 1

(57) Abstract: The invention describes the development of more potent peptide vaccines to prevent or treat infections or cancer. Small synthetic peptides from the known sequences of viral, bacterial, parasitic or tumor antigens are modified so they can spontaneously form complexes with a synthetic nucleic acid, such as Poly IC, that functions as an immunological adjuvant. The peptide-nucleic acid complexes are dramatically more immunogenic as compared to the separate components. The procedure for developing the vaccine involves the conjugation of a synthetic peptide containing a C residue to poly-K using a bi-functional cross-linking reagent (SMCC). The peptide/poly-K complex was then formulated with CMC and poly-IC to produce a self-adjuvant vaccine that was 36-fold more effective as compared to the same peptide administered mixed with the same adjuvant (but not complexed to it).



— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
29 November 2012

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/032708**A. CLASSIFICATION OF SUBJECT MATTER***A61K 39/39(2006.01)i, A61K 38/08(2006.01)i, A61K 47/48(2006.01)i, A61K 47/42(2006.01)i*

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)

A61K 39/39

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)

eKOMPASS(KIPO internal) & Keywords: adjuvant, poly arginine, cancer, synthetic peptide-based vaccine, tumor antigen, T cell epitope, E7 49-57, Trp1 455, addition of phenylalanine, fatty acid, addition of cysteine, poly-IC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WEIHSU CHEN et al. 'Induction of cytotoxic T-lymphocytes and antitumor activity by a liposomal lipopeptide vaccine' Molecular Pharmaceutics, 2008, Vol. 5, No. 3, pp. 464-471, ISSN 1543-8384.	1,2,5,8-11,17,18 ,24,26-28
Y	See abstract; table 1; introduction; materials and methods; figure 6.	3,4,6,7,12-16 ,19-23,25
Y	CHRISTA FIRBAS et al. 'Immunogenicity and safety of a novel therapeutic hepatitis C virus (HCV) peptide vaccine: A randomized, placebo controlled trial for dose optimization in 128 healthy subjects' Vaccine, 2006, Vol. 24, No. 20, pp. 4343-4353, ISSN 0264-410X. See abstract; tables 3 and 4; p. 4344, right-column.	3,4,25
Y	HIROHITO NARUSE et al. 'A potential peptide vaccine against two different strains of influenza virus isolated at intervals of about 10 years' PNAS, 1994, Vol. 91, No. 20, pp. 9588-9592, ISSN 0027-8424. See abstract; results.	6,7
Y	IVETTE CARO-AGUILAR et al. 'Chimeric epitopes delivered by polymeric synthetic linear peptides induce protective immunity to malaria' Microbes and Infection, 2005, Vol. 7, No. 13, pp. 1324-1337, ISSN 1286-4579. See pp. 1325 and 1330.	12,13,19,20

 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 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 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

27 SEPTEMBER 2012 (27.09.2012)

Date of mailing of the international search report

28 SEPTEMBER 2012 (28.09.2012)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
189 Cheongsu-ro, Seo-gu, Daejeon Metropolitan
City, 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

Choi Sung Hee

Telephone No. 82-42-481-8740



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/032708

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ZHENGRONG CUI et al. 'Synthetic double-stranded RNA poly(I:C) as a potent peptide vaccine adjuvant: therapeutic activity against human cervical cancer in a rodent model' <i>Cancer Immunol. Immunother.</i> , 2006, Vol. 55, No. 10, pp. 1267-1279, ISSN 0340-7004. See abstract; results.	14-16,21-23
Y	CHAO-YI WU et al. 'Improving therapeutic HPV peptide-based vaccine potency by enhancing CD4+ T help and dendritic cell activation' <i>Journal of Biomedical Science</i> , 2010, Vol. 17, No. 1, 88, ISSN 1021-7770. See abstract; results.	14-16,21-23

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/032708**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.: 29-35
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 29-35 pertain to methods for treatment of the human body by therapy, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
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:

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.:

- 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/032708

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
None			