



- (51) International Patent Classification:
A61K 39/12 (2006.01)
- (21) International Application Number:
PCT/US2012/044071
- (22) International Filing Date:
25 June 2012 (25.06.2012)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
PCT/US2011/041889 24 June 2011 (24.06.2011) US
- (71) Applicant (for all designated States except US): **LA JOLLA INSTITUTE FOR ALLERGY AND IMMUNOLOGY** [US/US]; 9420 Athena Circle, San Diego, CA 92037 (US).
- (72) Inventors; and
(71) Applicants : **SHRESTA, Sujan** [US/US]; 6820 Condon Drive, San Diego, CA 92122 (US). **YAUCH, Lauren** [US/US]; 6655 La Jolla Blvd., #20, La Jolla, CA 92037 (US). **SETTE, Alessandro** [US/US]; 5551 Linda Rosa Avenue, La Jolla, CA 92037 (US). **WEISKOPF, Daniela** [AT/US]; 4610 Dawes Street, San Diego, CA 92109 (US).
- (74) Agent: **BEDGOOD, Robert M.**; Pillsbury Winthrop Shaw Pittman LLP, P.O. Box 10500, Mclean, VA 22101 (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, 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).

[Continued on next page]

- (54) Title: PROTECTION AGAINST DENGUE VIRUS AND PREVENTION OF SEVERE DENGUE DISEASE

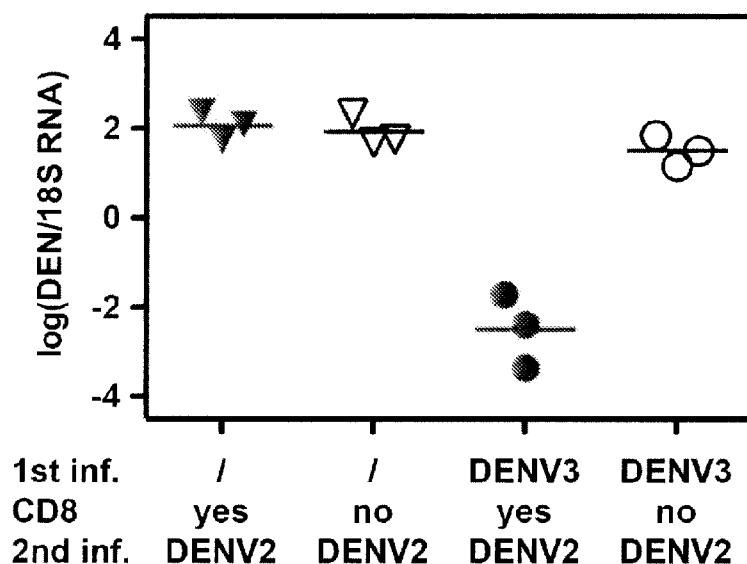


Figure 10

(57) Abstract: The invention provides uses, methods and compositions for eliciting, stimulating, inducing, promoting, increasing, or enhancing an anti-Dengue virus T cell response in a subject.

WO 2012/178196 A3



Published:

(88) Date of publication of the international search report:

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

28 March 2013

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/44071

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/12 (2012.01)

USPC - 424/218.1, 424/199.1, 536/23.72

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 39/12 (2012.01)

USPC - 424/218.1, 424/199.1, 536/23.72

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
424/184.1, 514/3.7

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

PubWEST; PatBase; Google Scholar

search terms: Dengue, DV, vaccin*, immuniz*, subsequ*, secondary, infec*, T, cell, lymphocyte, AB, antibody-dependant, enhanc*, vaccine, vaccination, immunization, T cell, T lymphocyte, CD8+, CD8, cytokin\$, CD27, TNFRSF7

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 2011/0150914 A1 (SHRESTA et al.) 23 June 2011 (23.06.2011) para [0005]; [0007]; [0009]-[0011]; [0022]; [0023]; [0029]; [0031]; [0032]; [0046]; [0085]; [0086]; [0089]; [0093]; [0104]; [0105]; [0112]; [0138]; [0205]; [0206]; claim 37.	1, 4-12, 28, 30-38, 40-42, 45-53, 69, 71-77, 79, 80 ----- 29, 39, 70, 78
Y	US 2004/0009469 A1 (APT et al.) 15 January 2004 (15.01.2004) para [0014]; [0039]; [0201]; [0202]; [0339].	29, 70
Y	US 2011/0033449 A1 (GLENNIE et al.) 10 February 2011 (10.02.2011) abstract; para [0039]; [0047]; [0049].	39, 78

☐ 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

29 November 2012 (29.11.2012)

Date of mailing of the international search report

13 DEC 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

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/44071

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.: 13-17 and 54-58
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, 4-12, 28-42, 45-53, and 69-80, drawn to methods and compositions for eliciting, stimulating, inducing, promoting, increasing, or enhancing an anti-Dengue virus T cell response in a subject

Group II: Claims 2, 4-12, 18-22, 28-41, 43, 45-53, 59-63, and 69-80, drawn to methods and compositions for vaccinating or providing a subject with protection against a Dengue virus infection

Group III: Claims 3-12, 23-41, 44-53, and 64-80, drawn to methods and compositions for treating a subject for a Dengue virus infection

--please see continuation on 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, 4-12, 28-42, 45-53, 69-80

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

International application No.

PCT/US 12/44071

Continuation of Box No III Observations where unity of invention is lacking

The inventions listed as Groups I-III 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 shared technical feature of the inventions listed as Groups I-III is a method for treating or protecting against Dengue virus infection in a subject without eliciting or sensitizing the subject to severe Dengue virus disease upon a secondary or subsequent Dengue virus infection, comprising administering to the subject an amount of a Dengue virus protein or subsequence thereof sufficient to treat or protect against Dengue virus infection. This shared technical feature fails to provide a contribution over the prior art, as evidenced by US 2004/0009469 A1 to Apt et al. (published 15 January 2004; hereinafter 'Apt'). Apt discloses a method of vaccinating or providing a subject with protection against a Dengue virus infection without eliciting or sensitizing the subject to severe dengue disease upon a secondary or subsequent Dengue virus infection (para [0217]- "Another characteristic of a recombinant C15/full length prM/full length E polypeptide of the invention is the ability to induce the production of a titer of neutralizing antibodies against at least one dengue virus of the at least one serotype. In one aspect, the polypeptide produces a titer of neutralizing antibodies against at least one dengue virus of each of at least two, at least three, or at least four serotypes. Some such polypeptides induce at least one neutralizing antibody response in a subject to or against at least one dengue virus of each of at least two, three or four serotypes without an occurrence of antibody-dependent enhancement (ADE) upon contact of the subject with the at least dengue virus of each of the at least two, three, or four serotypes, respectively"; para [0009] - "Subsequent infection with a heterologous Dengue virus can lead to the much more severe to fatal disease of dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). It is hypothesized that the presence of antibodies to the serotype causing the primary infection enhances the infection by a heterologous serotype in secondary infections. This phenomenon is referred to as antibody-dependent enhancement (ADE) of the disease") comprising administering to the subject an amount of a Dengue virus protein or subsequence thereof sufficient to vaccinate or provide the subject with protection against the Dengue virus infection (para [0277] - "In another aspect, a recombinant polypeptide of the invention induces a neutralizing antibody response to at least one dengue virus of all four dengue virus serotypes in a mammal to which such recombinant polypeptide (or polynucleotide encoding such recombinant polypeptide) is administered without an occurrence of antibody-dependent enhancement (ADE) upon infection of the mammal with the dengue virus"). In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature.

Further, the special technical feature of the inventions listed as Group I is eliciting, stimulating, inducing, promoting, increasing, or enhancing an anti-Dengue virus T cell response. This special technical feature is not shared by the inventions of Groups II and III. The special technical feature of the inventions listed as Group II is vaccinating or providing a subject with protection against a Dengue virus infection. This special technical feature is not shared by the inventions of Groups I and III. The special technical feature of the inventions listed as Group III is treating a subject for a Dengue virus infection. This special technical feature is not shared by the inventions of Groups I and II.

Unity of invention exists only when the same or corresponding technical feature is shared by the claimed inventions. Without a shared special technical feature, the inventions of Groups I-III lack unity with one another.