



- (51) **International Patent Classification:**
C07H 15/00 (2006.01) *C07K 16/00* (2006.01)
- (21) **International Application Number:**
PCT/US2014/010310
- (22) **International Filing Date:**
6 January 2014 (06.01.2014)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/748,880 4 January 2013 (04.01.2013) US
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- (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, BN, 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, IR, IS, JP, KE, KG, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, 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, KM, 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))
- (88) **Date of publication of the international search report:**
24 December 2014

(54) **Title:** VACCINES WITH HIGHER CARBOHYDRATE ANTIGEN DENSITY AND NOVEL SAPONIN ADJUVANT

(57) **Abstract:** The present invention provides vaccines comprising carbohydrate antigen conjugated to a diphtheria toxin (DT) as a carrier protein, wherein the ratio of the number of carbohydrate antigen molecule to the carrier protein molecule is higher than 5:1. Also disclosed herein is a novel saponin adjuvant and methods to inhibit cancer cells, by administering an effective amount of the vaccine disclose herein.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/10310

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07H 15/00; C07K 16/00 (2014.01)

CPC - C07H 15/04; C07H 15/10; C07K 16/00

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(8)- C07H 15/00; C07K 16/00 (2014.01)

CPC- C07H 15/04; C07H 15/10; C07K 16/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC: 536/17.9; 530/391.7; 530/300; 424/193.1; 424/197.11

Patents and NPL (classification, keyword; search terms below)

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

Databases: Google Scholar, Google Patent, PatBase

Search terms used: carbohydrate, oligosaccharide, antigen, DPT, diphtheria toxin, saponin

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 2012/0328646 A1 (Wong et al.) 27 December 2012 (27.12.2012) para [0005], [0012], [0013], [0015], [0023], [0091], [0120], [0151], [0182]; Table 1.	1-2, 4, 6-9, 12-15 and 34-37 ----- 3, 5, 10-11
Y	WO 2011/156774 A2 (Danishefsky et al.) 15 December 2011 (15.12.2011) para [0137]-[0138], [0210]	3, 5, 10-11
A	WO 1996/040242 A1 (Slaoui et al.) 19 December 1996 (19.12.1996) pg 1, ln 1-pg 3, ln 15.	1-15 and 34-37

☐ 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

01 October 2014 (01.10.2014)

Date of mailing of the international search report

31 OCT 2014

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/10310

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:
--Please see attached 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.:
1-15 and 34-37

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 14/10310

BOX III: lack of unity:

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 1-15 and 34-37 (in part) drawn to a vaccine containing a carbohydrate antigen or its immunogenic fragment and a toxoid protein, wherein the ratio of carbohydrate antigen to toxoid protein ranges from 5:1 to 39:1; a pharmaceutical composition containing the vaccine and a pharmaceutically acceptable carrier and to a method for inhibiting cancer cells, comprising administering an effective amount of the vaccine.

Group II: Claims 16-26 drawn to saponin compounds of formula (I), an OPT-821 saponin, and pharmaceutical compositions containing the same.

Group III: Claims 27-33 and 34-37 (in part) drawn to a vaccine containing a carbohydrate antigen or its immunogenic fragment and an OPT-821 saponin; a pharmaceutical composition containing the vaccine and a pharmaceutically acceptable carrier and to a method for inhibiting cancer cells, comprising administering an effective amount of the vaccine.

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:

Special technical features:

Group I includes the technical feature of a vaccine containing a carbohydrate antigen or its immunogenic fragment and a toxoid protein, wherein the ratio of carbohydrate antigen to toxoid protein ranges from 5:1 to 39:1, not required by Groups II-III.

Group II includes the technical feature of a saponin compound of formula (I), not required by Groups I and III.

Group III includes the technical feature of a vaccine containing a carbohydrate antigen or its immunogenic fragment and an OPT-821 saponin not required by Groups I-II.

Common technical features:

Groups I and III share the technical features of:

- a vaccine containing a carbohydrate antigen or its immunogenic fragment;
- a pharmaceutical composition containing the vaccine and a pharmaceutically acceptable carrier and
- a method for inhibiting cancer cells, comprising administering an effective amount of the vaccine.

These shared technical features, however, do not provide a contribution over the prior art as being anticipated by US 2012/0328646 A1 to Wong et al. (hereinafter 'Wong') which discloses a vaccine containing a carbohydrate antigen (para [0002], Globo H); a pharmaceutical composition containing the vaccine and a pharmaceutically acceptable carrier (para [0013], carrier protein; para [0014], DT-CRM197; para [0090]); and a method for inhibiting cancer cells, comprising administering an effective amount of the vaccine (para [0107]).

As said vaccine, pharmaceutical composition and method of treatment were known in the art at the time of the invention, these cannot be considered special technical features that would otherwise unify the groups.

Groups II and III share the technical feature of the OPT-821 saponin.

This shared technical feature, however, does not provide a contribution over the prior art as being anticipated by WO 2011/156774 A2 to Danishefsky et al. (hereinafter 'Danishefsky'), which discloses OPT-821 saponin as adjuvant for an immunogenic composition (para [0136]-[0137], pg 71, Table 3). As said saponin was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

The inventions of Group I-III therefore lack unity under PCT Rule 13.2, because they do not share a same or corresponding special technical feature providing a contribution over the prior art.