(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 August 2016 (18.08.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/131000 A3

(51) International Patent Classification:
A61K 39/00 (2006.01) *C07K 1/00* (2006.01)

(21) International Application Number:
PCT/US2016/017877

(22) International Filing Date:
12 February 2016 (12.02.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/116,318 13 February 2015 (13.02.2015) 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, 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, ST, 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).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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))*

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

(88) Date of publication of the international search report:
6 October 2016

(54) Title: TOLERANCE THERAPEUTIC FOR TREATING POLYPEPTIDE INDUCED ALLERGY

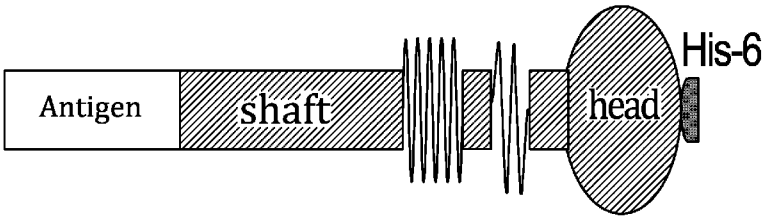

FIG. 1

(57) Abstract: The present disclosure is directed to compositions comprising one or more components of a polypeptide allergen combined with a reovirus-derived targeting protein, and related methods for the generation of tolerance against the polypeptide allergens.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/00, C07K 1/00 (2016.01)
CPC - C07K 2319/00, C07K 16/44
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 39/00, C07K 1/00 (2016.01)
CPC- C07K 2319/00, C07K 16/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC- 424/192.1, 530/403 (keyword search, terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST (USPT, PGPB, EPAB, JPAB), Google Patents/Scholar
Search Terms Used: Reovirus, p.sigma.1, sigma polypeptide, food, allergen, MHC, peanut, AraH2, targeting, autoantigen, M cells

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 2011/0135678 A1 (Pascual et al.) 09 June 2011 (09.06.2011) abstract, para [0011], [0020], [0031], [0039], [0060], [0067], [0074], [0075], [0079], [0105], [0108]	1-5, 18-19, 22-26 ---- 6
Y	US 2014/0010849 A1 (Northwestern University) 09 January 2014 (09.01.2014) abstract, para [0042]	6

☐ 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	Date of mailing of the international search report
20 June 2016 (20.06.2016)	26 JUL 2016
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. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
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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:
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 1-26, directed to an isolated fusion protein comprising a reovirus-derived targeting polypeptide and at least one allergen polypeptide. The fusion protein will be searched to the extent that the allergen polypeptide encompasses the first named allergen polypeptide, peanut allergen polypeptide Arah2. It is believed that claims 1-6, 18, 19, 22-26, encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass Arah2. Additional allergen polypeptide(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected allergen polypeptide(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. An exemplary election would be prolamin (claims 1-5, 7, 18-26).
- Please see extra sheet for continuation -

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.:
1-6, 18, 19, 22-26 limited to AraH2

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.
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Continuation of:

Box NO III. Observations where unity of invention is lacking

Group II: claims 27-30, drawn to a method for inducing tolerance to a polypeptide allergen.

The inventions listed as Groups I+ and II 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 special technical feature of a composition comprising an isolated fusion protein, not required by Group II.

Group II includes the special technical feature of a method for inducing tolerance to a polypeptide allergen, not required by Group I+.

Another special technical feature of the inventions listed as Group I+ is the specific allergen polypeptide, recited therein. Each of the inventions of Group I+ requires a unique allergen polypeptide, not required by the other inventions.

Common Technical Features

The inventions of Groups I+ and II share the technical feature of claim 1. However, these shared technical features do not represent a contribution over prior art in view of US 2007/0192905 A1 to Piller et al. (hereinafter 'Piller') and US 2011/0135678 A1 to Pascual et al. (hereinafter 'Pascual'). Piller teaches (instant claim 1) an isolated fusion protein comprising a plant lectin-derived targeting polypeptide and at least one allergen polypeptide (para [0131] Subunit Vaccines or Toleragens Containing a Peptide Segment, ?. Co-Expressed with Proteins or Peptides which Target Binding to Receptors on Epithelial Cells to Facilitate Deliver.; [0132] Essentially any vaccine or toleragen construct can be co-expressed as a fusion protein with proteins or peptides which target binding to epithelial cells in the gastrointestinal tract. For example, the plant lectin protein, Ulex europaeus agglutinin I can be coupled to vaccines or toleragens to facilitate uptake by specialized epithelial cells called "M" cells.). Piller does not specifically teach a reovirus-derived targeting peptide. Pascual teaches M cell-targeting Ag delivery systems using recombinant reovirus p sigma1. Recombinant p sigma 1 of reovirus has been genetically fused to OVA (OVA-p sigma 1) (para [0011]). It would have been obvious to one of ordinary skill in the art to have applied the reovirus p sigma1 of Pascual as the M cell-targeting polypeptide of Piller, because Pascual teaches that reovirus p sigma 1 can be used as a M cell-targeting polypeptide in a fusion protein (para [0011]).

Piller further teaches that allergen polypeptide is a food allergen (para [0215], Table 5, peanut allergen), an environmental allergen (Table 5, dust mite allergen), an autoantigen (para [0216], type II collagen), and Pascual teaches that that allergen polypeptide is biological therapeutic (para [0013], myelin proteins).

Piller further teaches a nucleic acid (para [0052]), a vector (para [0162]), a cultured cells transfected with a vector (para [0267], The synthetic fanC gene targeting expression to the cytosol of plant cells (pKP7) (FIG. 2) was used for transformation of soybean plants.).

As said technical features were known in the art at the time of the invention, these cannot be considered special technical feature that would otherwise unify the groups.

Groups I+ and II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.