

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
31 December 2008 (31.12.2008)

PCT

(10) International Publication Number
WO 2009/002380 A3

(51) International Patent Classification:
A61K 48/00 (2006.01) **A61K 39/395** (2006.01)

(21) International Application Number:
PCT/US2008/005924

(22) International Filing Date: 9 May 2008 (09.05.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/929,405 26 June 2007 (26.06.2007) US

(71) Applicant (for all designated States except US): **THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA** [US/US]; Center For Technology Transfer, Suite 200, 3160 Chestnut Street, Philadelphia, PA 19104-6283 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **PAYNE, Aimee, S.** [US/US]; 536 Hamilton Road, Merion Station, PA 19066 (US). **STANLEY, John, R.** [US/US]; 231 Righters Mill Road, Gladwyne, PA 19035 (US). **SIEGEL, Donald, L.** [US/US]; 2582 Brandon Court, Lansdale, PA 19446 (US). **YAMAGAMI, Jun** [JP/US]; 117n 15th Street, Apt. 2006, Philadelphia, PA 19102 (US). **ISHII, Ken** [JP/JP]; 3-50-5 Apt. #105, Honmachi Shibuya, Tokyo, 151-0071 (JP).

(74) Agent: **NGUYEN, Quang, D.**; Drinker Biddle & Reath LLP, One Logan Square, 18th And Cherry Streets, Philadelphia, PA 19103 (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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, 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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

(88) Date of publication of the international search report:
19 February 2009

(54) Title: ISOLATION OF ANTI-DESMOGLEIN 1 ANTIBODIES BY PHAGE DISPLAY OF PEMPHIGUS FOLIACEUS AUTOANTIBODIES

(57) Abstract: This invention relates to compositions and methods for the use of anti- autoimmune reagents that specifically bind to anti-desmoglein antibodies, which are responsible for pemphigus foliaceus. In addition, the invention relates to methods and compositions for inhibiting the expression or function of a variable region of an anti- desmoglein (anti-Dsg) pathogenic autoantibody.



WO 2009/002380 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/05924

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01N 33/53; A61K 39/395 (2008.04)

USPC - 435/7.1; 424/141.1

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)

USPC: 435/7.1; 424/141.1

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

USPC: 514/44; 424/145.1 435/7.1 (Text Search)

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

Electronic Data Bases: (EPAB,JPAB,PGPB,USPT); Google Search: Pemphigus, foliaceus, vulgaris, autoantibodies, Idiotype, CDR3, heavy chain, variable, phage, desmoglein

GenCore Sequence Search (AA): SEQ ID NO: 44,45,216

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	PAYNE et al. Targeting pemphigus autoantibodies through their heavy-chain variable region genes. Epub 29 Mar 2007. J Invest Dermatol. Jul 2007, 127(7):1681-91; pg 1682 left col para 4, pg 1682 right col para 1, pg 1682 table 1, pg 1683 right col para 2, pg 1684 fig 3	1, 6-8, 15, 16, 20 ----- 2, 24-26, 35-37, 41
Y	BRAUNINGER et al. Immunoglobulin Heavy Chain, Accession Number CAD88666. 23 Oct 2003 [Retrieved from the internet: <URL: http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=protein&id=29836858>] Pg 1	2
Y	PAYNE. Cloning and genetic characterization of human pemphigus autoantibodies. J Am Acad Dermatol. Aug 2006, 55(2):e2. Abstract	24-26, 35-37, 41
A	WO 2004/009618 A2 (VAN BERKEL et al.) 29 Jan 2004(29.01.2004) pg 175-176 sheet 7 SEQ ID NO: 8	3, 9, 17, 27, 38

☐ 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

13 November 2008 (13.11.2008)

Date of mailing of the international search report

08 DEC 2008

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 08/05924

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:

Group I, claims 1-3, 6-9, 15-17, 20, 24-27, 35-38, 41, drawn to an isolated anti-desmoglein 1 (Dsg1) antibody or fragment thereof and a method of its use, wherein claims 3, 9, 17, 27, 38 are limited to SEQ ID NO:216.

Group II+, claims 1-3, 6-9, 15-17, 20, 24-27, 35-38, 41, drawn to an isolated anti-desmoglein 1 (Dsg1) antibody or fragment thereof and a method of its use. With regard to claims 3, 9, 17, 27, 38 and SEQ ID NO:217-258, should additional fee be paid, Applicant is invited to elect a SEQ ID NO: to be searched.

Group III+, claims 1, 2, 4, 6-8, 10, 15, 16, 18-20, 24-26, 28, 35-37, 39, 41, drawn to an isolated anti-desmoglein 1 (Dsg1) antibody or fragment thereof and a method of its use. With regard to claims 4, 10, 18, 28, 39 and SEQ ID NO:173-215, should additional fee be paid, Applicant is invited to elect a SEQ ID NO: to be searched.

***** continued in Supplemental Box *****

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.:

Group I, claims 1-3, 6-9, 15-17, 20, 24-27, 35-38, 41, drawn to an isolated anti-desmoglein 1 (Dsg1) antibody or fragment thereof and a method of its use, wherein claims 3, 9, 17, 27, 38 are limited to SEQ ID NO:216.

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 08/05924

continuation of Box 3: LOU

Group IV+, claims 1, 2, 5-8, 11, 15, 16, 19, 20, 24-26, 29, 35-37, 40, 41, drawn to an isolated anti-desmoglein 1 (Dsg1) antibody or fragment thereof and a method of its use. With regard to claims 5, 11, 19, 29, 40 and SEQ ID NO:44-86, should additional fee be paid, Applicant is invited to elect a SEQ ID NO: to be searched.

Group V+, claim 12, drawn to an isolated nucleic acid sequence. With regard to SEQ ID NOs: 1-43 and 87-172, should additional fee be paid, Applicant is invited to elect a SEQ ID NO: to be searched.

Group VI+, claims 13, 14, 21-23, 30-34, drawn to an inhibitor of expression of an anti-desmoglein autoantibody or fragment thereof and a method of its use. With regard to claims 22, 23, 32, 33 and SEQ ID NOs: 1-43, 87-129, 130-172, should additional fee be paid, Applicant is invited to elect a SEQ ID NO: to be searched.

Group VII+, claims 42-45 and 48, drawn to a method of diagnosing pemphigus foliaceus (PF) in a subject by using an anti-autoimmune reagent that specifically binds to an anti-desmoglein 1 autoantibody or fragment thereof. With regard to claim 45 and SEQ ID NOs: 216-258, should additional fee be paid, Applicant is invited to elect a SEQ ID NO: to be searched.

Group VIII+, claims 42-44, 46, and 48, drawn to a method of diagnosing pemphigus foliaceus (PF) in a subject by using an anti-autoimmune reagent that specifically binds to an anti-desmoglein 1 autoantibody or fragment thereof. With regard to claim 46 and SEQ ID NOs: 173-215, should additional fee be paid, Applicant is invited to elect a SEQ ID NO: to be searched.

Group IX+, claims 42-44, 47, and 48, drawn to a method of diagnosing pemphigus foliaceus (PF) in a subject by using an anti-autoimmune reagent that specifically binds to an anti-desmoglein 1 autoantibody or fragment thereof. With regard to claim 47 and SEQ ID NOs: 44-86, should additional fee be paid, Applicant is invited to elect a SEQ ID NO: to be searched.

The inventions listed as Groups I-IX+ 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:

Groups I-IV+ and VII- IX+ do not include the inventive concept of a nucleic acid, as required by Groups V-VI+.

Groups I-IV+ and VII- IX+ do share the technical feature of an isolated anti-desmoglein 1 (Dsg1) antibody. However, this shared technical feature does not represent a contribution over the prior art of US 2002/0165188 A1 to Herlyn et al. that teaches an anti-desmoglein 1 (Dsg1) antibody (para [0026], [0041], [0043]). As said antibody was known at the time, as evidenced by the teaching of Herlyn et al., this cannot be considered a special technical feature that would otherwise unify the groups. In addition, there is no disclosure that the claimed SEQ ID NO: 173-258 and SEQ ID NO: 44-86 share a significant structural element that is essential to the common property or activity. Therefore, unity of invention is lacking.

As to Groups V-VI+, the claimed isolated nucleic acids of SEQ ID NOs: 1-43 and 87-172 and the inhibitors of their expression do not share a significant structural element that is essential to the common property or activity. In addition, US 2006/0286112 A1 to Kellerman et al. teaches an isolated nucleic acid that is ~90% identical to the claimed SEQ ID NO: 87.

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