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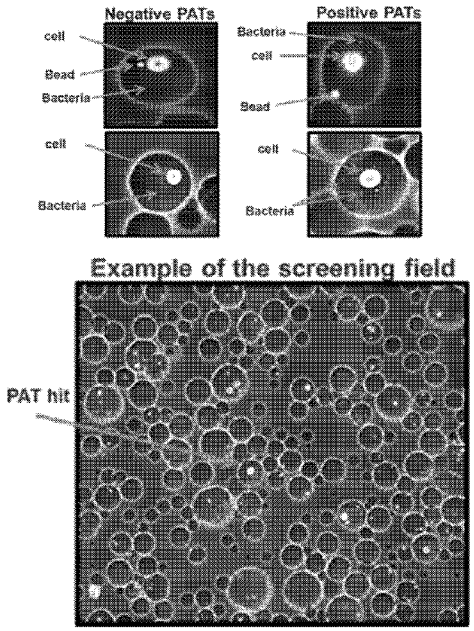
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[Continued on next page]

(54) Title: SCREENING METHODS FOR IDENTIFYING ANTIBODIES THAT BIND CELL SURFACE EPITOPES

FIG. 3



(57) Abstract: Provided are assays or methods for identifying antibodies that bind to microorganisms, *e.g.*, pathogenic microorganisms, such as bacteria other infectious agents. In some embodiments, the provided methods for identifying an antibody that binds the target microorganism involves gel encapsulation of antibody-producing cells in gel microdroplets with a target microorganism. Also provided are antibodies produced by the method. Also provided are antibodies that bind a conserved region or epitope across variants or species of *Acenitobacter* .

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Declarations under Rule 4.17:

— *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:
14 September 2017

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/015515

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/12 G01N33/569 G01N33/543
ADD.

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)
C07K G01N

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)
EPO-Internal, WPI Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/111014 A2 (CRYSTAL BIOSCIENCE INC [US]; HARRIMAN WILLIAM DON [US]) 11 September 2009 (2009-09-11) examples 1,6,8 -----	1,18,20, 46,48, 49,59, 61,104, 113-124, 126,127, 129
X	WO 2009/011808 A1 (HARVARD COLLEGE [US]; WEITZ DAVID A [US]; GRIFFITHS ANDREW [FR]; KOEST) 22 January 2009 (2009-01-22) claims 137-160 ----- -/--	104, 113-129

[X] Further documents are listed in the continuation of Box C.

[X] 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 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
7 July 2017	24/07/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Rutz, Berthold

3

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Bachir El Debs ET AL: "Functional single-cell hybridoma screening using droplet-based microfluidics", Proceedings of the National Academy of Sciences of the United States of America, 17 July 2012 (2012-07-17), pages 11570-11575, XP055235862, United States DOI: 10.1073/pnas.1204514109 Retrieved from the Internet: URL:http://www.pnas.org/content/109/29/11570.full.pdf [retrieved on 2015-12-11] page 11575, left-hand column	104,124, 126,127, 129
X	HONGXING HU ET AL: "Efficient cell pairing in droplets using dual-color sorting", LAB ON A CHIP, vol. 15, no. 20, 1 January 2015 (2015-01-01), pages 3989-3993, XP055220600, ISSN: 1473-0197, DOI: 10.1039/C5LC00686D page 3992, left-hand column; figure 1	104,124, 126,127, 129
A	KENNEY J S ET AL: "PRODUCTION OF MONOCLONAL ANTIBODIES USING A SECRETION CAPTURE REPORT WEB", BIOTECHNOLOGY. THE INTERNATIONAL MONTHLY FOR INDUSTRIAL BIOLOGY, NATURE PUBLISHING GROUP, US, vol. 13, no. 8, 1 August 1995 (1995-08-01), pages 787-790, XP001015788, ISSN: 0733-222X, DOI: 10.1038/NBT0895-787 the whole document	1-103, 124-129
A	GRAY F ET AL: "Secretion capture and report web: use of affinity derivatized agarose microdroplets for the selection of hybridoma cells", JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, NL, vol. 182, no. 2, 9 June 1995 (1995-06-09), pages 155-163, XP004021164, ISSN: 0022-1759, DOI: 10.1016/0022-1759(94)00319-R	1-103, 124-129

-/--

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	AKSELBAND YEVGENYA ET AL: "Isolation of rare isotype switch variants in hybridoma cell lines using an agarose gel microdrop-based protein secretion assay", ASSAY AND DRUG DEVELOPMENT TECHNOLOGIES, MARY ANN LIEBERT, INC. PUBLISHERS, US, vol. 1, no. 5, 1 October 2003 (2003-10-01) , pages 619-626, XP002602570, ISSN: 1540-658X	1-103, 124-129
A	WEAVER J C ET AL: "Gel microdrop technology for rapid isolation of rare and high producer cells", NATURE MEDICINE, NATURE PUB. CO, vol. 3, no. 5, 1 May 1997 (1997-05-01), pages 583-585, XP002116070, ISSN: 1078-8956, DOI: 10.1038/NM0597-583	1-103, 124-129
A	WO 02/097122 A1 (ONE CELL SYSTEMS INC [US]; JESPERSEN DIANA [US]; AKSELBAND YEVGENYA [U) 5 December 2002 (2002-12-05)	1-103, 124-129
Y	US 2015/023999 A1 (URWYLER SIMON [CH] ET AL) 22 January 2015 (2015-01-22) the whole document	105-123
Y	Ravinder Singh ET AL: "In silico Analysis of Acinetobacter baumannii Outer Membrane Protein BamA as a Potential Immunogen", Int. J. Pure Appl. Sci. Technol. International Journal of Pure and Applied Sciences and Technology ISSN, 1 January 2014 (2014-01-01), pages 32-39, XP055388385, Retrieved from the Internet: URL:http://www.ijopaasat.in/yahoo_site_admin/assets/docs/6_IJPAST-769-V21N2.180122520.pdf the whole document	105-123
A	US 2014/335092 A1 (SPELLBERG BRAD J [US] ET AL) 13 November 2014 (2014-11-13) the whole document	105-112
A	RENATA FAJARDO BONIN ET AL: "Identification of immunogenic proteins of the bacterium Acinetobacter baumannii using a proteomic approach", PROTEOMICS - CLINICAL APPLICATIONS, vol. 8, no. 11-12, 28 August 2014 (2014-08-28), pages 916-923, XP055388584, DE ISSN: 1862-8346, DOI: 10.1002/prca.201300133	105-112

-/--

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KELLY H. KIM ET AL: "The bacterial outer membrane [beta]-barrel assembly machinery", PROTEIN SCIENCE, vol. 21, no. 6, 1 May 2012 (2012-05-01), pages 751-768, XP055388383, US ISSN: 0961-8368, DOI: 10.1002/pro.2069 -----	105-112
A	A. E. ROSSITER ET AL: "The Essential -Barrel Assembly Machinery Complex Components BamD and BamA Are Required for Autotransporter Biogenesis", JOURNAL OF BACTERIOLOGY, vol. 193, no. 16, 15 August 2011 (2011-08-15), pages 4250-4253, XP055388381, US ISSN: 0021-9193, DOI: 10.1128/JB.00192-11 -----	105-112
A	DATABASE UniProt [Online] 24 November 2009 (2009-11-24), "RecName: Full=Outer membrane protein assembly factor BamA {ECO:0000256¦HAMAP-Rule:MF_01430}; Flags: Precursor;", XP002771800, retrieved from EBI accession no. UNIPROT:D0C6H3 Database accession no. D0C6H3 sequence -----	105-112
A,P	TAREK A. AHMAD ET AL: "Development of immunization trials against Acinetobacter baumannii", TRIALS IN VACCINOLOGY, vol. 5, 9 April 2016 (2016-04-09), pages 53-60, XP055388500, ISSN: 1879-4378, DOI: 10.1016/j.trivac.2016.03.001 -----	105-112

3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/015515

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:

see additional 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 an 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.:

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-104, 124-129(completely); 113-123(partially)

   method for identifying an antibody that binds a target microorganism comprising encapsulating candidate antibody-producing cells in microdroplets with a target microorganism, composition comprising a plurality of microdroplets each comprising a candidate antibody-producing cell and a target microorganism, library of microdroplets

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2. claims: 105-112(completely); 113-123(partially)

   antibody or antigen-binding fragment thereof, that binds to an epitope present in the at least one conserved region or domain of BamA (beta-barrel assembly machinery) of a Gram-negative bacterium, polynucleotide encoding the antibody or antigen-binding fragment, composition

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/015515

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009111014 A2	11-09-2009	AU 2009220203 A1	11-09-2009
		CA 2717070 A1	11-09-2009
		DK 2271657 T3	15-05-2017
		EP 2271657 A2	12-01-2011
		JP 5737707 B2	17-06-2015
		JP 2011512842 A	28-04-2011
		US 2010092955 A1	15-04-2010
		US 2012058903 A1	08-03-2012
		WO 2009111014 A2	11-09-2009
WO 2009011808 A1	22-01-2009	US 2009068170 A1	12-03-2009
		US 2012015382 A1	19-01-2012
		WO 2009011808 A1	22-01-2009
WO 02097122 A1	05-12-2002	AT 410680 T	15-10-2008
		CA 2447691 A1	05-12-2002
		EP 1399580 A1	24-03-2004
		JP 4194934 B2	10-12-2008
		JP 2004528574 A	16-09-2004
		US 2003143642 A1	31-07-2003
		US 2005019839 A1	27-01-2005
		WO 02097122 A1	05-12-2002
US 2015023999 A1	22-01-2015	AU 2012344293 A1	10-07-2014
		CA 2857423 A1	06-06-2013
		CN 104507499 A	08-04-2015
		CN 106380510 A	08-02-2017
		EP 2599496 A1	05-06-2013
		EP 2800584 A1	12-11-2014
		ES 2568071 T3	27-04-2016
		JP 2015501809 A	19-01-2015
		US 2015023999 A1	22-01-2015
		WO 2013079207 A1	06-06-2013
US 2014335092 A1	13-11-2014	AU 2012256075 A1	02-05-2013
		CN 103930131 A	16-07-2014
		EP 2707023 A2	19-03-2014
		US 2012301474 A1	29-11-2012
		US 2014335092 A1	13-11-2014
		WO 2012158529 A2	22-11-2012