

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ETB-01125	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2018/050212	International filing date (<i>day/month/year</i>) 10 September 2018 (10-09-2018)	(Earliest) Priority Date (<i>day/month/year</i>) 8 September 2017 (08-09-2017)
Applicant EVELO BIOSCIENCES, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 8 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6**bis**(a)).

c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____
☐ as suggested by the applicant
☐ as selected by this Authority, because the applicant failed to suggest a figure
☐ as selected by this Authority, because this figure better characterizes the invention
b. ☒ none of the figures is to be published with the abstract

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
- a. ☐ forming part of the international application as filed:
- ☐ in the form of an Annex C/ST.25 text file.
- ☐ on paper or in the form of an image file.
- b. ☒ furnished together with the international application under PCT Rule 13~~ter~~.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
- c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
- ☐ in the form of an Annex C/ST.25 text file (Rule 13~~ter~~.1(a)).
- ☐ on paper or in the form of an image file (Rule 13~~ter~~.1(b) and Administrative Instructions, Section 713).
2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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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:

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.

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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K14/195 C12R1/01 A61K35/74 C12N1/20
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 C12R A61K C12N

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, BIOSIS, Sequence Search, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2014/196913 A1 (BJÖRCK INGER [SE]; NILSSON ANNE [SE]; BÄCKHED FREDRIK [SE]; KOVATCHEVA) 11 December 2014 (2014-12-11) the whole document	9-16, 19-21, 82,83, 105,108, 116, 123-131
X	WO 2011/053653 A2 (MAYO FOUNDATION [US]; MURRAY JOSEPH A [US]; MARIETTA ERIC V [US]; BART) 5 May 2011 (2011-05-05) the whole document ----- -/-	9-16, 19-21, 82,83, 105,108, 116, 123-131



Further documents are listed in the continuation of Box C.



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

10 January 2019

Date of mailing of the international search report

26/02/2019

Name and mailing address of the ISA/

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Authorized officer

Kania, Thomas

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STUBBS S ET AL: "Effect of environmental haemin upon the physiology and biochemistry of Prevotella intermedia R78", LETTERS IN APPLIED MICROBIOLOGY, vol. 29, no. 1, July 1999 (1999-07), pages 31-36, XP002787785, ISSN: 0266-8254 page 33, right-hand column, paragraph 1 -----	159,160, 172-178
X	H. BOUALLAGUI ET AL: "Microbial monitoring by molecular tools of a two-phase anaerobic bioreactor treating fruit and vegetable wastes", BIOTECHNOLOGY LETTERS, vol. 26, no. 10, 1 May 2004 (2004-05-01), pages 857-862, XP055540159, Dordrecht ISSN: 0141-5492, DOI: 10.1023/B:BILE.0000025892.19733.18 the whole document -----	175-178
A	US 5 674 733 A (SALYERS ABIGAIL A [US] ET AL) 7 October 1997 (1997-10-07) -----	1-181
A	I. A. MACDONALD ET AL: "Stress-Induced Outer Membrane Vesicle Production by Pseudomonas aeruginosa", JOURNAL OF BACTERIOLOGY, vol. 195, no. 13, 1 July 2013 (2013-07-01), pages 2971-2981, XP055539937, US ISSN: 0021-9193, DOI: 10.1128/JB.02267-12 cited in the application -----	1-181
A	PRAMOD K. GIRI ET AL: "Exosomes Derived from M. Bovis BCG Infected Macrophages Activate Antigen-Specific CD4+ and CD8+ T Cells In Vitro and In Vivo", PLOS ONE, vol. 3, no. 6, 18 June 2008 (2008-06-18), page e2461, XP055293781, DOI: 10.1371/journal.pone.0002461 cited in the application -----	1-181
A	SEONG BIN PARK ET AL: "Outer Membrane Vesicles as a Candidate Vaccine against Edwardsiella", PLOS ONE, vol. 6, no. 3, 1 January 2011 (2011-01-01), page e17629, XP055183327, ISSN: 1932-6203, DOI: 10.1371/journal.pone.0017629 cited in the application -----	1-181
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DEBASHREE CHATTERJEE ET AL: "Vibrio cholerae 0395 Outer Membrane Vesicles Modulate Intestinal Epithelial Cells in a NOD1 Protein-dependent Manner and Induce Dendritic Cell-mediated Th2/Th17 Cell Responses", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 288, no. 6, 8 February 2013 (2013-02-08), pages 4299-4309, XP055539935, US ISSN: 0021-9258, DOI: 10.1074/jbc.M112.408302 cited in the application -----	1-181
A	GUNNSTEIN NORHEIM ET AL: "An OMV Vaccine Derived from a Capsular Group B Meningococcus with Constitutive FetA Expression: Preclinical Evaluation of Immunogenicity and Toxicity", PLOS ONE, vol. 10, no. 9, 21 September 2015 (2015-09-21), page e0134353, XP055524302, DOI: 10.1371/journal.pone.0134353 cited in the application -----	1-181

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Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2014196913	A1	11-12-2014	CN 105451576 A 30-03-2016
			DK 3016527 T3 12-11-2018
			EP 3016527 A1 11-05-2016
			ES 2692162 T3 30-11-2018
			HK 1218839 A1 17-03-2017
			SG 11201510750X A 26-02-2016
			US 2016113972 A1 28-04-2016
			WO 2014196913 A1 11-12-2014
WO 2011053653	A2	05-05-2011	US 2012213833 A1 23-08-2012
			US 2014105972 A1 17-04-2014
			US 2015290256 A1 15-10-2015
			US 2017189455 A1 06-07-2017
			US 2018021390 A1 25-01-2018
			WO 2011053653 A2 05-05-2011
US 5674733	A	07-10-1997	AT 169960 T 15-09-1998
			AU 2185792 A 08-01-1993
			CA 2110924 A1 10-12-1992
			DE 69226698 D1 24-09-1998
			DE 69226698 T2 24-12-1998
			EP 0587763 A1 23-03-1994
			US 5322784 A 21-06-1994
			US 5674733 A 07-10-1997
			WO 9221761 A1 10-12-1992

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-181

Pharmaceutical compositions comprising Prevotella extracellular vesicles (EVs), Prevotella bacteria or both, methods of generating engineered Prevotella bacteria resulting in increased or modified EV production, methods of culturing Prevotella for improved EV production under stress-inducing conditions, as well as a bioreactor comprising Prevotella bacteria.

1.1. claims: 1-131

Pharmaceutical compositions comprising Prevotella extracellular vesicles (EVs), Prevotella bacteria or both, as well as related subject-matter.

1.2. claims: 132-159

Methods of generating engineered Prevotella bacteria resulting in increased or modified EV production, as well as related subject-matter.

1.3. claims: 160-174

Methods of culturing Prevotella for improved EV production under stress-inducing conditions, as well as related subject-matter.

1.4. claims: 175-181

A bioreactor comprising Prevotella bacteria.
