

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 32724-42664/WO	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2019/017731	International filing date (<i>day/month/year</i>) 12 February 2019 (12-02-2019)	(Earliest) Priority Date (<i>day/month/year</i>) 12 February 2018 (12-02-2018)
Applicant CODIAK 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:

METHODS AND COMPOSITIONS FOR MACROPHAGE POLARIZATION

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

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/017731

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:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/017731

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.:

14-16, 39, 40, 63-66(completely); 1-11, 17-38, 41-60(partially)

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/US2019/017731

A. CLASSIFICATION OF SUBJECT MATTER

INV. C12N15/113 A61K31/7088 A61P35/00
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)

C12N A61K A61P

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, EMBL, Sequence Search, BIOSIS, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MEI-JU SU ET AL: "Pancreatic Cancer Cell Exosome-Mediated Macrophage Reprogramming and the Role of MicroRNAs 155 and 125b2 Transfection using Nanoparticle Delivery Systems", SCIENTIFIC REPORTS, vol. 6, no. 1, 22 July 2016 (2016-07-22), XP055588271, DOI: 10.1038/srep30110 pages 2,9,10; figures 6,7 -----	1-11, 14-60, 63-66
X	WO 2016/201323 A1 (UNIV TEXAS [US]) 15 December 2016 (2016-12-15)	1-11, 14-25, 28-60, 63-66
Y	paragraphs [0087], [0088], [0103] - [0105]; claims 1,2,10,18-20,34-40; example 1 ----- -/-	26,27



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

14 May 2019

Date of mailing of the international search report

25/07/2019

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/017731

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2017/161010 A1 (CODIAK BIOSCIENCES INC [US]) 21 September 2017 (2017-09-21) claims 1,5,9,10; example 12 -----	1-9, 14-21, 28-43
A	YAQIN ZHANG ET AL: "Adipocyte-derived microvesicles from obese mice induce M1 macrophage phenotype through secreted miR-155", JOURNAL OF MOLECULAR CELL BIOLOGY, vol. 8, no. 6, 25 September 2016 (2016-09-25), pages 505-517, XP055588319, ISSN: 1674-2788, DOI: 10.1093/jmcb/mjw040 page 506, left-hand column; figures 4,5,6 page 507, right-hand column - page 509, left-hand column -----	1-11, 14-60, 63-66
Y	WO 2014/082083 A1 (CARIS SCIENCE INC [US]) 30 May 2014 (2014-05-30) claims 1,14-16 -----	26,27
A	SAMARESH SAU ET AL: "Multifunctional nanoparticles for cancer immunotherapy: A groundbreaking approach for reprogramming malfunctioned tumor environment", JOURNAL OF CONTROLLED RELEASE, vol. 274, 31 January 2018 (2018-01-31), pages 24-34, XP055588512, NL ISSN: 0168-3659, DOI: 10.1016/j.jconrel.2018.01.028 page 25, right-hand column - page 26, right-hand column -----	1-11, 14-60, 63-66
A	WO 2017/053722 A1 (IONIS PHARMACEUTICALS INC [US]) 30 March 2017 (2017-03-30) sequence 392 -----	1-11, 14-60, 63-66
A	FERNANDO ARANDA ET AL: "Trial Watch : Immunostimulatory monoclonal antibodies in cancer therapy", ONCOIMMUNOLOGY, vol. 3, no. 2, 1 February 2014 (2014-02-01), page e27297, XP055588520, DOI: 10.4161/onci.27297 tables 1,2 ----- -/--	1-11, 14-60, 63-66

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/017731

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PETER STORZ: "The crosstalk between acinar cells with Kras mutations and M1-polarized macrophages leads to initiation of pancreatic precancerous lesions", ONCOIMMUNOLOGY, vol. 4, no. 6, 22 May 2015 (2015-05-22), page e1008794, XP055588430, DOI: 10.1080/2162402X.2015.1008794 the whole document -----	1-11, 14-60, 63-66
A	NAKADA Y ET AL: "ANTISENSE OLIGONUCLEOTIDES SPECIFIC TO MUTATED K-RAS GENES INHIBIT INVASIVENESS OF HUMAN PANCREATIC CANCER CELL LINES", PANCREATO, KARGER, BASEL, CH, vol. 1, no. 4, 2001, pages 314-319, XP009006374, ISSN: 1424-3903, DOI: 10.1159/000055830 the whole document -----	1-11, 14-60, 63-66

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/017731

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2016201323 A1	15-12-2016	AU 2016275046 A1 BR 112017026467 A2 CA 2988585 A1 CN 107980004 A EA 201890006 A1 EP 3307890 A1 JP 2018520125 A KR 20180017119 A US 2018177727 A1 WO 2016201323 A1	04-01-2018 11-09-2018 15-12-2016 01-05-2018 31-05-2018 18-04-2018 26-07-2018 20-02-2018 28-06-2018 15-12-2016
WO 2017161010 A1	21-09-2017	AU 2017232498 A1 BR 112018068746 A2 CA 3017586 A1 CN 109071597 A EP 3430024 A1 JP 2019513019 A KR 20180122433 A SG 11201807401R A WO 2017161010 A1	18-10-2018 22-01-2019 21-09-2017 21-12-2018 23-01-2019 23-05-2019 12-11-2018 27-09-2018 21-09-2017
WO 2014082083 A1	30-05-2014	AU 2013347838 A1 CA 2892490 A1 EP 2922861 A1 US 2015301058 A1 WO 2014082083 A1	11-06-2015 30-05-2014 30-09-2015 22-10-2015 30-05-2014
WO 2017053722 A1	30-03-2017	AR 106135 A1 AU 2016326619 A1 BR 112018004620 A2 CA 2998382 A1 CL 2018000429 A1 CN 108513588 A CO 2018003168 A2 EP 3353328 A1 JP 2018528781 A KR 20180051626 A TW 201723176 A US 2018273577 A1 WO 2017053722 A1 ZA 201802663 B	13-12-2017 10-05-2018 25-09-2018 30-03-2017 10-08-2018 07-09-2018 20-06-2018 01-08-2018 04-10-2018 16-05-2018 01-07-2017 27-09-2018 30-03-2017 30-01-2019

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 14-16, 39, 40, 63-66(completely); 1-11, 17-38, 41-60(partially)

An extracellular vesicle comprising one or more immunomodulating component(s) that, upon contact with a macrophage, selectively repolarizes the macrophage from an M2 to an M1 phenotype, wherein the immunomodulating component inhibits the KRAS gene (such as the oligonucleotide of SEQ ID NO: 6), related methods.

- 2-9. claims: 1-11, 17-38, 41-60(all partially)

An extracellular vesicle comprising one or more immunomodulating component(s) that, upon contact with a macrophage, selectively repolarizes the macrophage from an M2 to an M1 phenotype, wherein the immunomodulating component inhibits in each separate invention one of the genes selected from the group of HRAS, NRAS, HIF1-alpha, HIF1-beta, Spl, P300, LKB1 and AMPK, related methods.

10. claims: 12, 13, 61, 62(completely); 1-11, 17-38, 41-60(partially)

An extracellular vesicle comprising one or more immunomodulating component(s) that, upon contact with a macrophage, selectively repolarizes the macrophage from an M2 to an M1 phenotype, wherein the immunomodulating component inhibits the STAT3 gene, related methods.

- 11-22. claims: 1-11, 17-38, 41-60(all partially)

An extracellular vesicle comprising one or more immunomodulating component(s) that, upon contact with a macrophage, selectively repolarizes the macrophage from an M2 to an M1 phenotype, wherein the immunomodulating component inhibits in each separate invention one of the genes selected from the group of STAT6, n-MYC, c-MYC, HCAR1, A2AB, IDO, TDO, Arginase, Glutaminase, CEBP/beta, Pi3K-gamma, and PKM2, related methods.
