

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 165687010601	<b>FOR FURTHER ACTION</b>	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US2018/046477	International filing date ( <i>day/month/year</i> ) 13 August 2018	(Earliest) Priority Date ( <i>day/month/year</i> ) 11 August 2017
Applicant SYNVITROBIO, 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 5 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 43.6bis(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. 2  
 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/US2018/046477

**Box No. 1** 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 13ter.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 13ter.1(a)).  
 on paper or in the form of an image file (Rule 13ter.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:

ISA/225 mailed on 27 August 2018. No approved electronic sequence listing was submitted in response to the ISA/225.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/046477

**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.: 15, 16  
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:

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.:

**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/US2018/046477

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC(8) - C07K 14/195; C12N 9/12; C12P 21/00 (2018.01)  
 CPC - C07K 14/195; C12N 1/06; C12N 9/1247; C12P 21/02 (2018.08)

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)

See Search History document

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

USPC - 435/69.1; 435/70.1; 435/91.5 (keyword delimited)

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

See Search History document

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	SUN et al. "Protocols for Implementing an Escherichia coli Based TX-TL Cell-Free Expression System for Synthetic Biology," Journal of Visualized Experiments, 16 September 2013 (16.09.2013), Vol. 79, Pgs. 1-14. entire document	1-5 ----- 6-14
Y	KORNBLIHTT et al. "Alternative splicing: a pivotal step between eukaryotic transcription and translation," Nature Reviews Molecular Cell Biology, 06 February 2013 (06.02.2013), Vol. 14, No. 3, Pgs. 153-165. entire document	6-12, 14
Y	WO 2017/123748 A1 (NEW ENGLAND BIOLABS, INC. et al) 20 July 2017 (20.07.2017) entire document	8, 10, 11
Y	SHIMIZU et al. "Cell-free translation reconstituted with purified components," Nature Biotechnology, 31 August 2001 (31.08.2001), Vol. 19, No. 8, Pgs. 751-755. entire document	13
Y	ROSENBLUM et al. "Engine out of the chassis: Cell-free protein synthesis and its uses," FEBS Letters, 21 January 2014 (21.01.2014), Vol. 588, Iss. 2, Pgs. 261-268. entire document	14
A	BONNER et al. "Characterization of a set of T7 RNA polymerase active site mutants," Journal of Biological Chemistry, 07 October 1994 (07.10.1994), Vol. 269, No. 40, Pgs. 25120-25128. entire document	1-14
A	GE et al. "Cell-Free Protein Expression under Macromolecular Crowding Conditions," PLoS One, 08 December 2011 (08.12.2011), Vol. 6, Iss. 12, e28707, Pgs. 1-10. entire document	1-14

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

"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

"E" earlier application or patent but published on or after the international filing date

"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

"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)

"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

"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

"&" document member of the same patent family

Date of the actual completion of the international search

30 October 2018

Date of mailing of the international search report

07 DEC 2018

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents  
 P.O. Box 1450, Alexandria, VA 22313-1450  
 Facsimile No. 571-273-8300

Authorized officer

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300  
 PCT OSP: 571-272-7774

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/046477

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2014/0315245 A1 (SUTRO BIOPHARMA, INC.) 23 October 2014 (23.10.2014) entire document	1-14