

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1157443-002813		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US 22/82601	International filing date (<i>day/month/year</i>) 30 December 2022 (30.12.2022)	(Earliest) Priority Date (<i>day/month/year</i>) 31 December 2021 (31.12.2021)	
Applicant SURROZEN OPERATING, 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 6 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. 1
☒ 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.

b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.1(a)),

☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

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.: 4-7, 10-34
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:

---Please see continuation in first extra 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 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.:
1-3, 8-9, limited to SEQ ID NOs: 121, 141, 161, 221, 241, 261, 321, 341, 361

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
IPC - INV. C07K 16/00, C07K 16/08 (2023.01)
ADD. C07K 16/34 (2023.01)

CPC - INV. C07K 16/005, C07K 16/2863

ADD. C07K 2317/24, C07K 2317/31, C07K 2317/565

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
See Search History document

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.
A	WO 2019/126399 A1 (SURROZEN, INC.) 27 June 2019 (27.06.2019) p12, ln 14-17; Claim 1; Claim 2; p3, ln 7-12; SEQ ID NO 66	1-3, 8-9
A	US 2005/0282252 A1 (SIEGEL) 22 December 2005 (22.12.2005) para [0051]; DPK9 JK4	1-3, 8-9
A	WO 2019/126398 A1 (SURROZEN, INC.) 27 June 2019 (27.06.2019) Claim 13; SEQ ID NO 133	1-3, 8-9

☐ 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

"D" document cited by the applicant in the international application

"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

25 March 2023

Date of mailing of the international search report

AUG 09 2023

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. 571-273-8300

Authorized officer

Kari Rodriguez

Telephone No. PCT Helpdesk: 571-272-4300

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Continuation of Box No. III. Observations where unity of invention is lacking.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I+, Claims 1-3, 8-9, directed to a multispecific antibody or antibody fragment. The antibody will be searched to the extent that the antibody encompasses wherein: (A) the VH1 comprises: (i) a heavy chain complementarity-determining region 1 (CDRH1) of SEQ ID NO:121, (ii) a heavy chain complementarity-determining region 2 (CDRH2) of SEQ ID NO:141, (iii) a heavy chain complementarity-determining region 3 (CDRH3) of SEQ ID NO:161; and the VL1 comprises: (iv) a light chain complementarity-determining region 1 (CDRL1) of SEQ ID NO:221, (v) a light chain complementarity-determining region 2 (CDRL2) of SEQ ID NO:241; and (vi) a light chain complementarity-determining region 3 (CDRL3) of SEQ ID NO:261, and (B) the VH2 comprises: (i) a CDRH1 of SEQ ID NO:321; (ii) a CDRH2 of SEQ ID NO:341, and (iii) a CDRH3 of SEQ ID NO:361 (note, these are the first claimed CDR sequences for the inventive antibody). The first named invention was determined based on the first claimed CDR sequences (claim 1) for the inventive antibody embodiment. This first named invention has been selected based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines. It is believed that claims 1-3, 8-9 encompass this first named invention, and thus these claims will be searched without fee to the extent that the antibody encompasses wherein: (A) the VH1 comprises: (i) a heavy chain complementarity-determining region 1 (CDRH1) of SEQ ID NO:121, (ii) a heavy chain complementarity-determining region 2 (CDRH2) of SEQ ID NO:141, (iii) a heavy chain complementarity-determining region 3 (CDRH3) of SEQ ID NO:161; and the VL1 comprises: (iv) a light chain complementarity-determining region 1 (CDRL1) of SEQ ID NO:221, (v) a light chain complementarity-determining region 2 (CDRL2) of SEQ ID NO:241; and (vi) a light chain complementarity-determining region 3 (CDRL3) of SEQ ID NO:261, and (B) the VH2 comprises: (i) a CDRH1 of SEQ ID NO:321; (ii) a CDRH2 of SEQ ID NO:341, and (iii) a CDRH3 of SEQ ID NO:361. Additional antibody(ies) comprising additional CDR sequence(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected antibody(ies) comprising additional CDR sequence(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. An exemplary election would be an antibody comprising wherein: (A) the VH1 comprises: (i) a heavy chain complementarity-determining region 1 (CDRH1) of SEQ ID NO:121, (ii) a heavy chain complementarity-determining region 2 (CDRH2) of SEQ ID NO:141, (iii) a heavy chain complementarity-determining region 3 (CDRH3) of SEQ ID NO:161; and the VL1 comprises: (iv) a light chain complementarity-determining region 1 (CDRL1) of SEQ ID NO:221, (v) a light chain complementarity-determining region 2 (CDRL2) of SEQ ID NO:241; and (vi) a light chain complementarity-determining region 3 (CDRL3) of SEQ ID NO:261, and (B) the VH2 comprises: (i) a CDRH1 of SEQ ID NO:321; (ii) a CDRH2 of SEQ ID NO:341, and (iii) a CDRH3 of SEQ ID NO:363 (claim 1).

The inventions listed as Group I+ do not relate to a single special technical feature under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special technical features

The inventions of Groups I+ each include the special technical feature of a unique amino acid sequence. Each amino acid sequence comprises a unique peptide, and is considered a distinct technical feature.

Common technical features

No technical features are shared between the antibody amino acid sequences in each of Group I+ inventions and, accordingly, these inventions lack unity a priori.

Additionally, even if Group I+ inventions were considered to share the technical features of including:

a multispecific antibody or antibody fragment comprising at least: (A) a first antigen-binding region which specifically binds to frizzled class receptor 4 (Fzd4) and comprises a first heavy chain variable domain (VH1) and a first light chain variable domain (VL1), (B) a second antigen-binding region which specifically binds to low density lipoprotein receptor-related protein 5 and/or 6 (LRP5 and/or LRP6) and comprises at least a second heavy chain variable domain (VH2), wherein: (A) the VH1 comprises: CDRH1, CDRH2 and CDRH3 sequences, and the VL1 comprises: CDRL1, CDRL2 and CDRL3 sequences, and (B) the VH2 comprises: CDRH1, CDRH2 and CDRH3 sequences,

these shared technical features are previously disclosed by US 2021/0292422 A1 to Surrozen, Inc., (hereinafter 'Surrozen').

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Continuation of Box No. III. Observations where unity of invention is lacking.

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Surrozen teaches a multispecific antibody or antibody fragment comprising at least: (A) a first antigen-binding region which specifically binds to frizzled class receptor 4 (Fzd4) and comprises a first heavy chain variable domain (VH1) and a first light chain variable domain (VL1), (B) a second antigen-binding region which specifically binds to low density lipoprotein receptor-related protein 5 and/or 6 (LRP5 and/or LRP6) and comprises at least a second heavy chain variable domain (VH2), wherein: (A) the VH1 comprises: CDRH1, CDRH2 and CDRH3 sequences, and the VL1 comprises: CDRL1, CDRL2 and CDRL3 sequences, and (B) the VH2 comprises: CDRH1, CDRH2 and CDRH3 sequences (Claim 1 - 'A multispecific Wnt surrogate molecule, wherein the Wnt surrogate molecule comprises: (i) a plurality of regions that each specifically bind to a set of one or more Frizzled (Fzd) receptor epitopes (Fzd binding regions), wherein at least two Fzd binding regions bind to different sets of one or more Fzd receptor epitopes; and (ii) one or more regions that specifically bind to a Low-density lipoprotein (LDL) receptor-related protein 5 (LRP5) and/or a LDL receptor-related protein 6 (LRP6) (LRP5/6 binding regions).'; para [0020] - 'In some embodiments, at least one of the Fzd binding regions comprises one or more antigen-binding fragments of an antibody. In some embodiments, the one or more antigen-binding fragments are selected from the group consisting of: IgG, scFv, Fab, and VHH or sdAbs'; para [0083] - 'In this regard, an antigen-binding fragment of the herein described antibodies may comprise 1, 2, 3, 4, 5, or all 6 CDRs of a VH and VL sequence set forth herein from antibodies that bind one or more Fzd receptors or LRP5 and/or LRP6. In particular embodiments, an antigen-binding fragment may comprise all three VH CDRs or all three VL CDRs. Similarly, an antigen-binding fragment thereof may comprise all three CDRs of a VHH or sdAb'; para [0061] - 'FIGS. 12A-12E. The 2:2 tetravalent bispecific molecules, consisting of the two F1 and two L2 binding arms, are highly potent in inducing Wnt signaling.').

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

Therefore, Group I+ inventions lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.

continuation of item 4 above: claims 4-7, 10-34 are held unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).