



(51) International Patent Classification:

C12N 9/48 (2006.01) A61K 38/48 (2006.01)
C12N 15/62 (2006.01) A61P 31/14 (2006.01)

(21) International Application Number:

PCT/SG2022/050775

(22) International Filing Date:

27 October 2022 (27.10.2022)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

10202112143T 01 November 2021 (01.11.2021) SG

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG,

(54) Title: RECOMBINANT/FUSION POLYPEPTIDES COMPRISING MUTATED ANGIOTENSIN CONVERTING ENZYME 2 (ACE2)

Higher affinity ACE2 by computational prediction

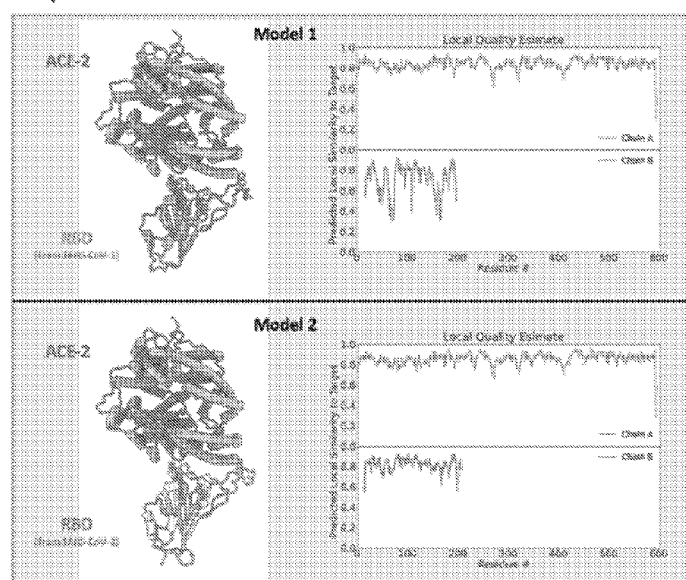


Fig. 1A

(57) Abstract: The invention relates to recombinant mutated angiotensin converting enzyme 2 (ACE2) comprising one or more amino acid substitutions at amino acid positions T27, F28, K31, H34, Y41 and Q42 which have improved binding affinity to SARS-CoV-1 and/or SARS-CoV-2. It also relates to combinatorial mutant ACE2 comprising T27Y/K31 H/H34A, T27YZ K31 H/H34V and T27Y/K31 Y/H34V and the use of said mutant ACE2 for treating and preventing coronavirus infection.



NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

- (84) Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *of inventorship (Rule 4.17(iv))*

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:

15 June 2023 (15.06.2023)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2022/050775

A. CLASSIFICATION OF SUBJECT MATTER

C12N 9/48 (2006.01) C12N 15/62 (2006.01) A61K 38/48 (2006.01) A61P 31/14 (2006.01)

According to International Patent Classification (IPC)

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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)

DATABASES: FAMPAT, MEDLINE, EMBASE, BIOSIS

SEARCH TERMS: SARS-CoV-1, SARS-CoV-2, COVID-19, Coronavirus, T27, F28, K31, H34, Y41, Q42, ACE2, Angiotensin Converting Enzyme 2 and related terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TANAKA, S. ET AL., A recombinant 'ACE2 Triple Decoy' that traps and neutralizes SARS-CoV-2 shows enhanced affinity for highly transmissible SARS-CoV-2 variants. <i>bioRxiv</i> , 9 March 2021 [Retrieved on 2023-04-24] <DOI: 10.1101/2021.03.09.434641> (Whole document especially Figures 1, 2E and S1)	1-31
X	HIGUCHI, Y. ET AL., Engineered ACE2 receptor therapy overcomes mutational escape of SARS-CoV-2. <i>Nature Communications</i> , 21 June 2021, Vol. 12, No. 1, pages 3802: 1-13 [Retrieved on 2023-04-24] <DOI: 10.1038/S41467-021-24013-Y> (Figures 1c, 5d; Supplementary Figures 2, 7 and 9-10)	1-31

☒ 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

24/04/2023

(day/month/year)

Date of mailing of the international search report

11/05/2023

(day/month/year)

Name and mailing address of the ISA/SG

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2022/050775

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GLASGOW, A. ET AL., Engineered ACE2 receptor traps potentially neutralize SARS-CoV-2. <i>Proceedings of the National Academy of Sciences</i> , 22 October 2020, Vol. 117, No. 45, pages 28046-28055 [Retrieved on 2023-04-24] <DOI: 10.1073/PNAS.2016093117> (Whole document especially Figures 2, 4; Supplemental experimental methods; Tables S3-S4)	1-31
X	WO 2021/183404 A1 (PLANET BIOTECHNOLOGY, INC.) 16 September 2021 (Paragraphs 0002, 0013, 0016, 0022, 0032, 0034, 0152, 0163-0164, 0167, 0173; Examples; Tables 5, 10; SEQ ID NO: 18)	1-31
X	WO 2021/188576 A1 (THE BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS.) 23 September 2021 (Page 2, Line 13 to Page 3, Line 18; Page 25, Lines 15-16; Tables 1-4; Examples 6-7; Figures 11, 32-33)	1-31

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2022/050775

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 13~~ter~~.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:

Although a sequence listing has been filed, it was not used for the purposes of this search.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/SG2022/050775

Note: This Annex lists known patent family members relating to the patent documents cited in this International Search Report. This Authority is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2021/183404 A1	16/09/2021	US 2022002699 A1	06/01/2022
WO 2021/188576 A1	23/09/2021	BR 112022018527 A2 KR 20220154796 A CA 3174683 A1 EP 4121170 A1 AU 2021239879 A1	25/10/2022 22/11/2022 23/09/2021 25/01/2023 29/09/2022