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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, MU, MW, MX, MY, MZ, NA, NG, 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.

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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

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))

(88) Date of publication of the international search report:

02 August 2024 (02.08.2024)

(54) Title: A T CELL RECEPTOR RECOGNIZING A HER2 MUTATION PRESENTED ON HLA-A*02:01 AND METHODS OF USE

(57) Abstract: This disclosure provides for engineered T cell Receptors (TCRs), cells comprising the TCRs, and methods of making and using the TCRs. The current disclosure relates to TCRs that specifically recognize a particular HER2 mutation, such as TCRs that recognize the Y772dupYVMA mutation in HER2 presented on HLA-A*02:01. Accordingly, aspects of the disclosure relate to an engineered T-cell Receptors (TCRs), nucleic acids encoding the TCRs, and cells comprising the nucleic acids and TCRs with respect to this antigen. Also provided are compositions comprising the cells, nucleic acids, or engineered TCRs of the disclosure, methods of making the cells and methods of using the embodiments of the disclosure for therapeutic treatments.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2023/082549

A. CLASSIFICATION OF SUBJECT MATTER IPC: A61K 35/17 (2024.01); C07K 15/725 (2024.01) CPC: A61K 39/4632; A61K 39/464406; A61K 39/4611; A61K 39/4622; C07K 14/7051 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	US 8,143,376 B2 (BOULTER et al.) 27 March 2012 (27.03.2012) entire document	1-4, 14-17, 27-31
A	WO 2021/086991 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 06 May 2021 (06.05.2021) entire document	1-4, 14-17, 27-31
A	US 2022/0213167 A1 (GIGAMUNE INC.) 07 July 2022 (07.07.2022) entire document	1-4, 14-17, 27-31
A	WO 2021/173756 A1 (BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM) 02 September 2021 (02.09.2021) entire document	1-4, 14-17, 27-31
A	WO 2022/098845 A1 (BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM et al.) 12 May 2022 (12.05.2022) entire document	1-4, 14-17, 27-31
☐ 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 10 April 2024 (10.04.2024)		Date of mailing of the international search report 04 June 2024 (04.06.2024)
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 MATOS TAINA Telephone No. 571-272-4300

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International application No.

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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:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2023/082549**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.: **5-10, 18-23, 32-44, 51-54, 56-142, 144-185, 187-198**
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:

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 examined, the appropriate additional examination fees need to be paid.

Group I: claims 1-4, 14-17, and 27-31 are drawn to polypeptides and engineered T-cell Receptors.

Group II: claims 45-50, 55, and 143 are drawn to peptides.

The inventions listed in Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The special technical features of Group I, polypeptides and engineered T-cell Receptors, are not present in Group II; the special technical features of Group II, peptides, are not present in Group I.

Additionally, even if Groups I-II were considered to share the technical features of a peptide comprising a sequence, these shared technical features do not represent a contribution over the prior art.

WO 2022/098845 A1 to Board of Regents, The University of Texas System et al. (hereinafter, "Texas") teaches a peptide comprising a sequence (a polypeptide comprising an antigen binding variable region comprising the amino acid sequence of a CDR3; Para. [0006]).

The inventions listed in Groups I-II therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.

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Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first 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.: **1-4, 14-17, 27-31**

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.