



(51) International Patent Classification:

C07K 14/725 (2006.01) A61K 35/17 (2015.01)

(21) International Application Number:

PCT/US2019/060570

(22) International Filing Date:

08 November 2019 (08.11.2019)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/758,397 09 November 2018 (09.11.2018) US

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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, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, 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, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

(54) Title: T CELL RECEPTORS SPECIFIC FOR MESOTHELIN AND THEIR USE IN IMMUNOTHERAPY

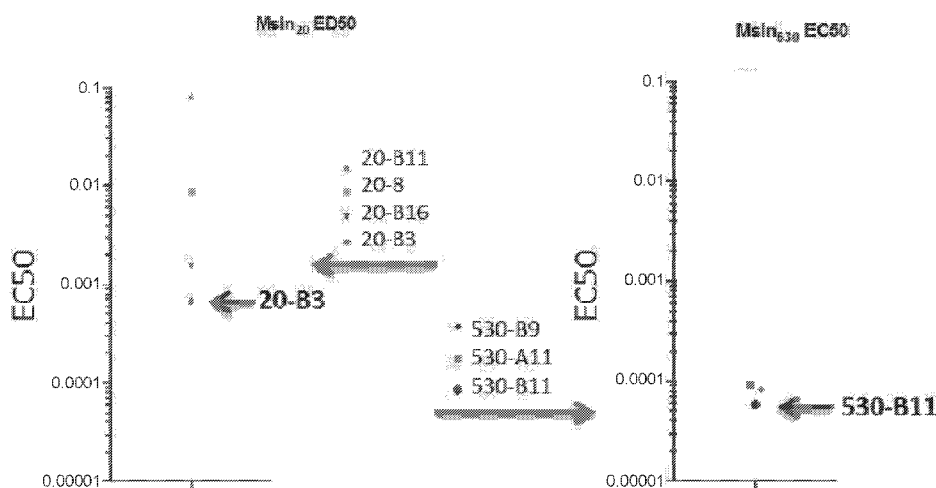


FIG. 6C

(57) Abstract: Binding proteins specific for Msln20-28 or Msln530-538 peptides are provided herein. Polynucleotides encoding the binding proteins, as well as compositions and recombinant host cells comprising the binding proteins or polynucleotides are also provided. The compositions and recombinant host cells may be used to treat a subject having mesothelioma, pancreatic cancer, ovarian cancer, lung cancer, a cancer wherein an Msln20-28 peptide is expressed on a tumor cell of the cancer, or a cancer wherein an Msln530-538 peptide is expressed on a tumor cell of the cancer.



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, 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).

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:

23 July 2020 (23.07.2020)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/060570

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K14/725 A61K35/17
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)
C07K A61K

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, Sequence Search, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	INGUNNN M. STROMNES ET AL: "T Cells Engineered against a Native Antigen Can Surmount Immunologic and Physical Barriers to Treat Pancreatic Ductal Adenocarcinoma", CANCER CELL, vol. 28, no. 5, 1 November 2015 (2015-11-01), pages 638-652, XP055382318, US ISSN: 1535-6108, DOI: 10.1016/j.ccell.2015.09.022 page 648, column 1 - column 2 figures 6,7 ----- -/-	1-8,10, 15-21, 38-97



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

6 March 2020

Date of mailing of the international search report

25/06/2020

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/060570

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 2018/129270 A1 (HUTCHINSON FRED CANCER RES [US]) 12 July 2018 (2018-07-12) paragraphs [0010], [0021], [0062] figure 4 -----	1-8,10, 15-21, 38-97
X	WO 2017/112944 A1 (HUTCHINSON FRED CANCER RES [US]; ADAPTIVE BIOTECHNOLOGIES CORP [US]) 29 June 2017 (2017-06-29) page 6, line 4 - line 10 page 6, line 19 - line 30 figure 3; examples 1-2 -& DATABASE EPO Proteins [Online] 27 April 2018 (2018-04-27), "Sequence 17 from Patent W02017112944.", XP002798113, retrieved from EBI accession no. EPOP:LP835765 Database accession no. LP835765 sequence -& DATABASE Geneseq [Online] 24 August 2017 (2017-08-24), "T cell receptor (TCR) beta chain variable domain, SEQ ID 15.", XP002798114, retrieved from EBI accession no. GSP:BEA52192 Database accession no. BEA52192 sequence -----	1-8,10, 15-21, 38-97
A	THOMAS M. SCHMITT ET AL: "Abstract A51: High-throughput method identifies rare, high-affinity, thymus-vetted T cell receptors (TCRs) for clinical translation", ENGINEERED IMMUNE CELLS AND SYNTHETIC IMMUNOTHERAPY, 1 September 2018 (2018-09-01), pages A51-A51, XP055672591, DOI: 10.1158/2326-6074.TUMIMM17-A51 the whole document -----	1-8,10, 15-21, 38-97
A	DATABASE Geneseq [Online] 17 May 2018 (2018-05-17), "Transgene construction related TCR construct encoding gene SEQ 59.", XP002798115, retrieved from EBI accession no. GSN:BFE48571 Database accession no. BFE48571 sequence ----- -/--	85-97

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/060570

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE EPO Proteins [Online] 30 June 2017 (2017-06-30), "Sequence 54 from Patent W02017089768.", XP002798116, retrieved from EBI accession no. EPOP:MS816951 Database accession no. MS816951 sequence -----	1-8,10, 15-21, 38-97

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/060570

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.:

3-8, 85-97(completely); 1, 2, 10, 15-21, 38-84(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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 3-8, 85-97(completely); 1, 2, 10, 15-21, 38-84(partially)

TCR comprising TCR a-chain variable domain: Seq ID No:102 and b-chain variable domain: Seq ID No:101 or variants, composition, polynucleotide, expression vector, host cell, unit dose, method of treatment, second medical use for cancer therapy

2. claims: 9, 11-14(completely); 1, 2, 10, 15-21, 38-84(partially)

TCR comprising TCR a-chain variable domain: Seq ID No:100 and b-chain variable domain: Seq ID No:99 or variants, composition, polynucleotide, expression vector, host cell, unit dose, method of treatment, second medical use for cancer therapy

3. claims: 24, 26-29(completely); 22, 23, 25, 31, 36-84(partially)

TCR comprising TCR a-chain variable domain: Seq ID No:96 and b-chain variable domain: Seq ID No:95 or variants, composition, polynucleotide, expression vector, host cell, unit dose, method of treatment, second medical use for cancer therapy

4. claims: 30, 32-35(completely); 22, 23, 25, 31, 36-84(partially)

TCR comprising TCR a-chain variable domain: Seq ID No:98 and b-chain variable domain: Seq ID No:97 or variants, composition, polynucleotide, expression vector, host cell, unit dose, method of treatment, second medical use for cancer therapy

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/060570

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2018129270 A1	12-07-2018	CA 3049244 A1	12-07-2018
		CN 110121336 A	13-08-2019
		EP 3565535 A1	13-11-2019
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WO 2017112944 A1	29-06-2017	EP 3394092 A1	31-10-2018
		US 2018369280 A1	27-12-2018
		WO 2017112944 A1	29-06-2017
