(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 July 2020 (16.07.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/146902 A3

(51) International Patent Classification:
C07K 16/18 (2006.01) *A61P 13/12* (2006.01)
A61P 35/00 (2006.01) *A61P 13/08* (2006.01)
C07K 14/71 (2006.01) *A61P 7/00* (2006.01)

(21) International Application Number:
PCT/US2020/013410

(22) International Filing Date:
13 January 2020 (13.01.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/791,661 11 January 2019 (11.01.2019) US
PCT/US2019/019566
26 February 2019 (26.02.2019) US
PCT/US2019/021556
11 March 2019 (11.03.2019) 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, 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, 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, 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))*

(88) Date of publication of the international search report:
27 August 2020 (27.08.2020)

(54) Title: ANTI-VARIABLE MUC1* ANTIBODIES AND USES THEREOF

(57) Abstract: The present application discloses an antibody, or fragment thereof, for the diagnosis, treatment or prevention of cancers wherein the antibody specifically binds to the PSMGFR peptide (SEQ ID NO:2) or a fragment thereof of the peptide.

WO 2020/146902 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/13410

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C07K 16/28, A61P 35/00, C07K 14/71, A61P 13/12, A61P 13/08, A61P 7/00 (2020.01)

CPC - C07K 16/3092, A61K 39/00117, A61K 39/0011, C07K 2317/622, C07K 2317/34, C07K 2317/52, C07K 2319/02, A61K 2039/5156, C07K 2317/24, C07K 14/4727, A61K 2039/505, C07K 16/2863, 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.
X --- Y --- A	US 2018/0112007 A1 (MINERVA BIOTECHNOLOGIES CORPORATION) 26 April 2018 (26.04.2018) Abstract; Claim 40; para [0002]; para [0007] - [0009]; para [0028]; para [0048]; para [0074]; para [0097]; para [0165]; para [0170]; para [0189]; SEQ ID NO:2; SEQ ID NO:131	1-2, 5-10, 12, 17, 19, (35, 36)/(1-2, 5-10, 12, 17, 19) --- 3, 11, 13-15, (35, 36)/(3, 11, 13-15) --- 18
Y	US 2017/0204191 A1 (BAMDAD et al.) 20 July 2017 (20.07.2017) Abstract; para [0010]; para [0052]	3, 11, 13-15, (35, 36)/(3, 11, 13-15)
Y	WO 2014/028668 A2 (MINERVA BIOTECHNOLOGIES CORPORATION) 20 February 2014 (20.02.2014) Abstract; para [0064-0065]; para [0068]	3, 15, (35, 36)/(3, 15)
A	US 2016/0257758 A1 (SORRENTO THERAPEUTICS, INC.) 8 September 2016 (08.09.2016) Claim 1; SEQ ID NO:23	18
A	WO 2010/042562 A2 (MINERVA BIOTECHNOLOGIES CORPORATION) 15 April 2010 (15.04.2010) Claim 20; para [00362]; SEQ ID NO:149; SEQ ID NO:318	18

☒ 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	Date of mailing of the international search report
17 June 2020	23 JUL 2020
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 Lee Young Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/13410

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2009/103969 A1 (QUEEN MARY & WESTFIELD COLLEGE) 27 August 2009 (27.08.2009) Claim 1	18
A	WO 2001/057277 A2 (MOLECULAR DYNAMICS INC et al.) 9 August 2001 (09.08.2001) Claim 27; SEQ ID NO:36113	18

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/13410

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.: 50-58, 67
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, 5-15, 17-19, (35, 36)(in part) limited to the first named antibody as described in extra sheet

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
Information on patent family members

International application No.
PCT/US 20/13410

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 1-49, 59-66, directed to an antibody, or fragment thereof, for the diagnosis, treatment or prevention of cancers. The antibody will be searched to the extent that the antibody specifically binds to the PSMGFR peptide (SEQ ID NO:2), or a fragment thereof comprising the N-10 peptide (SEQ ID NO:3), N-19 peptide (SEQ ID NO:4), N-23 peptide (SEQ ID NO:5), N-26 peptide (SEQ ID NO:6), which interacts with a peptide comprising conformational epitope SVSDV (SEQ ID NO:1751) and FPFS (SEQ ID NO:1747) within N-26 sequence ISDVSVSDVPFPFSAQSGA (SEQ ID NO:6), wherein mutation or deletion of FPFS (SEQ ID NO:1747) destroys binding of the antibody or fragment thereof to the N-26 peptide (note, these are the first claimed epitopes for binding antibody of the first invention), further wherein in said antibody heavy chain CDR1 comprises consensus sequence 90% identical to sequence: F at position 1, T at position 2, F at position 3, S at position 4, T, at position 5, Y at position 6, A, at position 7, M at position 8 and S at position 9; heavy Chain CDR2 comprises consensus sequence 90% identical to sequence: T at position 1, I at position 2, I at position 3, G at position 5, G at position 6, T at position 9, Y at position 10, Y at position 11, P at position 12 and DSVKG for positions 13-17; heavy chain CDR3 comprises consensus sequence 90% identical to sequence:_ G, at position 2, G at position 4, Y at position 7, D at position 12, A at position 14, and Y at position 15; light chain CDR1 comprises consensus sequence 90% identical to sequence: K at position 1, A at position 2, S at position 3, K at position 4, S at position 5, L at position 6, L at position 7, T at position 10, Y at position 15, and I, at position 16; light Chain CDR2 comprises consensus sequence 90% identical to sequence: L at position 1, A at position 2, S at position 3, N at position 4, L at position 5, E at position 6, and S at position 7; and light chain CDR3 comprises consensus sequence 90% identical to sequence: Q at position 1, H at position 2, S, at position 3, R, at position 4, E, at position 5, L at position 6, P at position 7, F at position 8 and T at position 9. It is believed that claims 1-3, 5-15, 17-19, (35, 36)(in part) encompass this first named invention, and thus these claims will be searched without fee to the extent that the antibody specifically binds to the PSMGFR peptide (SEQ ID NO:2) and fragments containing conformational epitope SVSDV (SEQ ID NO:1751) and FPFS (SEQ ID NO:1747) within N-26 sequence ISDVSVSDVPFPFSAQSGA (SEQ ID NO:6), wherein mutation or deletion of FPFS (SEQ ID NO:1747) destroys binding of the antibody or fragment thereof to the N-26 peptide, further wherein in said antibody heavy chain CDR1 comprises consensus sequence 90% identical to sequence: F at position 1, T at position 2, F at position 3, S at position 4, T, at position 5, Y at position 6, A, at position 7, M at position 8 and S at position 9; heavy Chain CDR2 comprises consensus sequence 90% identical to sequence: T at position 1, I at position 2, I at position 3, G at position 5, G at position 6, T at position 9, Y at position 10, Y at position 11, P at position 12 and DSVKG for positions 13-17; heavy chain CDR3 comprises consensus sequence 90% identical to sequence:_ G, at position 2, G at position 4, Y at position 7, D at position 12, A at position 14, and Y at position 15; light chain CDR1 comprises consensus sequence 90% identical to sequence: K at position 1, A at position 2, S at position 3, K at position 4, S at position 5, L at position 6, L at position 7, T at position 10, Y at position 15, and I, at position 16; light Chain CDR2 comprises consensus sequence 90% identical to sequence: L at position 1, A at position 2, S at position 3, N at position 4, L at position 5, E at position 6, and S at position 7; and light chain CDR3 comprises consensus sequence 90% identical to sequence: Q at position 1, H at position 2, S, at position 3, R, at position 4, E, at position 5, L at position 6, P at position 7, F at position 8 and T at position 9. Additional antibodies binding fragments and subsequences of PSMGFR comprising additional epitopes, or antibody derivatives will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected antibodies. 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 which interacts with a peptide comprising conformational epitope ASRYNLT (SEQ ID NO:1745), SVSDV (SEQ ID NO:1751), and FPFS (SEQ ID NO:1747) within the N-19 sequence ASRYNLT ISDVSVSDVPFPFSAQSGA (SEQ ID NO:4), wherein mutation or deletion of ASRYNLT (SEQ ID NO: 1745) destroys binding of the antibody or fragment thereof to the N-19 peptide (SEQ ID NO:4), further wherein in said antibody is 25E6 (claims 1, 2, 4-14, 16, 31, 32, (35, 36)(in part)).

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 Group I+ each include the special technical feature of a unique amino acid sequence. Each amino acid sequence encodes a unique antibody polypeptide, and is considered a distinct technical feature.

Common technical features

No technical features are shared between the antibody amino acid sequences of Groups I+ and, accordingly, these groups lack unity a priori.

Additionally, even if Group I+ inventions were considered to share the technical features of including: an antibody, or fragment thereof, for the diagnosis, treatment or prevention of cancers wherein the antibody specifically binds to the PSMGFR peptide or a fragment thereof, these shared technical features are previously disclosed by US 2017/0204196 A1 to Minerva Biotechnologies Corporation, (hereinafter 'Minerva').

------please see continuation on next extra sheet----------

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

------continued from previous sheet----------

Minerva teaches an antibody for the diagnosis, treatment or prevention of cancers wherein the antibody specifically binds to the PSMGFR peptide (Abstract - 'The present application discloses anti-NME antibodies and their use in treating or preventing diseases.'; para [0005] - 'The present application is directed to a method of treating or preventing cancer in a subject, comprising administering to the subject an antibody made against a member of the NME family. The NME family may be NME7 family. The antibody may bind to NME7. The antibody may bind to NME7-AB or NME-AB-like protein. The antibody may bind to NME7-X1. The antibody may inhibit binding between NME7 and its cognate binding partner. The cognate binding partner may be MUC1*. The cognate binding partner may be PSMGFR portion of the MUC1* extracellular domain.'; para [0070] - 'B) various cancer cell lines are probed for the expression of cleaved form MUC1* using anti-PSMGFR antibody.').

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 50-58, 67 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).

NOTE, the following errors in claim language are noted.

Claim 2 identifies C-5 peptide as SEQ ID NO:825 whereas SEQ ID NO:825 corresponds to C-10 according to sequence listing. For this application, claim 2 is reconstrued to replace C-5 peptide with C-10 peptide.

Claims 3 and 4 recite SEQ ID NO:1747 epitope as FPSA whereas SEQ ID NO:1747 corresponds to FPFS according to sequence listing. For this application, claims 3 and 4 are reconstrued to replace FPSA epitope with FPFS (SEQ ID NO:1747).

Claims 4 and 19 reciting mutation or deletion of ASRYNLT (SEQ ID NO: 1745) destroys binding of the antibody or fragment thereof to the N-26 peptide, is objected to because N-26 peptide does not contain ASRYNLT (SEQ ID NO: 1745). For this application, claims 4 and 19 are reconstrued to replace N-26 peptide with N-19 peptide that does contain ASRYNLT (SEQ ID NO: 1745).