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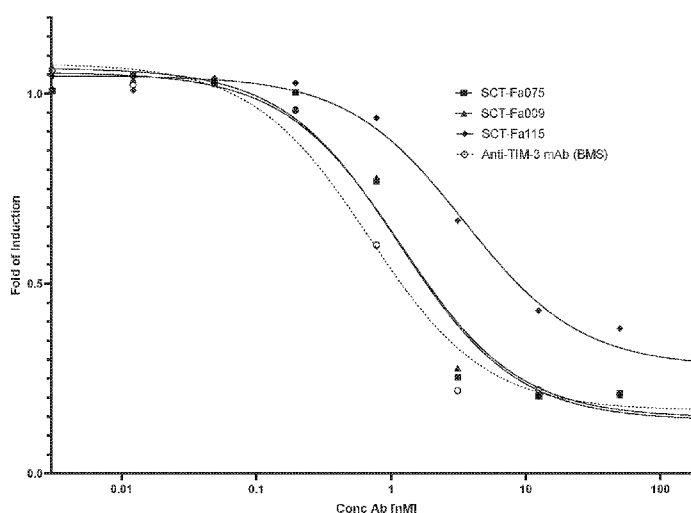
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(81) **Designated States** (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, 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.

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(54) Title: ANTI-TIM-3 ANTIBODIES

FIG. 1



Anti-TIM-3 mAb	EC50 (nM)
SCT-Fa009	1.12
SCT-Fa075	1.15
SCT-Fa115	3.48
Anti-TIM-3 mAb (BMS)	0.69

(57) **Abstract:** Provided are antibodies that specifically recognize T-cell immunoglobulin and mucin-domain containing-3 (TIM-3) protein. Specifically, the disclosure provides antibodies that bind human TIM-3 (SEQ ID NO:1) with the complementarity determining regions (CDRs) sequences of heavy chain variable (VH) region and light chain variable (VL) region sequences of each antibody disclosed. Further disclosed are pharmaceutical compositions comprising the antibodies for using in the methods for treating 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).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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))*

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/38997

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 39/395; A61K 39/00; A61K 39/42; C12P 21/08; C07K 16/00 (2020.01)

CPC - A61K 2039/505; C07K 16/28; C07K 2317/24; C07K 2317/565; C07K 16/24; C07K 16/10; C07K 16/1009; C07K 2317/60; C07K 2317/56; C07K 16/18

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 2013/0022623 A1 (KARSUNKY et al.) 24 January 2013 (24.01.2013), Abstract, para [0011], [0012], [0018], [0019], [0033], [0081], [0217], and SEQ ID NO: 122	1-2, 4-5, 7-8, 10
A	US 2012/0275996 A1 (Hsieh) 01 November 2012 (01.11.2012), Abstract, para [0088], [0107], and SEQ ID NO: 95 (122 a.a.), the region between amino acid residues 97-111	1-2, 4-5, 7-8, 10
A	WO 2018/153366 A1 (JIANGSU HENGRUI MEDICINE CO., LTD. et al.) 30 August 2018 (30.08.2018), Abstract; and pg 18, ln 23, SEQ ID NO: 6	1-2, 4-5, 7-8, 10
A	WO 2018/071910 A2 (CELLERANT THERAPEUTICS, INC.) 19 April 2018 (19.04.2018), Abstract; para [0196], and SEQ ID NO: 58	1-2, 4-5, 7-8, 10
A	HE et al., TIM-3, a promising target for cancer immunotherapy. Onco Targets Ther. 2018, Vol. 11, p. 7005-7009. Entire documentation especially Abstract; pg 7005, para 1, para 2, and para 3; pg 7006, col 2, para 1, para 2, and para 4; pg 7007, Table 1; and pg 7008, Table 2	1-2, 4-5, 7-8, 10
P,A	WOLF et al., TIM3 comes of age as an inhibitory receptor. Nat Rev Immunol. 2020, Vol. 20(3), p. 173-185. Epub 2019 Nov 01. Entire documentation especially Abstract; and pg 174, Fig 1	1-2, 4-5, 7-8, 10

☐ 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

16 November 2020

Date of mailing of the international search report

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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:
 - ☒ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☒ furnished subsequent to the international filing date for the purposes of international search only:
 - ☒ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
2. ☒ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

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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.: 11
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 searched, the appropriate additional search fees must be paid.

Groups I+, claims 1-10, directed to an antibody that binds human TIM-3 (SEQ ID NO:1) comprising a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3; or comprising a heavy-chain (VH) amino acid sequence and a light-chain (VL) amino acid sequence. The HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 will be searched to the extent that the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 having the amino acid amino acid sequence of SEQ ID NO: 369, SEQ ID NO:373, SEQ ID NO:374, SEQ ID NO:375, SEQ ID NO:376, and SEQ ID NO:377, respectively; and the heavy-chain (VH) amino acid sequence and the light-chain (VL) amino acid sequence will be searched to the extent that the heavy-chain (VH) having the amino acid sequence of SEQ ID NO: 12 and the light-chain (VL) having the amino acid sequence of SEQ ID NO: 241 (for antibody SCT-Fa009) (Specification: pg 49, Table 2, SCT-Fa009; pg 55, Table 3, SCT-Fa009). *****Continued in the 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 (in part), 2, 4 (in part), 5, 7 (in part), 8, and 10 / 1 (in part), 2, 4 (in part), 5, 7 (in part), 8, limited to SEQ ID NOs: 1, 12, 241, 369, 373-377

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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Continuation of:
Box No III (unlty of invention is lacking)

(Continuation of Groups I+) It is believed that claims 1(in part), 2, 4 (in part), 5, 7(in part), 8, and 10/[1(in part), 2, 4(in part), 5, 7(in part), 8] encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 having the amino acid amino acid sequence of SEQ ID NO: 369, SEQ ID NO:373, SEQ ID NO:374, SEQ ID NO:375, SEQ ID NO:376, and SEQ ID NO:377, respectively; and the heavy-chain (VH) having the amino acid sequence of SEQ ID NO: 12 and the light-chain (VL) having the amino acid sequence of SEQ ID NO: 241. Applicants must specify the claims that encompass any additionally elected HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 as well as associated heavy-chain (VH) amino acid sequence and a light-chain (VL) amino acid sequence. 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 the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 having the amino acid amino acid sequence of SEQ ID NO: 363, SEQ ID NO:492, SEQ ID NO:490, SEQ ID NO:366, SEQ ID NO:367, and SEQ ID NO:493, respectively; and the heavy-chain (VH) having the amino acid sequence of SEQ ID NO: 74 and the light-chain (VL) having the amino acid sequence of SEQ ID NO: 326 (for antibody SCT-Fa075) (Specification: Table 2, pg 51, SCT-Fa075; Table 3, pg 59, SCT-Fa075) [claims 1(in part), 3, 4 (in part), 6, 7(in part), 9, and 10/[1(in part), 3, 4(in part), 6, 7(in part), 9]].

The inventions listed as Groups I+ 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:

Special Technical Feature

Among Groups I+, each SEQ ID NO represents a structurally different peptide sequence.

Common Technical Features

The inventions of Groups I+ share the technical features of an antibody that binds human TIM-3 (SEQ ID NO:1) comprising: a) a HCDR1 having the amino acid sequence of a specified sequence, a HCDR2 having the amino acid sequence of a specified sequence, a HCDR3 having the amino acid sequence of a specified sequence, a LCDR1 having the amino acid sequence of a specified sequence, a LCDR2 having the amino acid sequence of a specified sequence, and a LCDR3 having the amino acid sequence of a specified sequence (part of claim 1); or
--an antibody that binds human TIM-3 (SEQ ID NO:1) comprising: a) a heavy-chain (or VH) comprising the amino acid sequence of a specified sequence and a light-chain (or VL) comprising the amino acid sequence of a specified sequence (part of claim 4 or part of claim 7).

Therefore, the common technical features shared by inventions of Groups I+ can be covered by:

An antibody that binds human TIM-3 (SEQ ID NO:1) comprising: a) a HCDR1 having the amino acid sequence of a specified sequence, a HCDR2 having the amino acid sequence of a specified sequence, a HCDR3 having the amino acid sequence of a specified sequence, a LCDR1 having the amino acid sequence of a specified sequence, a LCDR2 having the amino acid sequence of a specified sequence, and a LCDR3 having the amino acid sequence of a specified sequence (part of claim 1);
--wherein the antibody comprising a heavy-chain (or VH) comprising the amino acid sequence of a specified sequence and a light-chain (or VL) comprising the amino acid sequence of a specified sequence (part of claim 4 or part of claim 7).

However, these shared technical features do not represent a contribution over prior art as being anticipated by US 2013/0022623 A1 to KARSUNKY et al. (hereinafter 'Karsunky') as follows:

Karsunky discloses an antibody that binds human TIM-3 (SEQ ID NO:1) (Abstract - 'antibodies specific for TIM3 that can be used to detect cancer cells'; para [0217] - 'the anti-TIM3 antibody binds to TIM3 from a human'; para [0081] - 'T cell Immunoglobulin- and Mucin domain-containing molecule 3 (TIM3)...the human sequences can be found at ... Uniprot accession number Q8TDQ0 (SEQ ID NO:122)', wherein SEQ ID NO: 122 is 100% identical to the claimed SEQ ID NO: 1) comprising:

a) a HCDR1 having the amino acid sequence of a specified sequence, a HCDR2 having the amino acid sequence of a specified sequence, a HCDR3 having the amino acid sequence of a specified sequence (para [0011]-[0012] - 'internalizing TIM3-specific antibody competes for binding with... an antibody having... complementarity determining region (CDR) sequences of ... heavy chain CDR sequences of SEQ ID NOs:3-5', wherein 'heavy chain CDR sequences of SEQ ID NOs:3-5' comprising 'a HCDR1 having the amino acid sequence of a specified sequence, a HCDR2 having the amino acid sequence of a specified sequence, a HCDR3 having the amino acid sequence of a specified sequence', respectively),
--a LCDR1 having the amino acid sequence of a specified sequence, a LCDR2 having the amino acid sequence of a specified sequence, and a LCDR3 having the amino acid sequence of a specified sequence (para [0011]-[0012] - 'internalizing TIM3-specific antibody competes for binding with... an antibody having light chain complementarity determining region (CDR) sequences of SEQ ID NOs:8-10 and heavy chain CDR sequences of SEQ ID NOs:3-5', wherein 'light chain complementarity determining region (CDR) sequences of SEQ ID NOs:8-10' comprising 'a LCDR1 having the amino acid sequence of a specified sequence, a LCDR2 having the amino acid sequence of a specified sequence, and a LCDR3 having the amino acid sequence of a specified sequence', respectively);
--wherein the antibody comprising a heavy-chain (or VH) comprising the amino acid sequence of a specified sequence and a light-chain (or VL) comprising the amino acid sequence of a specified sequence (para [0018]-[0019] - 'internalizing TIM3-specific antibody is selected from ... an antibody having a light chain variable region sequence comprising SEQ ID NO:7 and a heavy chain variable region sequence of SEQ ID NO:2').

*****Continued in the next extra sheet*****

INTERNATIONAL SEARCH REPORT

International application No.

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Continuation of:
The previous extra sheet - Box No III (unity of invention is lacking)

Without a shared special technical feature, the inventions lack unity with one another.

Groups I+ therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Continuation of item 4: Claim 11 is not drafted in accordance with the second and third sentences of Rule 6.4 (a). This claim is an improper multiple dependent claim.

Note:

I) Claim 1 contains multiple first appeared abbreviations each without a full name introduced.

II) Claim 4 contains the first appeared abbreviations "VH" and "VL" each without a full name introduced; and further the limitation "TIGIT (SEQ ID NO:1)" in claim 4 is assumed to read as "TIM-3 (SEQ ID NO:1)" to be consistent with claim 1 and claim 7.