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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 December 2022 (29.12.2022)

WIPO | PCT

(10) International Publication Number
WO 2022/271771 A3

(51) International Patent Classification:
C07K 16/28 (2006.01) *A61K 39/395* (2006.01)

(21) International Application Number:
PCT/US2022/034443

(22) International Filing Date:
22 June 2022 (22.06.2022)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/213,540 22 June 2021 (22.06.2021) US

(71) Applicants: **THE GENERAL HOSPITAL CORPORATION** [US/US]; 55 Fruit Street, Boston, MA 02114 (US). **THE BRIGHAM AND WOMEN'S HOSPITAL, INC.** [US/US]; 75 Francis Street, Boston, MA 02115 (US).

(72) Inventors: **BRENNER, Michael**; 33 Huntington Rd., Newton, MA 02458 (US). **HABER, Daniel, A.**; 34 Monadnock Rd., Chestnut Hill, MA 02467 (US). **TING, David, T.**; 25 Farm St, Dover, MA 02030 (US). **MICALIZZI, Douglas**; 24r Marshall St., Unit 11, Somerville, MA 02145 (US). **MAHESWARAN, Shyamala**; 42 Eastern Avenue, Lexington, MA 02421 (US).

(74) Agent: **DECAMP, James, D.**; Clark & Elbing LLP, 101 Federal Street, 15th Floor, Boston, MA 20110 (US).

(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, IQ, IR, IS, IT, JM, 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:
— *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))*
— *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:
23 February 2023 (23.02.2023)

(54) Title: THERAPEUTIC TARGETING OF CADHERIN 11 IN CANCER

(57) Abstract: The present invention relates to methods, uses, and compositions for the treatment of cancer (e.g., a breast cancer or a pancreatic cancer). More specifically, the invention concerns the treatment of patients having cancer for the therapeutic inhibition of cancer cell growth and metastasis with an anti- Cadherin 11 monoclonal antibody with specific monoclonal antibody clones 23C6 or 3H10.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. C07K 16/28, A61K 39/395 (2022.01)

CPC - INV. A61K 38/177, C07K 16/2845; ADD. A61K 2039/505, C07K 14/705, A61K 39/3955, C07K 2317/24

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 2011/0274703 A1 (AGARWAL et al.) 10 November 2011 (10.11.2011) para [0010], [0054], [0075], [0077]	1-26, 85-93, 97-105
A	US 2015/0352225 A1 (REDWOOD BIOSCIENCE) 10 December 2015 (10.12.2015) para [0381], SEQ ID NO: 42	1-26, 85-93, 97-105
A	US 2020/0181249 A1 (Q32 BIO INC) 11 June 2020 (11.06.2020) claim 1, para [0243], SEQ ID NO: 229	1-26, 85-93, 97-105
A	GenBank submission PH1710, 17 March 1999 [online]. [Retrieved on 17 March 1999]. Retrieved from the internet <URL: https://www.ncbi.nlm.nih.gov/protein/PH1710> entire document	1-26, 85-93, 97-105
A	US 2009/0297530 A1 (UNIVERSITY OF TEXAS SYSTEM) 3 December 2009 (03.12.2009) claim 7, para [0349], SEQ ID NOs: 44, 46	1-26, 85-93, 97-105
A	US 2004/0023316 A1 (REITER et al.) 5 February 2004 (05.02.2004) para [0052], [0064], SEQ ID NO: 21	1-26, 85-93, 97-105

☐ 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
9 November 2022	DEC 14 2022
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 Kari Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

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 13*ter*.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 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.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:

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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.: 65-68, 76-84, 94-96 and 106-119
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 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.:
1-26, 85-93, 97-105, limited to SEQ ID NOs: 1-6; Note: Claims 61-64, 69-75 fall outside the scope of Group I and are therefore being excluded from the search of Group I.

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, 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 1-26, 61-64, 69-75, 85-93, 97-105, drawn to methods and compositions employing an anti-CDH11 antibody that comprises SEQ ID NOs: 1-6.

Group II: Claims 27-36, drawn to methods comprising determining expression of CDH11 gene in sample and comparing it to a control

Group III: Claims 37-60, 120-121, drawn to compositions comprising immunoconjugates of an anti-CDH11 antibody and a therapeutic agent.

Group IV: Claims 61-64, 69-75, drawn to composition comprising a nucleic acid molecule encoding CDH11antibody.

The inventions listed as Groups I through IV 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 Features

Group I requires an anti-CDH11 antibody that comprises SEQ ID NOs: 1-6, not required by groups II - IV.

Group II requires methods comprising determining expression of CDH11 gene in a sample, not required by groups I, III and IV.

Group III requires compositions comprising immunoconjugates, not required by groups I, II and IV.

Group IV requires composition comprising a nucleic acid molecule encoding CDH11 antibodies, not required by groups I – III.

Common Technical Features

The common technical feature shared by Groups I-IV, is an anti-CDH11 antibody, conjugate, or single chain antibody. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is taught by US 2011/0274703 A1 to Agarwal et al. (hereinafter 'Agarwal').

Agarwal teaches anti-CDH11 antibodies and conjugates (para [0010] "In one embodiment, the cadherin-11 antagonist is a cadherin-11 binding peptide. In one embodiment, the cadherin-11 binding peptide is an anti-cadherin-11 antibody or an antigen-binding antibody fragment.", para [0054] "The cadherin-11 antagonists may be conjugated to another agent such as an imaging agent or a cytotoxic agent.", para [0075] Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paratope ... In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.", para [0077] "The present invention also includes single chain antibodies.").

As the technical feature was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

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

Note: Claims 61-64, 69-75 fall outside the scope of Group I and are therefore being excluded from the search of Group I.