



- (51) **International Patent Classification:**
C07K 16/00 (2006.01) *A61K 39/395* (2006.01)
- (21) **International Application Number:**
PCT/US2011/047650
- (22) **International Filing Date:**
12 August 2011 (12.08.2011)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/373,072 12 August 2010 (12.08.2010) 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, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, 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.

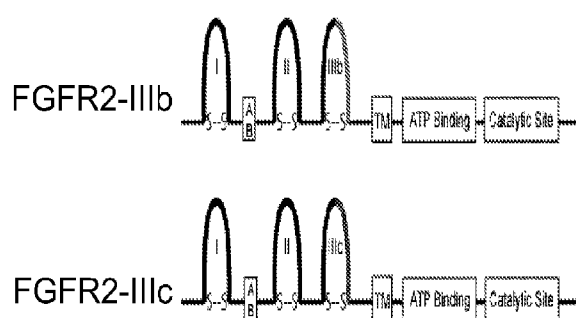
(84) **Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, 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, 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))

[Continued on next page]

(54) **Title:** ANTIBODY MOLECULES TO ONCOGENIC ISOFORMS OF FIBROBLAST GROWTH FACTOR RECEPTOR-2 AND USES THEREOF

**FIG. 1**

(57) **Abstract:** Antibody molecules that specifically bind to one or more isoforms expressed and/or associated with oncogenic phenotypes in a hyperproliferative cell (e.g., a cancerous or tumor cell) are disclosed. The isoform-binding antibody molecules can be used to treat, prevent and/or diagnose cancerous conditions and/or disorders. Methods of using the isoform-binding molecules to selectively detect oncogenic isoforms, to reduce the activity and/or induce the killing of a hyperproliferative cell expressing an oncogenic isoform in vitro, ex vivo or in vivo are also disclosed. Diagnostic and/or screening methods and kits for evaluating the function or expression of an oncogenic isoform are also disclosed.



— *with sequence listing part of description (Rule 5.2(a))*

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

14 June 2012

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 11/47650

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07K 16/00; A61K 39/395 (2012.01)

USPC - 530/388.22; 424/143.1

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)

IPC(8) - C07K 16/00; A61K 39/395 (2012.01)

USPC - 530/388.22; 424/143.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC(8) - C07K 16/00; A61K 39/395 (2012.01), USPC - 530/388.22; 424/143.1: keyword search, as below

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWest (PGPB,USPT,USOC,EPAB,JPAB), Google Scholar: FGFR, FGFR2, IIIb, IIIc, antibody, immunoglobulin, fab, scFv, binding protein, specific, cancer, prostate, breast, testicular, conjugated, functionalized, linked, linking, effector, toxin, radioactive, radiolabel, labeled, cytotoxic, epitope, determinant, schwerts. GenCore 6.3: SEQ ID NO: 144-149

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/100105 A2 (CHANG, et al.) 13 August 2009 (13.08.2009) pg 6, ln 14 to pg 7, ln 1; pg 8, ln 3 to pg 9, ln 29; pg 13, ln 8 to pg 14, ln 23; pg 16, ln 1-22; pg 17, ln 4-20; pg 18, ln 28 to pg 20, ln 1; pg 21, ln 19-22; pg 22, ln 8-31; pg 23, ln 3-27; pg 42, ln 9-12; pg 49, ln 20-23; pg 55, ln 3-4	1-5, 14, 16-27, 30, 32, and 34-56
A	US 2010/0196364 A1 (KIM, et al.) 5 August 2010 (05.08.2010) abstract; SEQ ID NO: 6	6-13, 15
A	US 2008/0260748 A1 (IWAMOTO, et al.) 23 October 2008 (23.10.2008) abstract; SEQ ID NO: 53-55	6-13, 15
A	US 2009/0137002 A1 (PETRUL, et al.) 28 May 2009 (28.05.2009) abstract; SEQ ID NO: 23	6-13, 15
A	US 2005/0019845 A1 (HARKINS, et al.) 27 January 2005 (27.01.2005) abstract; SEQ ID NO: 30	6-13, 15
A	US 2008/0300204 A1 (FEDEROFF, et al.) 4 December 2008 (04.12.2008) abstract; SEQ ID NO: 12	6-13, 15

☐ Further documents are listed in the continuation of Box C.

* 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

"I" 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

23 March 2012 (23.03.2012)

Date of mailing of the international search report

13 APR 2012

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. 571-273-3201

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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.:
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.

Group I+: claims 1-56, drawn to an antibody molecule that binds to human fibroblast growth factor receptor 2 (FGFR2) isoform IIIe or a fragment thereof, and shows less than 10% cross-reactivity with human FGFR2 isoform IIb. The first invention is restricted to an antibody that comprises CDRs/competes with antibody Atto-HuMab-01. Should an additional fee(s) be paid, Applicant is invited to elect an additional specific antibody(s) to be searched.

[NOTE: Claims 28-29, 31, 33 were excluded from the search, because they are drawn to a non-elected subject matter.]

- Please see extra sheet for continuation -

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.:
1-27, 30, 32, and 34-56, restricted to an antibody that comprises CDRs/competes with antibody Atto-HuMab-01

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.

Continuation of Box III: Lack of Unity of Invention

The inventions listed as Group 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:

The inventions of Group I+ share the technical feature of an antibody of claim 1. However, this shared technical feature does not represent a contribution over prior art as being anticipated by WO 2009/100105 A2 to Chang et al. (hereinafter "Chang") that discloses an antibody molecule that binds to human FGFR2 isoform IIIc or a fragment thereof (pg. 6, ln 14-16), and shows less than 10% cross-reactivity with human FGFR2 isoform IIIb (does not substantially bind to other non-oncogenic isoforms of the FGF receptors, such as other alternative splice variants of FGFR2 (e.g., FGFR2 IIIb)(pg. 6, ln 16-17), said antibody selectively binds to an amino acid sequence encoded by Exon III of FGFR2 corresponding to about amino acids 301 to 360 of FGFR2-IIIc (SEQ ID NO: 2) (pg. 6, ln 28-30); about amino acids 314 to 324 of FGFR2-IIIc (AAGVNTTDKEI, SEQ ID NO: 4)(pg. 6, ln 30); about amino acids 328 to 337 of FGFR2-IIIc (YIRNVTFEDA, SEQ ID NO: 6)(pg. 6, ln 30-31); about amino acids 350 to 353 of FGFR2-IIIc (ISFH, SEQ ID NO: 8)(pg. 6, ln 31-pg. 7, ln 1). As said antibody 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.

Another special technical feature of the inventions listed as Group I+ is the specific antibody recited therein. As no significant structural similarities can readily be ascertained among the antibodies, the inventions do not share a special technical feature. 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.