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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 September 2012 (07.09.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/118915 A3

(51) International Patent Classification:
C12N 15/113 (2010.01) *C12N 15/63* (2006.01)
A61K 31/7088 (2006.01) *A61P 35/00* (2006.01)
A61K 48/00 (2006.01) *G01N 33/15* (2006.01)

(21) International Application Number:
PCT/US2012/027185

(22) International Filing Date:
1 March 2012 (01.03.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/448,009 1 March 2011 (01.03.2011) US

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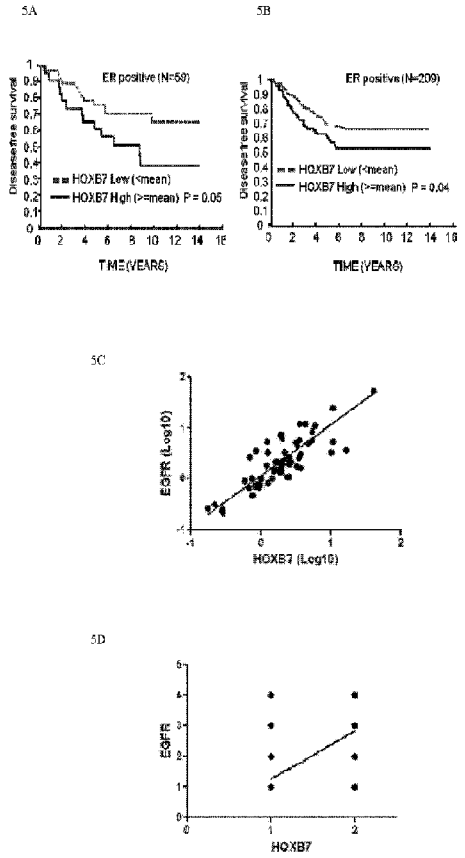
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, 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, RW, SC, SD,

[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR TREATMENT OF TAMOXIFEN RESISTANT BREAST CANCER



(57) Abstract: The inventors found that the gene, HOXB7, was frequently overexpressed in breast cancer, and is a major upstream regulator of events leading to tamoxifen resistance. The present invention provides double-stranded short interfering nucleic acid (siNA) molecules that targets the HOXB7 gene in cells, and also provides methods of use of this siNA molecule for methods of screening, diagnosis and prediction of treatment outcomes as well as treatment of cancer.

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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, RW, 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))*

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

(88) Date of publication of the international search report:
22 November 2012

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/027185

A. CLASSIFICATION OF SUBJECT MATTER

C12N 15/113(2010.01)i, A61K 31/7088(2006.01)i, A61K 48/00(2006.01)i, C12N 15/63(2006.01)i, A61P 35/00(2006.01)i, G01N 33/15(2006.01)i

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)

C12N 15/113; A61K 39/395; C12N; A61K 31/7105; C12Q 1/68

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models
Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) , Pubmed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010-0285031 A1 (SUKUMAR, S. et al.) 11 November 2010 See claims 14, 17; paras. [0005], [0075]-[0077], [0079], [0109]-[0114],	1-9,11-14,18-20
Y	[0325]-[0339], [0487], [0490], [0508]-[0513].	10
Y	BRAIG, S. et al. 'MicroRNA miR-196a is a central regulator of HOX-B7 and BMP4 expression in malignant melanoma' Celullar and Molecular Life Sciences. Vol.67(20), pp.3535-3548(18 May 2010)	10
A	See the abstract; Fig. 3e.	1-9,11-14,18-20
A	WO 03-012052 A2 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES et al.) 13 February 2003 See the abstract.	1-14,18-20
A	WO 2008-115419 A2 (GENOMIC HEALTH, INC. et al.) 25 September 2008 See the abstract.	1-14,18-20
A	WO 2008-115470 A2 (EAST CAROLINA UNIVERSITY et al.) 25 September 2008 See the abstract.	1-14,18-20

☒ 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 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
25 SEPTEMBER 2012 (25.09.2012)	**26 SEPTEMBER 2012 (26.09.2012)**
Name and mailing address of the ISA/KR Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon Metropolitan City, 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer KIM, JI YUN Telephone No. 82-42-481-8288

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/027185

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.: 15,17
because they relate to subject matter not required to be searched by this Authority, namely:
Said claims pertain to methods for treatment of the human body, thus relate to a subject-matter which International Searching Authority is not required to search under PCT Art. 17(2)(a)(i) and Rule 39.1(iv).

2. ☒ Claims Nos.: 16
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:
Claim 16 refers to the method of claim 14 which does not relate to a method. Thus, the subject-matter of claim 16 is unclear.

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:

1. ☐ As all required addtional 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 fee, this Authority did not invite payment of any additional fee.

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.:

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

International application No.
PCT/US2012/027185

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	JIN, K. et al. 'The HOXB7 protein renders breast cancer cells resistant to tamoxifen through activation of the EGFR pathway' Proceedings of the National Academy of Sciences. Vol.109(8), pp.2736-2741 (20 June 2011) See the whole document.	1-14,18-20

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2012/027185

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2010-0285031 A1	11.11.2010	WO 2007-136857 A2	29.11.2007
		WO 2007-136857 A3	20.11.2008
WO 03-012052 A2	13.02.2003	AU 2002-329667 A1	17.02.2003
		AU 2002-329667 A8	17.02.2003
		WO 03-012052 A3	31.03.2005
WO 2008-115419 A2	25.09.2008	CA 2680591 A1	25.09.2008
		EP 2140020 A2	06.01.2010
		US 2009-0258795 A1	15.10.2009
		WO 2008-115419 A3	19.03.2009
WO 2008-115470 A2	25.09.2008	WO 2008-115470 A3	20.11.2008