

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 February 2009 (05.02.2009)

PCT

(10) International Publication Number
WO 2009/018303 A3

(51) International Patent Classification:
C12Q 1/68 (2006.01)

(21) International Application Number:
PCT/US2008/071532

(22) International Filing Date:
30 July 2008 (30.07.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/962,795 31 July 2007 (31.07.2007) 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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, 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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, 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))

(88) Date of publication of the international search report:
30 December 2009

(54) Title: METHODS FOR REVERTING METHYLATION BY TARGETING DNMT3A AND DNMT3B

(57) Abstract: Methods for restoring a desired pattern of DNA methylation, inducing re-expression of methylation-silenced tumor suppressor genes (TSGs), and/or inhibiting tumorigenicity both in vitro and in vivo in a subject in need thereof by administering an effective amount of one or more miR-29s sufficient to target one or more of DNMT3A and DNMT3B are disclosed.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/71532

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12Q 1/68 (2009.01)

USPC - 435/6

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): C12Q 1/68 (2009.01)

USPC: 435/6

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
435/91.1, 435/91.2, 536/24.5, 536/25.32

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

PubWEST(USPT,PGPB,EPAB,JPAB); DialogPRO--Chemical Engineering and Biotechnology Abstracts, INSPEC, NTIS (National Technical Information Service), PASCAL, Current Contents Search, MEDLINE

Search Terms: miR29a, miR-29b, miR-29c, DNMT3A, DNMT3B, FHIT, WWOX, lung cancer.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	WO 2007/081720 A2 (Croce, et al.) 19 July 2007 (19.07.2007), pg 52, ln 1-2; pg 62, ln 24-25; pg 66, ln 19; pg 67, ln 22-23; pg 69, ln 21-27; pg 70, ln 16-18; pg 77, table 4; pg 85, ln 1, 13	13, 31-33 ----- 9-12, 14, 15
X ----- Y	US 2006/0105360 A1 (Croce, et al.) 18 May 2006 (18.05.2006), para [0014], [0015], [0016], [0017], [0019], [0020], [0021], [0022], [0042], [0045], [0047], [0050], [0051], [0052], [0066], [0067], [0070], [0072], [0073], [0074], [0076], [0078], [0084], [0085], [0087], [0088], [0091], [0092], [0096], [0106], [0120], [0137], [0144], [0157], [00160], [0172], [0179], [0182], [0203], [0205], [0245], claim 61	18, 21-30, 34-41, 46-50, 63-66 ----- 1-10, 12, 16, 17, 19, 20, 45, 67-75
Y	Koturbash, et al., Role of epigenetic effectors in maintenance of the long-term persistent bystander effect in spleen in vivo, Carcinogenesis (2007) vol 28, no 8, pg 1831-1838, pg 1836, col 2, ln 6; pg 1837, col 1, para 3, ln 5-7	1-10, 12, 14-16, 19, 20,
Y	US 2007/0050146 A1 (Bentwich, et al.) 1 March 2007 (01.03.2007), para [0014], [0074], [0167]	11, 14, 15, 17, 19, 20
Y	WO 2005/080601 A2 (Moorhouse, et al.) 01 September 2005 (01.09.2005), pg 14, ln 12-14; pg 17, ln 23-25; pg 18, ln 17-18; pg 25, ln 17-18, ln 25-29; pg 26, ln 4-5; pg 27, ln 20-21, ln 27.	67-72
Y	US 2005/0256072 A1 (Aronin, et al.) 17 November 2005 (17.11.2005), para [0084], [0091], [0108]).	45, 73-75
Y	WO/2007/084486 A2 (Renne, et al.) 26 July 2007 (26.07.2007), para [0008], [0031], [0034] [0041].	45

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

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search

03 March 2009 (03.03.2009)

Date of mailing of the international search report

17 APR 2009

Name and mailing address of the ISA/US

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P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

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PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/71532

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2005/017111 A2 (Hatzigeorgiou, et al.) 24 February 2005 (24.02.2005), pg 3, para 5, ln 3; pg16, para 4, ln 1; pg 16, para 5, ln 6-10.	69-72

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/71532

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.: 38-44, 51-62
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 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.:

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.