



(43) International Publication Date
16 February 2012 (16.02.2012)

(10) International Publication Number
WO 2012/021867 A3

- (51) International Patent Classification:
C12Q 1/68 (2006.01) *G06F 19/18* (2011.01)
- (21) International Application Number:
PCT/US2011/047681
- (22) International Filing Date:
12 August 2011 (12.08.2011)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
61/373,730 13 August 2010 (13.08.2010) 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))
 - with sequence listing part of description (Rule 5.2(a))
- (88) Date of publication of the international search report:
5 July 2012

(54) Title: A COMPREHENSIVE METHYLOME MAP OF MYELOID AND LYMPHOID COMMITMENT FROM HEMATOPOIETIC PROGENITORS

(57) Abstract: Provided herein are differentially methylated regions (DMRs) of multipotent progenitor cells (MPPs) and oligopotent progenitor cells and methods of use thereof. The invention provides methods for detecting and analyzing alterations in the methylation status of DMRs in such progenitor cells as well as methods for differentiating such cells.



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2011/047681**A. CLASSIFICATION OF SUBJECT MATTER***C12Q 1/68(2006.01)i, G06F 19/18(2011.01)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)

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	ATTEMA, J. L. et al. 'Epigenetic characterization of hematopoietic stem cell differentiation using miniChIP and bisulfite sequencing analysis' Proceedings of the National Academy of Sciences. Vol.104(30), pp.12371-12376 (18 July 2007)	1-4,6-9,55,56
A	See the abstract; Fig. 4.	5,10-42,46-54
X	BAIOCCHI, M. et al. '5-azacytidine reactivates the erythroid differentiation potential of the myeloid-restricted murine cell line 32D Ro' Experimental Cell Research. Vol.285(2), pp.258-267 (1 May 2003)	10,12-21
A	See the abstract; Fig. 5.	1-9,11,22-42,46-56
X	GUO, Y. et al. 'Effects of 5-aza-2' deoxycytidine on proliferation, differentiation and p15/INK4b regulation of human hematopoietic progenitor cells' Leukemia. Vol.20(1), pp.115-121 (January 2006)	22-29,31-42
A	See the abstract; Figs. 3-5; Table 1.	1-21,30,46-56

☒ 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

21 MAY 2012 (21.05.2012)

Date of mailing of the international search report

21 MAY 2012 (21.05.2012)

Name and mailing address of the ISA/KR

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Facsimile No. 82-42-472-7140

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2011/047681

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GAUTREAU, L. et al. 'Gene coexpression analysis in single cells indicates lymphomyeloid copriming in short-term hematopoietic stem cells and multipotent progenitors' Journal of Immunology. Vol.184(9), pp.4907-4917 (5 April 2010) See the abstract.	1-42,46-56
A	KITAJIMA, K. et al. 'Redirecting differentiation of hematopoietic progenitors by a transcription factor, GATA-2' Blood, Vol.107(5), pp.1857-1863 (1 March 2006) See the abstract.	1-42,46-56
PX	JI, H. et al. 'Comprehensive methylome map of lineage commitment from haematopoietic progenitors' Nature, Vol.467(7313), pp.338-342 (15 August 2010) See the whole document.	1-42,46-56

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2011/047681**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.: 45
because they relate to subject matter not required to be searched by this Authority, namely:
Said claim pertains 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.: 43, 44, 57
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:
Claims 43, 44 and 57 relate to a cell, a population of cells, and a cell bank defined only by a method of production. However, which cells may fall within this scope is so unclear that the subject-matter for which protection is not clearly defined.
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:

[Invention 1] A method of identifying the differentiation potential of a cell by comparing the methylation status of a DMR(differentially methylated region) sequences as set forth in Table 2a, first row(chr6, Gata2 gene), and related methods and products (claims 1-57, all in partial).

[Invention 2~11327] same as invention 1, but relating to the other genes listed in the Table 2a~2h (claims 1-57, all in partial).

The common technical feature among inventions 1-11327 is 'a DMR which is identified from comparing haematopoietic progenitors'. However, ATTEMA, J. L. et al. already discloses several DMR by comparing the methylation status between HSC and progenitor cells. Thus, the common technical feature is not considered to contribute over the prior art as a whole and the present application does not meet the requirements of unity of invention (Rule 13.1 PCT).

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 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.:
1-42, 46-56(all partially)

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

Information on patent family members

International application No.

PCT/US2011/047681Patent document
cited in search reportPublication
datePatent family
member(s)Publication
date

None