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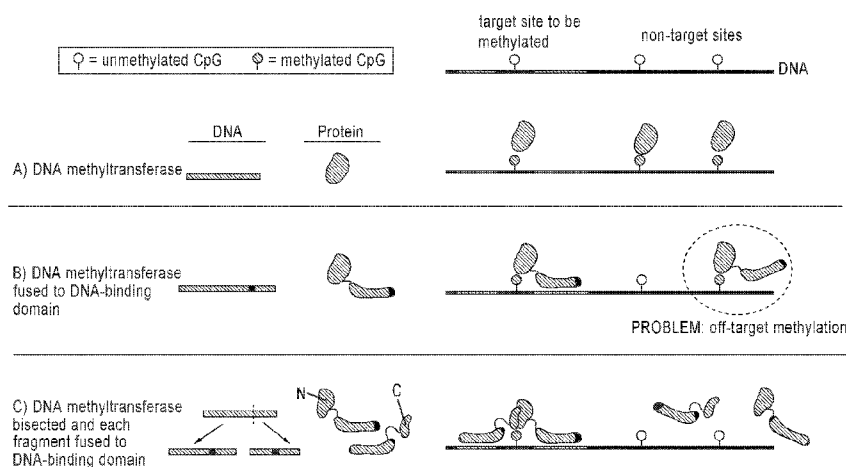


Figure 1

(57) Abstract: The present invention provides methods of systems and methods of site specific methylation.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2015/059984

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 48/00; C12N 9/10; C12N 15/54; C12N 15/85 (2017.01)

CPC - A61K 48/00; C07K 2319/81; C12N 9/1007; C12N 15/85; C12N 15/907; C12N 2800/24; C12N 2800/40; C12Y 201/01; C12Y 201/01037 (2017.02)

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

USPC - 514044R; 435/6.11; 435/7.21; 435/375; 536/24.31 (keyword delimited)

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.
X — Y	CHAIKIND et al. "Directed evolution of improved zinc finger methyltransferases," PLoS One, 08 May 2014 (08.05.2014), Vol. 9, No. 5, e96931, Pgs. 1-8. entire document	22 ----- 1-21, 23, 34-38
X — Y	KLUG et al. "Functional analysis of promoter CpG methylation using a CpG-free luciferase reporter vector," Epigenetics, 28 August 2006 (28.08.2006), Vol. 1, No. 3, Pgs. 127-130. entire document	24-30 ----- 31
Y	US 2002/0188103 A1 (BESTOR) 12 December 2002 (12.12.2002) entire document	1-21, 23, 34-38
Y	WO 2014/018423 A2 (THE BROAD INSTITUTE, INC. et al) 30 January 2014 (30.01.2014) entire document	16-18, 21, 31
Y	RIVENBARK et al. "Epigenetic reprogramming of cancer cells via targeted DNA methylation," Epigenetics, 01 April 2012 (01.04.2012), Vol. 7, No. 4, Pgs. 350-360. entire document	34-38
P, X	WO 2015/070083 A1 (EDITAS MEDICINE, INC.) 14 May 2015 (14.05.2015) entire document	1-31, 34-38
P, X	WO 2015/138582 A1 (THE JOHNS HOPKINS UNIVERSITY) 17 September 2015 (17.09.2015) entire document	1-31, 34-38

☐ 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

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"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

12 July 2017

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2015/059984

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.: 32, 33
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.