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- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

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(54) Title: METHODS AND REAGENTS FOR DETECTING CpG METHYLATION WITH A METHYL CpG BINDING PROTEIN (MBP)

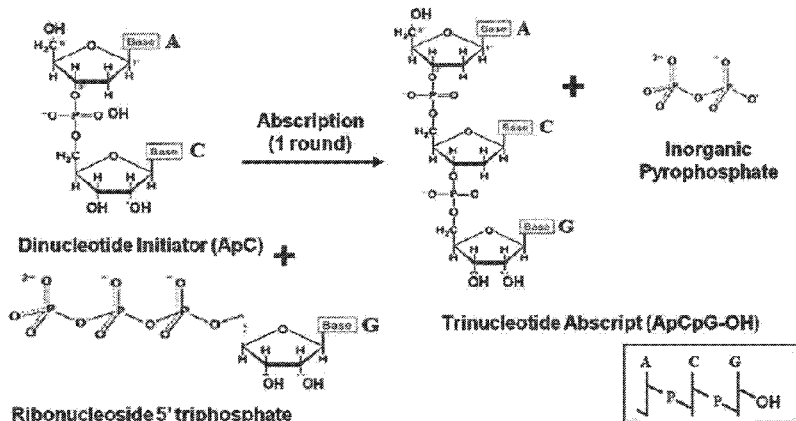


Figure 1

(57) Abstract: The present invention provides a simple and sensitive technology for the detection of CpG methylation in DNA without chemical modification of sample DNA by bisulfite treatment or PCR amplification. Signal generation is based on an Ab-scription (Abortive Transcription) technology in which DNA signal generators called Abortive Promoter Cassettes (APCs) are bound to target mCpG sites via mCpG target specific probes based on methyl binding polypeptides or methyl binding domains thereof. RNA polymerase produces uniform, short RNA molecules from synthetic promoters in APCs as signals of the presence of methylated CpGs. Detection of CpG methylation and hypermethylation of DNA targets such as CpG islands provides a convenient means for detecting and monitoring cancer in a subject.



WO 2009/140666 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/044269**A. CLASSIFICATION OF SUBJECT MATTER***C12Q 1/68(2006.01)i, C07K 19/00(2006.01)i, C12N 15/11(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)

IPC 8 C12Q 1/68

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

N.A.

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

eKOMPASS (KIPO internal), WPI, USPTO, PAJ, PubMed, INSPECT "absorption, absorb, abortive transcription, complex, methyl CpG, detect, methyl binding protein, etc."

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X/ A	Rauch T. wr al., (2005) "Methylated-CpG island recovery assay: a new technique for the rapid detection of methylated-CpG islands in cancer", Lab. Invest. Vol.85, pp. 1172-1180. - see abstract; page 1172, the 2nd paragraph of the right column ~ page 1173, the 2nd paragraph of the left column; page 1174, the left column	21,22,24-27/ 1-20, 23, 28-41
X/ A	US 2006-240460 A1 (Pfeifer, GP., et al., US) 26 Oct 2006 - see abstract; [0036]; and claims	21-27/ 1-20, 28-41
A	US 07045319 B2 (Hanna, MM., US) 16 May 2006 - see abstract; Fig.20; col.7, line 57 ~ col.8, line 5; col.14, lines 51 ~ 65; Fig.22; col.16, lines 28 ~ 38; Fig.30; and claims	1-41
A	WO 2003-038042 A2 (Ribomed Biotechnologies, INC, US) 08 May 2003 - see abstract; Fig.20; Fig.22; Fig.31; and claims	1-41
A	US 2004-0157257 A1 (Hanna, MM., US) 12 Aug 2004 - see abstract; Fig.20; Fig.22; Fig.30; and claims	1-41

 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

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Name and mailing address of the ISA/KR

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2009/044269**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.: 42
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 42 is directed to an array comprising 1 to about 1000 CpG island capture probes, of which sequences are not defined. The sequences of said probes are, however, the major constituents required for enabling the invention set out in claim 42. The scope for which protection is sought is not only unclear and indefinite but also unsupported by Description [Art. 6 PCT]
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 ISA found multiple inventions as follows:

Group 1 : claims 1-20, 28-41 are directed to a subject matter featuring a mCpG detector of claim 1 comprising a methyl-CpG binding Polypeptide (MBP) linked to an abortive promoter cassette (APC), and

Group 2 : claims 21-27 are directed to a subject matter featuring a fusion polypeptide comprising a MBP and an affinity tag.

The single general concept linking the two groups is merely a MBP, which is, however, described in US 2006-240460 A1 (26 Oct 2006). Hence the inventions listed as Groups 1 & 2 do not relate to a single general inventive concept under PCT Rule 13.1 because the above mentioned common concept fails to make a contribution over the prior art within the meaning of PCT Rule 13.2.

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.:

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/US2009/044269

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2006-240460 A1	26.10.2006	US 07425415 B2	16.09.2008
US 07045319 B2	16.05.2006	AU 2002-360306 A8 CA 2465158 A1 EP 1451366 A2 EP 1622923 A2 JP 2006-507792 T JP 2006-525022 A US 2005-0064414 A1 US 2005-0026150 A1 US 2004-0234996 A1 US 2003-0099950 A1 US 2004-0054162 A1 US 2004-0137461 A1 US 2004-0157257 A1 WO 2004-096997 A2 WO 2003-038042 A2	29.10.2002 08.05.2003 01.09.2004 08.02.2006 09.03.2006 09.11.2006 24.03.2005 03.02.2005 25.11.2004 29.05.2003 18.03.2004 15.07.2004 12.08.2004 11.11.2004 08.05.2003
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