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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, BN, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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.

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(54) **Title:** METHODS OF DETECTING MUTATIONS AND EPIGENETIC CHANGES

(57) **Abstract:** Disclosed are methods for assessing the methylation and mutation status of nucleic acid in a sample. The methods provide for methylation-dependent modification of the nucleic acid in a sample, and subsequently nucleic acid amplification processes to distinguish between mutated and non-mutated target sequence.

# INTERNATIONAL SEARCH REPORT

International application No <b>PCT/IB2012/003094</b>
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A. CLASSIFICATION OF SUBJECT MATTER  
**INV. C12Q1/68**  
 ADD.

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**

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
**EPO-Internal , WPI Data, BIOSIS, Sequence Search , EMBASE**

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X	EP 2 309 005 A1 (EPLGENOMICS AG [DE] ) 13 April 2011 (2011-04-13) paragraph [0108] -----	1-5 ,9-18
X	WO 2008/084219 A1 (ONCOMETHYLOME SCIENCES SA [BE] ; BALDOCK SHARON CLAIRE [GB] ; VAN ENGELA) 17 July 2008 (2008-07-17) SEQ ID NO:26 and 27 correspond to SEQ ID NOs :15 and 16 of the present appl icati on . ; tabl e 24  -----  -/- .	21

Further documents are listed in the continuation of Box C.       See patent family annex.

\* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p>
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Date of the actual completion of the international search  <b>11 June 2013</b>	Date of mailing of the international search report  <b>19/06/2013</b>
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  <p style="text-align: center;"><b>Gabriel s, Jan</b></p>
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International application No

PCT/IB2012/003094

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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Information on patent family members

International application No <b>PCT/IB2012/003094</b>
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