



- (51) International Patent Classification:
C12Q 1/68 (2006.01)
- (21) International Application Number:
PCT/EP2012/057225
- (22) International Filing Date:
19 April 2012 (19.04.2012)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
11162979.6 19 April 2011 (19.04.2011) EP
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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, 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.

- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, 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:
13 December 2012

(54) Title: PROSTATE CANCER MARKERS

(57) Abstract: The invention relates to the identification and selection of novel genomic regions (biomarker) and the identification and selection of novel genomic region combinations which are hypermethylated in subjects with prostate cancer compared to subjects without prostate cancer. Nucleic acids which selectively hybridize to the genomic regions and products thereof are also encompassed within the scope of the invention as are compositions and kits containing said nucleic acids and nucleic acids for use in diagnosing prostate cancer. Further encompassed by the invention is the use of nucleic acids which selectively hybridize to one of the genomic regions or products thereof to monitor disease regression in a patient and the efficacy of therapeutic regimens.



INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/057225

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, BIOSIS, CHEM ABS Data, EMBASE, FSTA, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MICHAEL WEBER ET AL: "Chromosome-wide and promoter-specific analyses identify sites of differential DNA methylation in normal and transformed human cells", NATURE GENETICS, NATURE PUBLISHING GROUP, NEW YORK, US, vol. 37, no. 8, 1 August 2005 (2005-08-01), pages 853-862, XP002634922, ISSN: 1061-4036, DOI: 10.1038/NG1598 [retrieved on 2005-07-10] abstract; Fig. 1 and legend ----- -/--	1-22

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 another 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 28 September 2012	Date of mailing of the international search report 24/10/2012
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 Leber, Thomas

INTERNATIONAL SEARCH REPORT

International application No.
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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.:
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:

see additional sheet

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 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.:

1-19, 21, 22

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

International application No
PCT/EP2012/057225

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ILANA KESHET ET AL: "Evidence for an instructive mechanism of de novo methylation in cancer cells", NATURE GENETICS, vol. 38, no. 2, 1 February 2006 (2006-02-01), pages 149-153, XP055000439, ISSN: 1061-4036, DOI: 10.1038/ng1719 abstract; whole document</p>	1-22
Y	<p>-----</p> <p>Y. TOKUMARU: "Optimal Use of a Panel of Methylation Markers with GSTP1 Hypermethylation in the Diagnosis of Prostate Adenocarcinoma", CLINICAL CANCER RESEARCH, vol. 10, no. 16, 15 August 2004 (2004-08-15), pages 5518-5522, XP055005127, ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-04-0108 whole document; Table 2</p>	1-11
Y	<p>-----</p> <p>HOQUE MOHAMMAD OBAIDUL ET AL: "Quantitative methylation-specific polymerase chain reaction gene patterns in urine sediment distinguish prostate cancer patients from control subjects", JOURNAL OF CLINICAL ONCOLOGY, AMERICAN SOCIETY OF CLINICAL ONCOLOGY, US, vol. 23, no. 27, 20 September 2005 (2005-09-20), pages 6569-6575, XP002485531, ISSN: 0732-183X, DOI: 10.1200/JCO.2005.07.009 the whole document</p>	1-7
Y	<p>-----</p> <p>"Supplementary table for XP002485531", 20 September 2005 (2005-09-20), XP055005228, Retrieved from the Internet: URL:http://www.jcojournal.org/content/23/27/6569/T4.expansion.html [retrieved on 2011-08-19] the whole document</p> <p>-----</p> <p style="text-align: center;">-/--</p>	1-11

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/057225

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JACINTO FILIPE V ET AL: "Methyl-DNA immunoprecipitation (MeDIP): hunting down the DNA methylome.", BIOTECHNIQUES JAN 2008 LNKD-PUBMED:18254377, vol. 44, no. 1, January 2008 (2008-01), XP001525871, ISSN: 0736-6205 the whole document	1-11
Y	----- KE XI-SONG ET AL: "Global profiling of histone and DNA methylation reveals epigenetic-based regulation of gene expression during epithelial to mesenchymal transition in prostate cells", BMC GENOMICS, BIOMED CENTRAL, LONDON, GB, vol. 11, no. 1, 25 November 2010 (2010-11-25), page 669, XP021086270, ISSN: 1471-2164, DOI: 10.1186/1471-2164-11-669 the whole document	1-11
Y	----- MATHEWS LESLEY A ET AL: "Epigenetic regulation of CpG promoter methylation in invasive prostate cancer cells", MOLECULAR CANCER, BIOMED CENTRAL, LONDON, GB, vol. 9, no. 1, 7 October 2010 (2010-10-07), page 267, XP021078005, ISSN: 1476-4598, DOI: 10.1186/1476-4598-9-267 the whole document	1-11
A	----- EP 2 213 749 A1 (EPIGENOMICS AG [DE]) 4 August 2010 (2010-08-04) sequence 57	1-22
A	----- Cottrell S. ET AL: "JA282616 = SEQ ID NO:57 of EP2280084", ² 2 February 2011 (2011-02-02), pages 1-2, XP055011564, Retrieved from the Internet: URL: http://www.ncbi.nlm.nih.gov/pubmed/ [retrieved on 2011-11-08] the whole document	1-22
A	----- "SEQ ID NO:198370 of US6812339", ² 2 November 2004 (2004-11-02), XP055011755, Retrieved from the Internet: URL: http://www.ncbi.nlm.nih.gov/pubmed/ [retrieved on 2011-11-10] the whole document	1-22
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/057225

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	"Nucleic acid hybridising to the 5' and 3' vicinity of SEQ ID NO:2 and to this sequence as such", 29 December 2010 (2010-12-29), XP55039305, Retrieved from the Internet: URL:http://www.ncbi.nlm.nih.gov/pubmed/ [retrieved on 2012-09-26]	12,16, 18,21,22
Y	the whole document	13-15,17
X	"Nucleic acid hybridising to the 5' and 3' vicinity of SEQ ID NO:19 and to this sequence as such", 5 April 2011 (2011-04-05), XP55039307, Retrieved from the Internet: URL:http://www.ncbi.nlm.nih.gov/pubmed/ [retrieved on 2012-09-26]	12,16, 18,21,22
Y	the whole document	13-15,17
X	"Nucleic acid hybridising to the 5' and 3' vicinity of SEQ ID NO:49 and to this sequence as such", 26 September 2001 (2001-09-26), XP55039308, Retrieved from the Internet: URL:http://www.ncbi.nlm.nih.gov/pubmed/ [retrieved on 2012-09-26]	12,16, 18,21,22
Y	the whole document	13-15,17
A	US 6 812 339 B1 (VENTER J CRAIG [US] ET AL) 2 November 2004 (2004-11-02) col. 6, lines 16-22; col. 14, lines 39-54; col. 14, line 64 - col. 15, line 62; the whole document	1-22

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2012/057225

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 2213749	A1	04-08-2010	AT 438740 T 15-08-2009
			AU 2005322435 A1 06-07-2006
			CA 2593546 A1 06-07-2006
			EP 1831399 A2 12-09-2007
			EP 2213749 A1 04-08-2010
			EP 2280084 A1 02-02-2011
			EP 2284279 A1 16-02-2011
			EP 2311984 A1 20-04-2011
			ES 2331146 T3 22-12-2009
			JP 2008522590 A 03-07-2008
			JP 2012120538 A 28-06-2012
			US 2009197250 A1 06-08-2009
			WO 2006071466 A2 06-07-2006
US 6812339	B1	02-11-2004	NONE

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-11

A method for diagnosis of prostate cancer comprising analysing the methylation pattern of at least one of the genomic-region-pairs as defined in Table 2.

2-112. claims: 12-19(completely); 21, 22(partially)

A nucleic acid molecule that hybridises in the vicinity of a genomic region as defined by SEQ ID NO:1-110.

113. claims: 20(completely); 21, 22(partially)

Use of an antibody that is specific for (thus binds to) a genomic region as defined by SEQ ID NO:1-110.
