



(43) International Publication Date
12 July 2012 (12.07.2012)

(10) International Publication Number
WO 2012/094682 A3

(51) International Patent Classification:
C12Q 1/70 (2006.01)

(21) International Application Number:
PCT/US2012/020684

(22) International Filing Date:
9 January 2012 (09.01.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/430,797 7 January 2011 (07.01.2011) US

(71) Applicant (*for all designated States except US*): **QIAGEN
GAITHERSBURG, INC.** [US/US]; 1201 Clopper Road,
Gaithersburg, MD 20878 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **RANGWALA,
Sameera** [US/US]; 1201 Clopper Road, Gaithersburg, MD
20878 (US). **KOBAYASHI, Lori** [US/US]; 7124 Sharps-
burg Pike, Boonsboro, MD 21713 (US). **GAY, Tanya**
[US/US]; 1201 Clopper Road, Gaithersburg, MD 20878
(US).

(74) Agent: **SHAW MCBEE, Susan, E.**; Baker, Donelson,
Bearman, Caldwell & Berkowitz.P.C, 920 Massachusetts
Ave., NW, Washington, DC 20001 (US).

(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:
6 December 2012

(54) Title: MATERIALS AND METHOD FOR GENOTYPING AND QUANTIFYING A HIGH-RISK HUMAN PAPILLO-
MAVIRUS

(57) Abstract: Nucleic acids, assays, and methods for the detection and quantification of high risk HPV types are disclosed.



WO 2012/094682 A3

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2012/020684

A. CLASSIFICATION OF SUBJECT MATTER

INV. C12Q1/70

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, Sequence Search, EMBASE, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/057993 A1 (VERENIGING VOOR CHRISTELIJK HO [NL]; MEIJER CHRISTOPHORUS JOANNES LAMB) 7 May 2009 (2009-05-07) abstract	1,2,12, 13,16, 20-22, 28,30-34
X	CLAD ANDREAS ET AL: "Performance of the Aptima high-risk human papillomavirus mRNA assay in a referral population in comparison with Hybrid Capture 2 and cytology.", JOURNAL OF CLINICAL MICROBIOLOGY MAR 2011 LNKD- PUBMED:21191046, vol. 49, no. 3, 29 December 2010 (2010-12-29), pages 1071-1076, XP002675145, ISSN: 1098-660X abstract	1,2,12, 13,22

☒ 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

19 June 2012

Date of mailing of the international search report

25/10/2012

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

Costa Roldán, Nuria

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/020684

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.:
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.:

6, 7, 35-38, 47(completely); 1-5, 12-34(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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 6, 7, 35-38, 47(completely); 1-5, 12-34(partially)

A nucleic acid primer or probe specific for a target sequence in the E6/E7 region of high-risk HPV-16 genome, wherein:(a) said nucleic acid primer or probe has 80% identity or greater across its entire length to both the target sequence and at least one nucleic acid sequence in E6/E7 region of a genome of a subtype thereof; and (b) said nucleic acid primer or probe does not hybridize to a nucleic acid derived from a different HPV type. A nucleic acid primer or probe that has 70%-100% identity to a sequence selected from the group of sequences directed to HPV-16, i.e. SEQ ID NOs: 1 to 3. Primer sets / kits / compositions and genotyping assay claims all comprising, primers or probes specific for a target sequence in the E6/E7 region of high-risk HPV-16 genome.

2. claims: 8, 9, 39-42, 48(completely); 1-5, 12-34(partially)

As for invention 2, however, comprising primers / probes targeting E6/ E7 of high-risk HPV-18 genome.

3. claims: 10, 11, 43-46, 49(completely); 1-5, 12-34(partially)

As for invention 3, however, comprising primers / probes targeting E6/ E7 of high-risk HPV-45 genome.

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2012/020684

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LI ET AL: "Detection of human papillomavirus genotypes with liquid bead microarray in cervical lesions of northern Chinese patients", CANCER GENETICS AND CYTOGENETICS, ELSEVIER SCIENCE PUBLISHING, NEW YORK, NY, US, vol. 182, no. 1, 6 March 2008 (2008-03-06), pages 12-17, XP022513163, ISSN: 0165-4608, DOI: 10.1016/J.CANCERGENCYTO.2007.12.007 abstract	1,2,12, 22
X	----- GHEIT TARIK ET AL: "Development of a sensitive and specific assay combining multiplex PCR and DNA microarray primer extension to detect high-risk mucosal human papillomavirus types", JOURNAL OF CLINICAL MICROBIOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, DC, US, vol. 44, no. 6, 1 June 2006 (2006-06-01), pages 2025-2031, XP002427648, ISSN: 0095-1137, DOI: 10.1128/JCM.02305-05 abstract	1,2,12, 22
X	----- HAN J ET AL: "Simultaneous amplification and identification of 25 human papillomavirus types with Tempex technology", JOURNAL OF CLINICAL MICROBIOLOGY 200611 US LNKD- DOI:10.1128/JCM.01762-06, vol. 44, no. 11, November 2006 (2006-11), pages 4157-4162, XP002675146, ISSN: 0095-1137 abstract	1,2,12, 22
X	----- EP 1 806 410 A2 (MERCK & CO INC [US]) 11 July 2007 (2007-07-11)	4,14,15, 20-27, 30,31, 33,34 28
A	abstract	
X	----- DATABASE EMBL [Online] 19 July 2007 (2007-07-19), "Sequence 25 from Patent EP1806410.", XP002675256, retrieved from EBI accession no. EMBL:CS642417 Database accession no. CS642417 the whole document ----- -/--	1-3,6,7, 35

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2012/020684

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 7 812 144 B2 (KARLSEN FRANK [NO]) 12 October 2010 (2010-10-12) abstract -----	4,20-27, 29-31, 33,34
X	DATABASE EMBL [Online] 14 December 2010 (2010-12-14), "Sequence 26 from patent US 7812144.", XP002675257, retrieved from EBI accession no. EMBL:GX640151 Database accession no. GX640151 the whole document -----	1-3,6,7
X	WO 2008/139938 A1 (NAT UNIV CORP TOKYO MED & DENT [JP]; RNAI CO LTD [JP]; UNIV OKAYAMA NA) 20 November 2008 (2008-11-20) abstract -----	1-3,5-7, 17-19, 30,31, 35,37, 38,47
X	DATABASE Geneseq [Online] 22 January 2009 (2009-01-22), "HPV-16 E7/E6 gene target sequence, bases 752-774.", XP002675258, retrieved from EBI accession no. GSN:ATS82292 Database accession no. ATS82292 the whole document -----	1-3,5-7, 17-19, 35,37, 38,47
X	DATABASE Geneseq [Online] 22 January 2009 (2009-01-22), "HPV-16 E7/E6 gene target sequence, bases 698-720.", XP002675259, retrieved from EBI accession no. GSN:ATS82290 Database accession no. ATS82290 the whole document -----	1-3,6,7, 17-19, 35,37,38
X	WO 2010/004251 A1 (ONCOMETHYLOME SCIENCES SA [BE]; ESTELLER MANEL [ES]; SPENCER MATTHEW P) 14 January 2010 (2010-01-14) abstract ----- -/--	35,36

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2012/020684

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE Geneseq [Online]</p> <p>1 April 2010 (2010-04-01), "HPV16 E7 gene forward RT-PCR primer SEQ ID 49.", XP002675260, retrieved from EBI accession no. GSN:AXU96631 Database accession no. AXU96631 the whole document</p>	35,36
A	<p>-----</p> <p>US 2005/032038 A1 (FISHER CHRISTOPHER [US] ET AL) 10 February 2005 (2005-02-10) abstract</p>	35-38
A	<p>-----</p> <p>DATABASE Geneseq [Online]</p> <p>21 April 2005 (2005-04-21), "E7 coding region (1-87) amplifying sense PCR primer, SEQ ID NO: 37.", XP002675261, retrieved from EBI accession no. GSN:ADX15568 Database accession no. ADX15568 sequence</p> <p>-----</p>	35-38

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2012/020684

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009057993 A1	07-05-2009	AU 2007360826 A1 CA 2704151 A1 EP 2209920 A1 JP 2011502477 A US 2010304362 A1 WO 2009057993 A1	07-05-2009 07-05-2009 28-07-2010 27-01-2011 02-12-2010 07-05-2009
EP 1806410 A2	11-07-2007	EP 1806410 A2 SI 1421200 T1	11-07-2007 30-04-2007
US 7812144 B2	12-10-2010	AT 354677 T AU 2003201639 A1 AU 2008205436 A1 BR 0306723 A CA 2472026 A1 CN 1639357 A DE 60311961 T2 DK 1463839 T3 EP 1463839 A2 EP 1715062 A2 EP 2267155 A2 EP 2272988 A2 ES 2282599 T3 HK 1065827 A1 JP 4558322 B2 JP 2005514038 A JP 2010131020 A MX PA04006440 A NZ 533703 A PT 1463839 E SI 1463839 T1 US 2005118568 A1 US 2009253124 A1 US 2009275044 A1 WO 03057914 A2	15-03-2007 24-07-2003 04-09-2008 21-12-2004 17-07-2003 13-07-2005 18-10-2007 02-07-2007 06-10-2004 25-10-2006 29-12-2010 12-01-2011 16-10-2007 06-07-2007 06-10-2010 19-05-2005 17-06-2010 31-03-2005 26-05-2006 31-05-2007 31-08-2007 02-06-2005 08-10-2009 05-11-2009 17-07-2003
WO 2008139938 A1	20-11-2008	NONE	
WO 2010004251 A1	14-01-2010	NONE	
US 2005032038 A1	10-02-2005	AU 7078100 A EP 1206581 A2 JP 2003507078 A US 6200746 B1 US 2005032038 A1 WO 0114584 A2	19-03-2001 22-05-2002 25-02-2003 13-03-2001 10-02-2005 01-03-2001