



- (51) **International Patent Classification:**
C12Q 1/68 (2006.01) *C12Q 1/02* (2006.01)
- (21) **International Application Number:**
PCT/US2012/053530
- (22) **International Filing Date:**
31 August 2012 (31.08.2012)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/532,777 9 September 2011 (09.09.2011) US
- (71) **Applicant (for all designated States except US):** **SE-QUENTA, INC.** [US/US]; 400 East Jamie Court, Suite 301, South San Francisco, CA 94080 (US).
- (72) **Inventors; and**
- (75) **Inventors/Applicants (for US only):** **FAHAM, Malek** [US/US]; 400 East Jamie Court, Suite 301, South San Francisco, CA 94080 (US). **MOORHEAD, Martin** [CH/US]; 400 East Jamie Court, Suite 301, South San Francisco, CA 94080 (US). **WILLIS, Thomas** [US/US]; 400 East Jamie Court, Suite 301, South San Francisco, CA 94080 (US).
- (74) **Agents:** **SEIDEL, Jeffrey, J.** et al.; **WILSON SONSINI GOODRICH & ROSATI**, 650 Page Mill Road, Palo Alto, CA 94304-1050 (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, 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, 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, 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))

- (88) **Date of publication of the international search report:**
2 May 2013

(54) **Title:** SEQUENCE-BASED MEASURES OF IMMUNE RESPONSE

(57) **Abstract:** The invention is directed to methods of measuring an immune response by comparing sequence-based clonotype frequency data from successively measured clonotype profiles. In particular, the invention includes immunotherapies of cancers, such as lymphomas, that include sensitive pre- and post-vaccination sequence-based measurements of changes in a patient's immune repertoire, thereby providing a sensitive measure of the likelihood of treatment success.



A. CLASSIFICATION OF SUBJECT MATTER*C12Q 1/68(2006.01)i, C12Q 1/02(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)

C12Q 1/68; A61K 39/395; C12Q 1/02; A61K 38/00; G01N 33/567; G01N 33/53; A61M 25/06

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: immune response, clonotype, sequencing, T cell, B cell, cancer, vaccination, etc.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2011-0104671 A1 (DORNAN, DAVID et al.) 05 May 2011 See claims 1 and 23.	12-14
A	US 2011-0207135 A1 (FAHAM, MALEK et al.) 25 August 2011 See claim 1.	12-14
A	WO 2007-134220 A2 (UNIVERSITY OF MARYLAND BIOTECHNOLOGY INSTITUTE) 22 November 2007 See claim 10.	12-14
A	US 6605272 B2 (NOVAK, JULIA E. et al.) 12 August 2003 See claims 1, 2, and 12.	12-14
A	US 2009-0233301 A1 (LEE, SHING-MOU) 17 September 2009 See claims 1 and 4.	12-14
A	US 2011-0105343 A1 (PUEDRAN, BALI et al.) 05 May 2011 See claims 1, 40.	12-14
A	US 2004-0235061 A1 (WILKIE, BRUCE N. et al.) 25 November 2004 See claims 1-3.	12-14



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

25 FEBRUARY 2013 (25.02.2013)

Date of mailing of the international search report

26 FEBRUARY 2013 (26.02.2013)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon Metropolitan
City, 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

HEO, Joo Hyung

Telephone No. 82-42-481-8150



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/053530

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PA	GAWAD, C. et al., `Massive evolution of the immunoglobulin heavy chain locus in children with B precursor acute lymphoblastic leukemia`, Blood, 28 August 2012, Vol.120, No.22, pp.4407-4417, ISSN 0006-4971(p), ISSN 1528-0020(e). See whole document.	12-14

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/053530**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.: 1-11,15-25
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 1-11 and 15-25 pertain to methods for treatment of the human body by surgical procedure, as well as diagnostic methods, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
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:

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/US2012/053530

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2011-0104671 A1	05.05.2011	AU 2008-323701 A1 CA 2704499 A1 CN 101910414 A EP 2222875 A1 IL 205391 D0 JP 2011-504102 A KR 10-2010-0095564 A MX 2010005080 A WO 2009-062125 A1	14.05.2009 14.05.2009 08.12.2010 01.09.2010 30.12.2010 03.02.2011 31.08.2010 28.07.2010 14.05.2009
US 2011-0207135 A1	25.08.2011	None	
WO 2007-134220 A2	22.11.2007	CA 2652086 A1 EP 2021460 A2 EP 2021460 A4 US 2010-0323401 A1 WO 2007-134220 A3	22.11.2007 11.02.2009 17.11.2010 23.12.2010 27.11.2008
US 6605272 B2	12.08.2003	AU 1997-43397 B2 AU 2000-33962 A1 AU 2000-33962 B2 AU 2000-37312 A1 AU 2000-37312 B2 CA 2273960 A1 CA 2273960 C CA 2364251 A1 CA 2364251 C CA 2366921 A1 CA 2445677 A1 CA 2445677 C CA 2445953 A1 CN 100500846 C CN 101575377 A CN 102406937 A CN 1208065 C0 CN 1213748 C0 CN 1244121 A0 CN 1378595 A0 CN 1424926 A0 CN 1827639 A0 CN 1927883 A CN 1927883 B EP 1001759 A2 EP 1001759 B1 EP 1156797 A2 EP 1156797 B1 EP 1165791 A2 EP 1165791 B1 EP 1557167 A1	17.01.2002 28.09.2000 25.03.2004 28.09.2000 04.11.2004 26.03.1998 30.12.2003 14.09.2000 14.09.2000 14.09.2000 26.03.1998 02.01.2007 26.03.1998 17.06.2009 11.11.2009 11.04.2012 29.06.2005 10.08.2005 09.02.2000 06.11.2002 18.06.2003 06.09.2006 14.03.2007 21.09.2011 24.05.2000 20.07.2005 28.11.2001 24.10.2007 02.01.2002 31.10.2007 27.07.2005

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/053530

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		EP 1881070 A2	23.01.2008
		EP 1881070 A3	05.03.2008
		EP 1881070 B1	03.10.2012
		EP 2295577 A2	16.03.2011
		EP 2295577 A3	08.08.2012
		JP 2001-521490 A	06.11.2001
		JP 2002-537839 A	12.11.2002
		JP 2002-538200 A	12.11.2002
		JP 3739098 B2	25.01.2006
		JP 4405686 B2	13.11.2009
		KR 10-0528815 B1	16.11.2005
		KR 10-0528816 B1	16.11.2005
		KR 10-0743640 B1	27.07.2007
		KR 10-2002-0005615 A	17.01.2002
		US 05952392 A	14.09.1999
		US 2002-0128446 A1	12.09.2002
		US 2003-0073651 A1	17.04.2003
		US 2003-0125524 A1	03.07.2003
		US 2004-0110932 A1	10.06.2004
		US 2004-0260065 A1	23.12.2004
		US 2007-0014800 A1	18.01.2007
		US 2007-0041974 A1	22.02.2007
		US 2007-0048259 A1	01.03.2007
		US 2007-0048260 A1	01.03.2007
		US 2007-0048845 A1	01.03.2007
		US 2007-0049529 A1	01.03.2007
		US 2007-0054320 A1	08.03.2007
		US 2007-0059825 A1	15.03.2007
		US 2007-0066807 A1	22.03.2007
		US 2007-0066808 A1	22.03.2007
		US 2007-0092485 A1	26.04.2007
		US 2007-0098682 A1	03.05.2007
		US 2007-0098683 A1	03.05.2007
		US 2007-0099269 A1	03.05.2007
		US 2007-166794 A1	19.07.2007
		US 2010-0222557 A1	02.09.2010
		US 2010-0297063 A1	25.11.2010
		US 2010-0297064 A1	25.11.2010
		US 6307024 B1	23.10.2001
		US 6440980 B1	27.08.2002
		US 6686178 B2	03.02.2004
		US 7091190 B2	15.08.2006
		US 7473765 B2	06.01.2009
		US 7491800 B2	17.02.2009
		US 7569670 B2	04.08.2009
		US 7572892 B2	11.08.2009
		US 7579441 B2	25.08.2009
		US 7592425 B2	22.09.2009
		US 7611699 B2	03.11.2009
		US 7626002 B2	01.12.2009

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/053530

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		US 7829075 B2	09.11.2010
		US 7998468 B2	16.08.2011
		US 8017343 B2	13.09.2011
		US 8110180 B2	07.02.2012
		US 8227575 B2	24.07.2012
		US E041129 E1	16.02.2010
		WO 00-53167 A2	14.09.2000
		WO 00-53761 A2	14.09.2000
		WO 98-11887 A2	26.03.1998
US 2009-0233301 A1	17.09.2009	TW 200938840 A	16.09.2009
US 2011-0105343 A1	05.05.2011	WO 2010-060051 A2	27.05.2010
		WO 2010-060051 A3	22.07.2010
US 2004-0235061 A1	25.11.2004	AU 2002-308331 A8	03.12.2002
		CA 2487099 A1	28.11.2002
		EP 1395114 A2	10.03.2004
		WO 02-094009 A2	28.11.2002