



- (51) International Patent Classification:
C12Q 1/68 (2006.01)
- (21) International Application Number:
PCT/EP2012/060097
- (22) International Filing Date:
30 May 2012 (30.05.2012)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
00921/11 30 May 2011 (30.05.2011) CH
- (71) Applicant (for all designated States except US): **NEBION AG** [CH/CH]; Hohlstrasse 515, CH-8045 Zuerich (CH).
- (72) Inventors; and
(75) Inventors/Applicants (for US only): **LAULE, Oliver** [DE/DE]; Heimbachweg 5, 79713 Bad Säckingen (DE). **BLEULER, Stefan** [CH/CH]; Grepperstrasse 14, CH-6403 Küsnacht am Rigi (CH). **ZIMMERMANN, Philip** [CH/CH]; Bettlachstrasse 153a, CH-2540 Grenchen (CH).
- (74) Agent: **RENTSCH PARTNER AG**; Fraumünsterstrasse 9, CH-8045 Zürich (CH).
- (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,

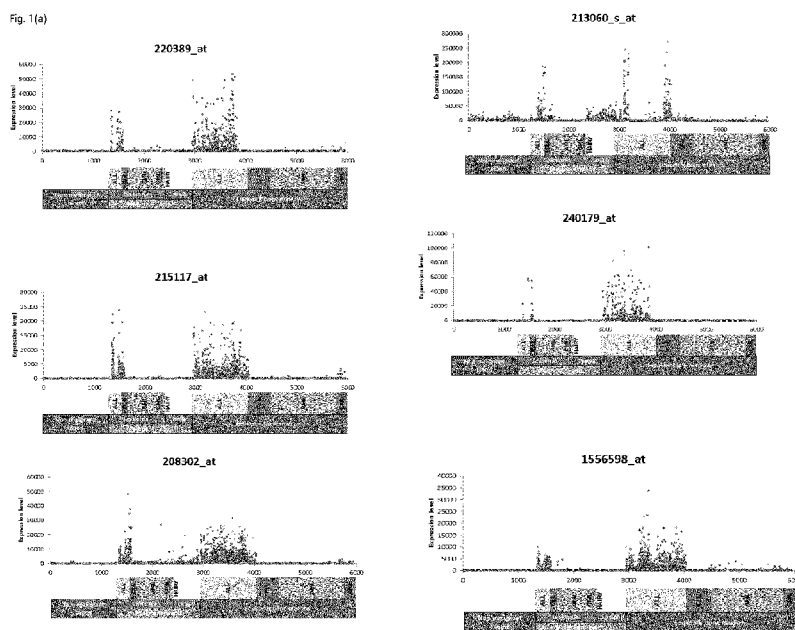
CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, 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, 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:
28 February 2013

(54) Title: MARKER FOR THE DETECTION AND CLASSIFICATION OF LEUKEMIA FROM BLOOD SAMPLES



(57) Abstract: The invention relates to a method for detecting leukemia from patient samples, preferably blood samples, and to preferably classify it into specific types of leukemia, comprising the steps of: (a) determining the expression level of at least one marker gene; and (b) comparing the expression level of the at least one marker gene to a reference to predict leukemia, preferably a specific type of leukemia; wherein the at least one marker gene corresponds to at least one of the genes listed in one or more of Tables I to VI and/or is represented by at least one probe set or at least one target sequence listed in one or more of Tables I to VI. The invention further relates to a kit to perform the method, to the use of the marker genes and to a reagent for detecting leukemia.



INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/060097

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	S. CHIARETTI ET AL: "Gene Expression Profiles of B-lineage Adult Acute Lymphocytic Leukemia Reveal Genetic Patterns that Identify Lineage Derivation and Distinct Mechanisms of Transformation", CLINICAL CANCER RESEARCH, vol. 11, no. 20, 15 October 2005 (2005-10-15), pages 7209-7219, XP055038821, ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-04-2165 abstract page 7215, column 2 page 7218; table 4 ----- -/--	1,10-17, 23,25



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

21 September 2012

Date of mailing of the international search report

10/01/2013

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

Celler, Jakub

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/060097

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2007/011856 A2 (UNIV COLUMBIA [US]; DELLA-FAVERA RICCARDO [US]) 25 January 2007 (2007-01-25) abstract page 19; figure 1 page 6, paragraph 20 page 7, paragraph 23 page 8, paragraph 28 -----	1,2,8, 10-17, 23,25
A	VASCONCELOS Y ET AL: "Gene expression profiling of chronic lymphocytic leukemia can discriminate cases with stable disease and mutated Ig genes from those with progressive disease and unmutated Ig genes", LEUKEMIA, MACMILLAN PRESS LTD, US, vol. 19, no. 11, 25 August 2005 (2005-08-25), pages 2002-2005, XP002367298, ISSN: 0887-6924, DOI: 10.1038/SJ.LEU.2403865 abstract table 1 -----	1,2,8, 10-17, 23,25
X	BACHER U ET AL: "Gene expression profiling for diagnosis and therapy in acute leukaemia and other haematologic malignancies", CANCER TREATMENT REVIEWS, SAUNDERS, US, vol. 36, no. 8, 1 December 2010 (2010-12-01), pages 637-646, XP027487300, ISSN: 0305-7372, DOI: 10.1016/J.CTRV.2010.05.002 [retrieved on 2010-06-08] abstract page 642, column 1 -----	1,10-17, 23,25
X	WO 2010/056351 A2 (STC UNM [US]; WILLMAN CHERYL L [US]; HARVEY RICHARD [US]; KANG HUINING) 20 May 2010 (2010-05-20) abstract page 57 -----	1,10-17, 23,25
X	DATABASE Genbank [Online] NCBI; 23 October 2006 (2006-10-23), "Homo sapiens coiled-coil domain containing 81 mRNA (cDNA clone)", XP002683874, retrieved from ncbi.nlm.nih.gov Database accession no. BC126412 -----	14,25
A	the whole document -----	15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2012/060097

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007011856 A2	25-01-2007	US 2008280297 A1 WO 2007011856 A2	13-11-2008 25-01-2007
WO 2010056351 A2	20-05-2010	US 2011230372 A1 WO 2010056351 A2	22-09-2011 20-05-2010

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/060097

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.:

1, 2, 8, 10-17, 23, 25(all 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: 1, 2, 8, 10-17, 23, 25(all partially)

Subject matter of the above claims, as characterised by the feature of the gene CCDC81 (SEQ ID NO: 1) of Table I of the present application.

2-6. claims: 1, 2, 8, 10-17, 23, 25(all partially)

Subject matter of the above claims, as characterised by the feature of the genes of Table I of the present application, respectively, with the exception of the gene CCDC81 (SEQ ID NO: 1), which represents the first invetin, above.

7. claims: 1, 3, 8, 10-16, 18, 23, 25(all partially)

Subject matter of the above claims, as characterised by the feature of the genes of Table II of the present application, i. e. the feature of AML.

8-13. claims: 1, 4, 8, 10-16, 19, 23, 25(all partially)

Subject matter of the above claims, as characterised by the feature of the genes of Table III of the present application, respectively.

14. claims: 1, 5, 8, 10-16, 20, 23, 25(all partially)

Subject matter of the above claims, as characterised by the feature of the genes of Table IV of the present application, i. e. the feature of CML.

15. claims: 1, 6, 8, 10-16, 21, 23, 25(all partially)

Subject matter of the above claims, as characterised by the feature of the genes of Table V of the present application, i. e. the feature of hairy cell leukemia.

16. claims: 1, 7, 8, 10-16, 22, 23, 25(all partially)

Subject matter of the above claims, as characterised by the feature of the genes of Table VI of the present application, i. e. the feature of multiple types of leukemia.

17. claims: 9, 24(completely); 1-8, 10-23, 25(partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Subject matter of the above claims, as characterised by the
feature of the genes of Table VII of the present
application, i. e. the feature of contrasting gene.
