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17 June 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 2003/102235 A3

(54) Title: SPECIFIC GENETIC MARKETS FOR CYTOGENETICALLY DEFINED ACUTE MYELOID LEUKAEMIA

(57) Abstract: A method of assigning a patient having or suspected of having acute myeloid leukaemia (AML) to a cytogenetically defined AML class, the method comprising providing a sample from the patient, using gene expression profiling to determine the expression level of at least one informative gene in the sample, and using the at least one determined expression level to assign the sample to an AML class. The invention also includes a method of assigning a patient having or suspected of having AML to an AML class, comprising providing a sample from the patient, determining the expression level of at least one informative gene selected from the genes listed in Table 1 or Table 2 or Table 3 in the sample, and using the at least one determined expression level to assign the sample to an AML class.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/02315

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C12Q1/68

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)  
 IPC 7 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 practical, search terms used)

SEQUENCE SEARCH, EMBASE, BIOSIS, 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          | VIRTANEVA K ET AL: "EXPRESSION PROFILING REVEALS FUNDAMENTAL BIOLOGICAL DIFFERENCES IN ACUTE MYELOID LEUKEMIA WITH ISOLATED TRISOMY 8 AND NORMAL CYTOGENETICS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 98, no. 3, 30 January 2001 (2001-01-30), pages 1124-1129, XP002952627 ISSN: 0027-8424 cited in the application the whole document<br>---<br>-/-- | 1-16,29,<br>30,<br>41-46,<br>55,57 |

Further documents are listed in the continuation of box C.

Patent family members are listed in 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 document 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

5 April 2004

Date of mailing of the international search report

13. 04. 2004

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/02315

| 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 5 633 136 A (CANAANI ELI ET AL)<br>27 May 1997 (1997-05-27)<br><br>the whole document   | 1-16,29,<br>30,<br>41-46,<br>55,57 |
| X  | ---<br>PABST ET AL.: "AML1-ETO downregulates the<br>granulocytic differentiation factor<br>C/EBPalpha in t(8;21) myeloid leukemia"<br>NATURE MEDICINE,<br>vol. 7, no. 4, April 2001 (2001-04), pages<br>444-451, XP002255850<br>the whole document   | 1-16,29,<br>30,<br>41-46,<br>55,57 |
| X  | ---<br>KOHLMANN ALEXANDER ET AL: "U937 cell line<br>transfected with Zinc-inducible<br>PML-RARalpha is a suitable model system<br>for acute promyelocytic leukemia: A<br>comparison of gene expression profiles in<br>cell lines and clinical samples."<br>BLOOD,<br>vol. 98, no. 11 Part 2,<br>16 November 2001 (2001-11-16), pages<br>160b-161b, XP001160824<br>43rd Annual Meeting of the American<br>Society of Hematology, Part 2;Orlando,<br>Florida, USA; December 07-11, 2001,<br>November 16, 2001<br>ISSN: 0006-4971<br>the whole document | 1-16,29,<br>30,<br>41-46,<br>55,57 |
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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/02315

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: **1-30, 34-54 (all partially), 56**  
because they relate to subject matter not required to be searched by this Authority, namely:  
**see FURTHER INFORMATION sheet PCT/ISA/210**
  
2.  Claims Nos.: **1-30, 34-54 (all partially)**  
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:  
**see FURTHER INFORMATION sheet PCT/ISA/210**
  
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 II Observations where unity of invention is lacking (Continuation of item 2 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 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.:  
**1-6, 29, 30, 34-46, 55, 57 (all partially)**

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No. PCT/ GB 03/02315

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 56 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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Continuation of Box I.1

Claims Nos.: 1-30, 34-54 (all partially), 56

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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Continuation of Box I.2

Claims Nos.: 1-30, 34-54 (all partially)

The methods and compositions of claims 1-30 and 34-40, respectively, relate to an extremely large number of possible set of genes. In fact, the claims contain so many possible permutations that a lack of clarity (and conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been limited to compositions and methods comprising a specific gene listed in tables 1, 2 or 3.

The above reasoning also applies to claims 41-54, which relate to the use of the compositions and kits of claims 34-39 and 40, respectively.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/ GB 03/ 02315

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. Claims: 1-16, 29, 30, 34-46, 55, 57 (all partialy)

Inventions 1-102

Nucleic acid array comprising one gene; kits comprising primers to amplify said gene; use of said gene; and methods using said gene, array and/or kit,

wherein said gene is that corresponding to the following Genebank Accession Number:

- for invention 1: X05409
- for invention 2: X16662
- for inventions 3-102: Genbank accession numbers as listed in the last column of Table 1, pages 68-71, starting from AA883870 until Y00093

2. Claims: 1-14, 17, 18, 29, 30, 34-45, 47, 48, 55, 57 (all partialy)

Inventions 103-159

Nucleic acid array comprising one gene; kits comprising primers to amplify said gene; use of said gene; and methods using said gene, array and/or kit,

wherein said gene is that corresponding to the following Genebank Accession Number:

- for invention 103: L10373
- for invention 104: U78735
- for inventions 105-159: Genbank accession numbers as listed in the last column in Table 1 in pages 71-72, starting from X96719 until Y11525

3. Claims: 1-14, 19, 20, 29, 30, 34-45, 49, 50, 55, 57 (all partialy),

Inventions 160-211

Nucleic acid array comprising one gene; kits comprising primers to amplify said gene; use of said gene; and methods using said gene, array and/or kit,

wherein said gene is that corresponding to the following Genebank Accession Number:

- for invention 160: X13916
- for invention 161: AF001548
- for inventions 162-211: Genebank Accession Numbers as listed in the last column in Table 1 in pages 72-74,

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/ GB 03/ 02315

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

starting from X96719 until Z35278

4. Claims: 1-14, 21, 22, 29, 30, 34-45, 51, 55,  
57 (all partially)

Inventions 212-269

Nucleic acid array comprising one gene; kits comprising primers to amplify said gene; use of said gene; and methods using said gene, array and/or kit,

wherein said gene is that corresponding to the following Genebank Accession Number:

- for invention 212: L43964
- for invention 213: AL050034
- for inventions 214-269: Genebank Accession Numbers as listed in the last column in Table 1 in pages 74-76, starting from M94345 until M63582

5. Claims: 1-14, 23, 24, 29, 30, 34-45, 52, 55,  
57 (all partially)

Inventions 270-273

Nucleic acid array comprising one gene; kits comprising primers to amplify said gene; use of said gene; and methods using said gene, array and/or kit,

wherein said gene is that corresponding to the following Genebank Accession Number:

- for invention 270: L13698
- for inventions 271-273: Genebank Accession Numbers as listed in the last column in Table 1 in pages 76, starting from S82592 until U64198

6. Claims: 1-14, 25, 26, 29, 30, 34-45, 53, 55,  
57 (all partially)

Invention 274

Nucleic acid array comprising one gene; kits comprising primers to amplify said gene; use of said gene; and methods using said gene, array and/or kit, wherein said gene is that corresponding to the Genebank Accession Number AL050089

7. Claims: 1-14, 27-30, 34-45, 54, 55, 57 (all partially)

Inventions 275-310

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Nucleic acid array comprising one gene; kits comprising primers to amplify said gene; use of said gene; and methods using said gene, array and/or kit,

wherein said gene is that corresponding to the following  
Genebank Accession Number:

-for invention 275: M74297

-for invention 276: U41813

-for inventions 277-310: Genbank accession numbers as listed  
in the last column in Table 1 in pages 76-77, starting from  
M26679 until M63582

8. Claims: 31-33

Invention 311

Methods of identifying at least a set of informative genes  
whose expression correlates with at least one respective  
cytogenetically defined AML class



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/02315

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