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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.

(54) Title: METHODS OF DIAGNOSING COLORECTAL CANCER AND/OR BREAST CANCER, COMPOSITIONS, AND METHODS OF SCREENING FOR COLORECTAL CANCER AND/OR BREAST CANCER MODULATORS

(57) Abstract: Described herein are methods that can be used for diagnosis and prognosis of breast and/or colorectal cancer. Also described herein are methods that can be used to screen candidate bioactive agents for the ability to modulate breast and/or colorectal cancer. Additionally, methods and molecular targets (genes and their products) for therapeutic intervention in breast and/or colorectal cancer are described.



WO 2002/059609 A3

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 01/48368

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 G01N33/574 C12Q1/68 A61K39/395 C07K16/18

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 G01N

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)
 EPO-Internal, Sequence Search, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! XP002249319 accession no. EBI Database accession no. aw780303 abstract	1-3, 5-11, 14, 18-26, 28-32
X	WO 00 30673 A (GENENTECH INC) 2 June 2000 (2000-06-02) claims	1-3, 5, 6, 8-11, 14, 18, 28-31
E	WO 01 94629 A (AVALON PHARMACEUTICALS) 13 December 2001 (2001-12-13) Seq ID No 2646 page 16, paragraph 3 - page 18, paragraph 2 ----- -/--	28, 32

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
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Date of the actual completion of the international search 29 July 2003	Date of mailing of the international search report 13.11.03
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Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <p style="text-align: center; font-size: 1.2em;">Luis Alves, D.</p>
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/48368

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>"ASCO Clinical Practice Guidelines on Tumour Markers in Breast and Colorectal Cancer" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 33, no. 1, January 1997 (1997-01), page 2, XP004282374 ISSN: 0959-8049 abstract</p> <p style="text-align: center;">-----</p>	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/48368

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.: 4, 12, 13, 15-17
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 5, 6, 18 to 28 and 31 are directed to methods comprising steps carried out on the human/animal body or to methods of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: 4, 12, 13, 15 to 17
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.:
see PCT/ISA/210 ANNEX

Remark on Protest

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 4, 12, 13, 15 to 17

Present claim 4 is directed to methods comprising a step of evaluating the activity of CHA4 or CBK8, respectively. However, the application does not disclose any specific activity to be tested in order to be able to carry out the claimed method. General definitions such as those given in the description on p.50, last paragraph to p.51, second paragraph, do not provide a basis for carrying out the claimed method. Thus, claim 4 lacks support (Article 6 PCT) and disclosure (Article 5 PCT) to such an extent that a meaningful search is not possible.

Claims 12 and 13 are directed to a product defined by reference to a desirable effect on the activity of CHA4 or CBK8, respectively. For the same reasons as above the requirements of Article 5 and 6 PCT are not fulfilled, and a meaningful search is not possible for the subject-matter of claims 12 and 13.

The same reasoning applies to the subject-matter of claims 15 to 17. Thus, a meaningful search cannot be carried out for said claims.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-3, 5-11, 14, 18-23 (all partially), 24-26 (all completely), 28-32 (all partially)

Methods of screening for modulators of CHA4 (Seq ID NO 8 (DNA), Seq ID NO 10 (protein)), methods of diagnosing colorectal or breast cancer based on the determination of CHA4, antibodies to CHA4 and methods of treatment based on the administration of CHA4 inhibitors.

2. claims: 1-3, 5-11, 14, 18-23 (all partially), 27 (completely), 28-32 (all partially)

Methods of screening for modulators of CBK8 (Seq ID NO 9 (DNA), Seq ID NO 11 (protein)), methods of diagnosing colorectal cancer based on the determination of CBK8, antibodies to CBK8 and methods of treatment based on the administration of CBK8 inhibitors.

3. claim: 7 (partially)

Methods of diagnosing colorectal or breast cancer based on the determination of the expression of Seq ID NO 1.

4. claim: 7 (partially)

Methods of diagnosing colorectal cancer based on the determination of the expression of Seq ID NO 2.

5. claim: 7 (partially)

Methods of diagnosing colorectal cancer based on the determination of the expression of Seq ID NO 3.

6. claim: 7 (partially)

Methods of diagnosing colorectal cancer based on the determination of the expression of Seq ID NO 4.

7. claim: 7 (partially)

Methods of diagnosing colorectal cancer based on the determination of the expression of Seq ID NO 6.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/48368

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