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(54) Title: DIAGNOSING OR PREDICTING THE COURSE OF BREAST CANCER

(57) Abstract: A method of diagnosing the presence or predicting the course of breast cancer by measuring the expression of a combination of Marker genes comprising a tissue-specific gene and a non-tissue specific gene in a cell or tissue sample derived from a patient. In one aspect of the invention, the genes are mammaglobin and CK19. Kits, nucleic acid primers and probes and controls are provided.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/19616

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: C12Q 1/68(2006.01);C12P 19/34(2006.01);C07H 21/02(2006.01),21/04(2006.01)
 USPC: 435/6,91.2;536/23.1,23.5
 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)
 U.S. : 435/6,91.2; 536/23.1,23.5
 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)
 Medline, Pubmed, GenBank

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KUN Y. et al. Classifying the estrogen receptor status of breast cancers by expression profiles reveals a poor prognosis subpopulation exhibiting high expression of the ERBB2 receptor. Hum Mol Genet. 2003 Dec 15;12(24):3245-58.	1-12
X	LEYGUE E. et al. Mammaglobin, a potential marker of breast cancer nodal metastasis. J Pathol. 1999 Sep;189(1):28-33.	30, 31, 39
A	AFFYMETRIX Details for HG_U133A:201650_AT, pages 1-3, downloaded on 06/11/2008 from www.affymetrix.com	
A	AFFYMETRIX Details for HG_U133A:203040_S_AT, pages 1-4, downloaded on 06/11/2008 from www.affymetrix.com	
A	AFFYMETRIX Details for HG_U133A:206378_AT, pages 1-2, downloaded on 06/11/2008 from www.affymetrix.com	

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	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 11 June 2008 (11.06.2008)	Date of mailing of the international search report 07 JUL 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Stephen Kapushoc Telephone No. 571-272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/19616

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:
Please See Continuation 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 additional fees, this Authority did not invite payment of any 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.:
- 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

International application No.
PCT/US05/19616

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	COBB J.P. et al. Sepsis gene expression profiling: murine splenic compared with hepatic responses determined by using complementary DNA microarrays. Crit Care Med. 2002 Dec;30(12):2711-21.	
A	ENARD W. et al. Intra- and interspecific variation in primate gene expression patterns. Science. 2002 Apr 12;296(5566):340-3.	
A	CHEUNG V.G. et al. Natural variation in human gene expression assessed in lymphoblastoid cells. Nat Genet. 2003 Mar;33(3):422-5.	

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-22, drawn to methods for gene-expression based analysis of breast cancer.

Group 2, claim(s) 23-39, drawn to kits comprising nucleic acids.

The inventions listed as Groups 1 and 2 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The common technical feature between the groups are nucleic acid sequences that are expressed in breast cancer tissues. However, such sequences were known in the prior art, and the mammaglobin sequence and its analysis are taught by Leygue et al (1999). As such the common technical feature is not a special technical feature.