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(54) Title: GENETIC MARKERS FOR PREDICTING DISEASE AND TREATMENT OUTCOME

(57) Abstract: The present invention provides for a method for identifying patients that are suitably treated by a therapy, such as a therapy involving administration of a fluoropyrimidine drug and/or a platinum drug. The method includes determining the expression level of at least one gene selected from a phospholipase 2 (PLA2) gene, a thymidine phosphorylase (TP) gene, and a glutathione S-transferase P1 (GSTP-1) gene in suitable sample isolated from the patient. Overexpression of the gene or genes identifies the patient as not being suitable for the therapy.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/63230

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: C12Q 1/68(2006.01)

USPC: 435/6
 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

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)
 Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/012361 A2 (UNIVERSITY OF SOUTHERN CALIFORNIA) 02 February 2006 (02.02.2006) see abstract, page 6, lines 28-31; page 20, lines 4-6.	1, 5-14
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Y		2-4
Y	US 2004/0203065 A1 (YANG et al.) 14 October 2004 (14.10.2004) see page 6, paragraph 0061.	2-4
Y	US 2005/0202465 A1 (WANG et al.) 15 September 2005 (15.09.2005) see page 1, paragraph 0005.	2-3
X	WO 2004/011625 A2 (UNIVERSITY OF SOUTHERN CALIFORNIA) 05 February 2004 (05.02.2004) see claims 2, 5; page 9, lines 29-30; page 10, lines 19-22.	15-22

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 29 November 2007 (29.11.2007)	Date of mailing of the international search report 18 AUG 2008
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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 Maury Audet Telephone No. 571-272-1600 <i>Janie Ford for</i>
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/63230

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.

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 the PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional fees must be paid.

Group I, claims 1-14 are drawn to a method for determining whether a patient suffering from a gastrointestinal (GI) cancer is suitably treated by a therapy comprising the administration of a fluoropyrimidine or a platinum drug, the method comprising determining the expression level of at least one gene selected from the group consisting of phospholipase 2 (PLA2) gene, thymidine phosphorylase (TP) gene, and glutathione S-transferase P1 (GSTP-1) gene in suitable sample isolated from the patient, wherein overexpression of the gene(s) identifies the patient as not suitable for the therapy.

Group II, claims 15-22 are drawn to a method for identifying patients suffering from a gastrointestinal cancer that are at risk for suffering from undesirable side effects from administration of a fluoropyrimidine drug and a platinum drug, comprising determining the expression level of at least one gene selected from the group consisting of XRCC1 gene and IL-8 gene in suitable sample isolated from the patient, wherein overexpression of the gene(s) identifies the patient as being at a risk for side effects.

The International Searching Authority considers that the international application does not comply with the requirement of unity of invention (PCT Rule 13.1, 13.2 and 13.3) for the reason indicated below:

The inventions between groups I-II are linked by the technical feature of a "treatment of gastrointestinal (GI) cancer comprising a fluoropyrimidine or a platinum drug and determining expression of genetic markers". However, this feature is not special because it does not constitute advancement over the prior art. WO2006/012361 A2 teaches a method for determining the increased risk for recurrence of gastrointestinal cancer using genetic markers (e.g. GSTP-1) and treatment with chemotherapeutic drug selected from the group consisting of fluoropyrimidine, a platinum drug etc. (see abstract and especially claims 1-2 and 16).

Furthermore, each group involves method steps or genetic markers not required by the other groups. Thus, Groups I-II lack unity of invention.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/63230

Continuation of B. FIELDS SEARCHED Item 3:

PGPUB, EPO, JPO, NCBI, Google (search terms: phospholipase (PLA2), fluoropyrimidine, thymidine phosphorylase (TP), GSTP-1, expression, platinum, 5-FU, COX-2, oxaliplatin, cancer)