Abstract:

Title:

J. BRIGHAM
Health, AMERICA
Applicants

Publication
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International
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International
World

221
Corporate
Government

Longwood
Suite

2008

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Boston,

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Boston,

2008

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60/899,942
6 February 2007 (06.02.2007)

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English

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(72) Inventors; and


(74) Agent: BRADLEY, Karri, Kuenzli; Klarquist Sparkman, LLP, One World Trade Center, Suite 1600, 121 Sw Salmon Street, Portland, OR 97204 (US).


(54) Title: A GENE EXPRESSION PROFILE THAT PREDICTS OVARIAN CANCER SUBJECT RESPONSE TO CHEMOTHERAPY

(57) Abstract: A gene profiling signature is disclosed herein. The gene signature can predict whether a subject with ovarian cancer will be chemorefractory, chemoresistant or chemosensitive. Thus, methods are disclosed for determining whether a subject with ovarian cancer will be sensitive to treatment with a chemotherapeutic agent. Methods are also provided for increasing sensitivity to the chemotherapeutic agent if the presence of differential expression indicates that the ovarian cancer has a decreased sensitivity to chemotherapeutic agent.
A. CLASSIFICATION OF SUBJECT MATTER

INV. 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)

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)

EPO-Internal, BIOSIS, WPI Data, EMBASE, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate of the relevant passages</th>
<th>Relevant to claim No</th>
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<td>X</td>
<td>US 2005/176669 A1 (AL-MURRANI SAMER [US]) 11 August 2005 (2005-08-11) abstract, claims 31, 36 and 37, tab.1, [0100], [0011], [0012], [0018], [0098] and [0134]</td>
<td>1-44</td>
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Further documents are listed in the continuation of Box C

See patent family annex

Date of the actual completion of the international search: 25 March 2009

Date of mailing of the international search report: 09/04/2009

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: Berillon-Lapopin, L
### INTERNATIONAL SEARCH REPORT

#### DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>X</td>
<td>US 2006/275810 Al (GEORGES ELIAS [CA] ET AL) 7 December 2006 (2006-12-07) abstract; claims 1,82,89</td>
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Continuation of Box II: 2

Claims Nos.: 1,2,4-19,23-44 (all partly)

1. Claim 1 relates to a method for determining if a subject with ovarian cancer is sensitive to a treatment with chemotherapeutic agent by detecting the expression of at least 6 genes of tables 1 and 5, encompassing 105 and 31 genes, respectively. This claim relate thus to an exceedingly high number of possible gene combinations. This imposes a severe an undue burden on all wishing to ascertain the scope of said claim, which is not in compliance with the clarity requirements of Art. 6 PCT. Thus, claim 1 lacks clarity to such an extend that a meaningful search of the whole claimed subject-matter of said claim could not be carried out (PCT guidelines, 9.19 and 9.24). Consequently, search was limited to the clearly defined gene combination, namely the one cited in claim 3 consisting of COL5A1, COL1A1, DUSP1, REV3L, RNASEL, and POLH.

The same limitation applies for claims 2 and 4-19, 23-28 dependent thereon.

2. The same reasoning and limitation as for claim 1 apply for the following independent claims:
   - claim 29 which refers to a method for evaluating the chemoresponsiveness in a subject with ovarian cancer by analysing the expression of all genes of table 1 or table 5, and wherein the differential expression of at least 6 genes indicates a decreased sensitivity,
   - claim 34 which refers to a method for identifying an agent that alters the activity of chemotherapeutic sensitivity-related molecules listed tables 1, 5 or both,
   - claim 40 referring to a method of treating a mammal by administrating the agent identified in claim 34, and
   - claim 41 which relates to a kit for detecting said genes.

The same limitation applies also for claims 30-33, 35-39 and 42-44 dependent thereon, respectively.

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, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.
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. [X] Claims Nos.: 1,2,4-19,23-44 (al partly) 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).

This International Searching Authority found multiple inventions in this International application, as follows:

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.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicants protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicants 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.
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<td>US 2005176669 A1</td>
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