Title: MOLECULAR SIGNATURES OF COMMONLY FATAL CARCINOMAS

Abstract: This invention provides methods, kits, and algorithms for obtaining molecular signatures of cells based on their gene expression profiles. Devices for carrying out molecular signature analysis of unknown samples are also provided.
### INTERNATIONAL SEARCH REPORT

**International application No.**

PCT/US02/16028

#### A. CLASSIFICATION OF SUBJECT MATTER

- **IPC(7)**: C12Q 1/68; C07H 21/02, 21/04
- **US CL.**: 435/6; 556/23.1, 24.3

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; 556/23.1, 24.3

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)

WEST, PubMed

#### C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>

- **“A”** - document defining the general state of the art which is not considered to be of particular relevance
- **“E”** - earlier application or patent published on or after the international filing date
- **“L”** - document which may throw doubts on priority claimed 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**: 14 May 2003 (14.05.2003)

**Date of mailing of the international search report**: 16 Jun 2004

**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.**: (703)305-3230

**Authorized officer**: Janice Ziske

**Telephone No.**: (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)
INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim 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. ☐ Claim 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:
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 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.: 1-30

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1998)
BOX II. 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 I, claim(s) 1-30, drawn to a kit for identifying an origin of a tumor, the kit comprising two probes which can detect expression products of two genes from Table 3 and a method of identifying an origin of a tumor by detecting expression levels of at least two genes identified in Table 3.

Group II, claim(s) 31-41, drawn to a method for identifying an origin of a tumor by providing a predictor set for two or more genes, detecting in a tumor an expression level for a gene diagnostic for a tumor, calculating a vector distance from the expression level obtained from the tumor sample to each of the levels in the predictor set, determining the shortest vector distance.

Group III, claim(s) 42-48, drawn to a method for obtaining a predictor set for classifying a sample into one or more classes, by obtaining a value for one or more features for each of plurality of members of each of the classes, determining a Wilcoxon rank score for each of the features and ranking the features by predictive accuracy.

Group IV, claim(s) 49-56, drawn to a method for screening a subject for prostate cancer by detecting a level of expression of at least one gene in a sample of prostate tissue, comparing the value with a level of expression of the gene in a sample from a disease free subject.

Group V, claim(s) 57-64, drawn to a method for screening a subject for ovarian cancer by detecting a level of expression of at least one gene in a sample of ovarian tissue, comparing the value with a level of expression of the gene in a sample from a disease free subject.

Group VI, claim(s) 65, drawn to a method for monitoring the progression of prostate cancer in a subject by detecting a level of expression of at least one gene in a sample of prostate tissue, wherein an increase in the level of expression of the gene over time is indicative of the progression of the prostate cancer.

Group VII, claim(s) 66, drawn to a method for monitoring the progression of ovarian cancer in a subject by detecting a level of expression of at least one gene in a sample of ovarian tissue, wherein an increase in the level of expression of the gene over time is indicative of the progression of the ovarian cancer.

Group VIII, claim(s) 67, drawn to a method of identifying agents for use in treatment of prostate cancer by contacting a sample of diseased prostate cells with a candidate agent, detecting a level of expression of at least one gene in the sample and comparing the levels of expression of the gene before and after addition of the candidate agent.

Group IX, claim(s) 68, drawn to a method of identifying agents for use in treatment of ovarian cancer by contacting a sample of diseased ovarian cells with a candidate agent, detecting a level of expression of at least one gene in the sample and comparing the levels of expression of the gene before and after addition of the candidate agent.

Group X, claim(s) 69 and 70, drawn to a method of inhibiting undesired proliferation of a prostate cell by administering to the cell an effective amount of an agent that can decrease expression of at least one gene.

Group XI, claim(s) 71 and 72, drawn to a method of inhibiting undesired proliferation of an ovarian cell by administering to the cell an effective amount of an agent that can decrease expression of at least one gene.

Group XII, claim(s) 73, drawn to a method for monitoring the efficacy of a treatment with an agent of a subject having prostate cancer by obtaining pre- and post-administration samples from the subject, obtaining expression levels of at least one gene in the samples and comparing the expression levels in pre- and post-administration samples.

Group XIII, claim(s) 74, drawn to a method for monitoring the efficacy of a treatment with an agent of a subject having ovarian cancer by obtaining pre- and post-administration samples from the subject, obtaining expression levels of at least one gene in the samples and comparing the expression levels in pre- and post-administration samples.
The inventions listed as Groups I-XII 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 special technical feature of Group I is detection of the expression of two genes in a sample, the special technical feature of Group II is identification of tumor origin by calculating a vector distance from the predictor set to the expression level from the tumor sample and determining the shortest vector distance, the special technical feature of Group III is identification of a predictor set, the special technical feature of Groups IV and V is screening for prostate cancer or ovarian cancer, respectively, the special technical feature of Groups VI and VII is monitoring the progression of prostate cancer or ovarian cancer, respectively, the special technical feature of Groups VIII and IX is identifying agents for treatment of prostate cancer or ovarian cancer, respectively, the special technical feature of Groups X and XI is inhibiting proliferation of prostate cancer or ovarian cancer cells, respectively, and special technical feature of Groups XII and XIII is monitoring the efficacy of a treatment of prostate cancer or ovarian cancer subject, respectively.