MALIGNANCY-RISK SIGNATURE FROM HISTOLOGICALLY NORMAL BREAST TISSUE

Identify IDC signature:
IDC (n = 42) vs. Normal (n = 143)

Identify "IDC-like" normal tissues:
11 normal tissues identified

Patients (80)
Tissues (185)

DC-like normal tissues (11)

Derive malignancy-risk score:
Identify genes common to 11 IDC-like normal tissues

117 genes

Signature
Predominant Gene Function
1038 genes
adhesion + proliferation

Figure 23.
(88) Date of publication of the international search report:
7 January 2010
A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12Q 1/68 (2009.01)
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)
IPC(8): C12Q 1/68 (2009.01)
USPC: 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)
WEST (PGPB,USPT,EPAB,IPAB): breast cancer, breast, cancer, predicting, signature, atypical hyperplasia, mastectomy, fibroadenoma, ipsilateral, likelihood, risk; esp:censt: breast, Moffitt, chen, yeatman; Google Scholar: breast cancer ipsilateral tissue sample mastectomy hyperplasia; NCBi: GSE2034

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>
<tbody>
<tr>
<td>X</td>
<td>MA et al. Gene expression profiles of human breast cancer progression. Proceed. Nat. Acad. Sci. USA, 12 May 2003, Vol 100, No. 10, pages 5974-5979, especially page 5974, abstract; page 5978, Table 1; page 5979, left column, third paragraph.</td>
<td>29</td>
</tr>
<tr>
<td>Y</td>
<td>US 2007/0269432 A1 (NAKAMURA et al.) 22 November 2007 (22.11.2007), abstract: para [0006], [0015], [0016], [0017], [0018], [0019], [0020], [0027], [0020], [0024], [0027], [0023], [0024], [0242].</td>
<td>1-16, 30, 32, 34-39</td>
</tr>
<tr>
<td>Y</td>
<td>WANG et al. Gene-expression profiles to predict distant metastasis of lymph-node-negative primary breast cancer. Lancet. 19 February 2005, Vol 365, pages 671-679, especially page 671, abstract; page 671, left col, first para; page 672, Figure 1; page 676, right col, first full para; page 676, Table 4.</td>
<td>30, 32, 34-39</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C.

Date of the actual completion of the international search
7 May 2009 (07.05.2009)

Date of mailing of the international search report
26 MAY 2009

Authorized officer:
Lee W. Young

PCT Helpdesk: 571-272-4300
PCT CSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Y</td>
<td>US 2006/0195266 A1 (YETMAN) 31 August 2006 (31.08.2006), abstract; para [0048]).</td>
<td>36-39</td>
</tr>
</tbody>
</table>
INTERNATIONAL SEARCH REPORT

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:

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, claims 1-39, drawn to a computer readable medium, a kit comprising an array, an array, a malignancy-risk gene signature and method for predicting breast cancer in an individually comprising the use of the malignancy-risk gene signature. The first invention encompass the malignancy-risk gene signature disclosed in Table 3. The claims encompassed by the first invention is: 1-16, 29-30, 32 and 34-39. Applicant may have additional malignancy-risk gene signatures, disclosed in claims 17/33, tables 7-8, 31A, 32B, 33A, 33b, 34B, 35A, 35B and 36A searched for an additional fee, wherein claims 17/33 and each tables is an invention. With payment for additional search, Applicant must specify the malignancy-risk gene signatures, disclosed in 17/33, tables 7-8, 31A, 32B, 33A, 33b, 34B, 35A, 35B and 36A to be searched.

The special technical feature of the listed inventions is the specific malignancy-risk gene signatures disclosed in each of the listed tables and claims 17/33. The special technical feature of each invention differs from one another. The inventions do not have a shared special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

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 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.: 1-16, 29-30, 32 and 34-39 (claims limited to table 6 or the table 3 subset)

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.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)