Title: METHOD OF DETECTION AND DIAGNOSIS OF ORAL AND NASOPHARYNGEAL CANCERS

Abstract: The present invention relates to cancer and in particular to oral and nasopharyngeal cancers. In particular, the present invention relates to a method of detection and diagnosis of oral squamous cell carcinoma (OSCC) and nasopharyngeal cancers by determining the expression levels of certain genes. The method comprising (a) determining in a biological sample from the patient the amount of the expression level of at least one gene selected from the group consisting of GNA-12 and IFITM3; and (b) comparing the determined expression levels of said genes in said biological sample with the level in a reference. The invention also relates to polypeptides, antibodies and nucleic acids of the invention for use in medicine and a kit for performing the invention.
A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

C12Q 1/68 (2006.01)  A61K 39/395 (2006.01)  C40B 40/10 (2006.01)
A61K 31/7105 (2006.01)  A61P 35/00 (2006.01)  GOIN 53/574 (2006.01)
A61K 38/17 (2006.01)  C40B 40/08 (2006.01)  GOIN 53/65 (2006.01)

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)

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)

EPDOC, WPIDS, CAPLUS, BIOTECHABS, MEDLINE, BIOSIS: GNA12, IFITM3, cancer (and like terms)

GENOMQUEST: motif search of GNA12 and IFITM3 primers in Table 2. GenePAST searches of GNA12 and IFITM3

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>ARORA S et al. 'Identification of Differentially Expressed Genes in Oral Squamous Cell Carcinoma'. Molecular Carcinogenesis, 2005, Vol. 42, pages 97-108. See the whole document, particularly Sequencing of cDNA Fragments and Computer analysis section and Table 1.</td>
<td>1-11, 27-30</td>
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<td>WO 1999/038973 A2 (CORIXA CORPORATION) 5 August 1999. See the whole document, particularly SEQ ID NO: 119 and 124, page 33 lines 21-30, page 2 line 29 to page 3 line 9, page 31 lines 21-29, page 19 line 22 to page 20 line 2, page 20 line 3 to page 21 line 5 and claims 42-43 and 46.</td>
<td>1-24, 26-30</td>
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<td>As above.</td>
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X Further documents are listed in the continuation of Box C  X 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
  'E' earlier application or patent but published on or after the international filing date
  '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)
  '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:
21 January 2010

Date of mailing of the international search report: 08.FEB 2010

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<td>P3X</td>
<td>CHEONG SC et al. 'Gene expression in human oral squamous cell carcinoma is influenced by risk factor exposure'. Oral Oncology, 2009, Vol. 45, pages 712-719. See the whole document, particularly the abstract, <em>Materials and methods</em> section and Table 2.</td>
<td>1-2, 4-7, 9-10, 27-30</td>
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<td>P3X</td>
<td>LIU S et al. 'Gαπ-Mediated Pathway Promotes Invasiveness of Nasopharyngeal Carcinoma by Modulating Actin Cytoskeleton Reorganization'. Cancer Research, 2009, Vol. 69, No. 15, pages 6122-6130. See the whole document, particularly the abstract, <em>Ga_{12} signaling activated in NPC tumorigenesis</em> section, <em>Immunohistochemical assays of Ga_{12} expression in NPC tumorigenesis</em> section and <em>Ga_{12} depletion inhibited cell migration and invasion and reversed fibroblastic changes in NPC cells</em> section.</td>
<td>1-3, 5-11, 17-19, 27-28, 30</td>
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Internationalsearch 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)

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

This International Application does not comply with the requirements of unity of invention because it does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept.

[Continued in Supplemental Box]

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.: 

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.
Supplemental Box
(To be used when the space in any of Boxes I to IV is not sufficient)

Continuation of Box No: III

In assessing whether there is more than one invention claimed, I have given consideration to those features which can be considered to potentially distinguish the claimed combination of features from the prior art. Where different claims have different distinguishing features they define different inventions.

This International Searching Authority has found that there are different inventions as follows: Invention 1. Claims 1-30 (all partially) are directed to the diagnosis and/or treatment of cancer by the measurement of the expression of GNA-12. It is considered that the use of GNA-12 in diagnosing and/or treating cancer comprises a first distinguishing feature.

Invention 2. Claims 1-30 (all partially) are directed to the diagnosis and/or treatment of cancer by the measurement of the expression of IFITM3. It is considered that the use of IFITM3 in diagnosing and/or treating cancer comprises a second distinguishing feature.

PCT Rule 13.2, first sentence, states that unity of invention is only fulfilled when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. PCT Rule 13.2, second sentence, defines a special technical feature as a feature which makes a contribution over the prior art.

The only feature common to all of the claims is the determination of differential gene expression in cancers. However this concept is not novel in the light of:


The cited art discloses the use of gene expression profiles of oral squamous cell carcinoma (OSCC) to identify new gene targets for diagnosis and therapy. Using differential display reverse transcription polymerase and reverse Northern blot analysis, 26 cDNAs were identified as being overexpressed in tumours. Therefore the determination of differential gene expression in cancers, including OSCC, is known.

Furthermore, one of the cDNAs identified in the cited art was an Interferon-inducible transmembrane protein 1-8U (IFITM3) homolog (see Sequencing of cDNA Fragments and Computer analysis section and Table 1). This means that IFITM3 is known to be associated with cancer and, more specifically, differentially expressed in OSCC.

GNA-12 is also known to be associated with cancer. The following citations are examples that disclose the association of GNA-12 with different cancers:


Each of these documents discloses the involvement of GNA-12 in cancers. Therefore GNA-12 is known to be associated with various cancers.

This means that the common feature can not constitute a special technical feature within the meaning of PCT Rule 13.2, second sentence, since it makes no contribution over the prior art.

Because the common feature does not satisfy the requirement for being a special technical feature it follows that it cannot provide the necessary technical relationship between the identified inventions. Therefore the claims do not satisfy the requirement of unity of invention a posteriori.
This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX