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(54) Title: GENE EXPRESSION IN BLADDER TUMORS

(57) Abstract: Methods for analyzing tumor cells, particularly bladder tumor cells employ gene expression analysis of samples. Gene expression patterns are formed and compared to reference patterns. Alternatively gene expression patterns are manipulated to exclude genes which are expressed in contaminating cell populations. Another alternative employs subtraction of the expression of genes which are expressed in contaminating cell types. These methods provide improved accuracy as well as alternative basis for analysis from diagnostic and prognostic tools currently available.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 00/00367

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 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)

IPC 7 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, PAJ, WPI Data, BIOSIS, EMBASE, CHEM ABS Data, MEDLINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NELSON ET AL: "An expressed-sequence-tag database of the human prostate: sequence analysis of 1168 cDNA clones" GENOMICS,US,ACADEMIC PRESS, SAN DIEGO, vol. 1, no. 47, 1998, pages 12-25, XP002076079 ISSN: 0888-7543	1,2,4,5, 23-25
Y	the whole document  ---  -/--	3,6,7, 11-22,26

Further documents are listed in the continuation of box C.

Patent family members are listed in 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 document 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.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 December 2000	29/12/2000

Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  Hagenmaier, S
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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 00/00367

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KRIZMAN DAVID B ET AL: "Construction of a representative cDNA library from prostatic intraepithelial neoplasia." CANCER RESEARCH, vol. 56, no. 23, 1996, pages 5380-5383, XP002155223 ISSN: 0008-5472	1,2,4,5, 23-25
Y	the whole document	3,6,7, 11-22,26
X	----- HAWKINS V ET AL: "PEDB: THE PROSTATE EXPRESSION DATABASE" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 27, no. 1, 1999, pages 204-208, XP000933960 ISSN: 0305-1048	1,2,4,5, 23-25
Y	the whole document	3,6,7, 11-22,26
X	----- WO 96 30389 A (MILLENNIUM PHARM INC) 3 October 1996 (1996-10-03)	22-26
Y	the whole document	1-7, 11-21
X	----- WO 98 53319 A (KINZLER KENNETH W ;VOGELSTEIN BERT (US); UNIV JOHNS HOPKINS (US)) 26 November 1998 (1998-11-26)	22-25
Y	the whole document	1-7, 11-21,26
X	----- ZHANG L ET AL: "Gene expression profiles in normal and cancer cells" SCIENCE, US, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, vol. 276, 23 May 1997 (1997-05-23), pages 1268-1272, XP002083785 ISSN: 0036-8075	22-25
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Y	----- ORNTOFT TORBEN F ET AL: "Molecular alterations in bladder cancer." UROLOGICAL RESEARCH, vol. 26, no. 4, August 1998 (1998-08), pages 223-233, XP000971351 ISSN: 0300-5623	3,6,7, 11-22,26
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## INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KNOWLES MARGARET A: "Molecular genetics of bladder cancer: Pathways of development and progression." CANCER SURVEYS, vol. 31, 1998, pages 49-76, XP000971199 1998 Cold Spring Harbor Laboratory Press 10 Skyline Dr., Plainview, New York 11803, USA ISBN: 0-87969-529-3 the whole document ---	3,6,7, 11-22,26
Y	WO 97 16206 A (GETZENBERG ROBERT H ;BAHNSON ROBERT R (US)) 9 May 1997 (1997-05-09) the whole document ---	3,6,7, 11-22,26
A	WO 97 28446 A (UNIV MIAMI) 7 August 1997 (1997-08-07) the whole document ---	
P,Y	DE 198 18 619 A (METAGEN GES FUER GENOMFORSCHUN) 28 October 1999 (1999-10-28) the whole document ---	1-7, 11-26
P,Y	WO 99 47674 A (CORIXA CORP) 23 September 1999 (1999-09-23) See example 3, page 40- page 41 -----	1-7, 11-26

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 8-10

Present claims 8-10 relate to a method of detecting an invasive tumor in a patient defined by reference to a desirable characteristic or property, namely detecting in a sample of a body fluid a marker which is more prevalent in submucosal, smooth muscle, or connective tissue than in the body fluid wherein the marker is an mRNA or protein expression product of a gene, wherein an increased amount of the marker in the body fluid indicated a tumor which has become invasive in the patient.

The claims cover all methods having this characteristic or property without defining the claimed subject matter by technical features and the application provides no technical support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 for such methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). Consequently, no search has been carried out for these claims.

The applicant's attention is drawn to the fact that claims, or parts of 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.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/IB 00/00367
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