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(54) Title: DIFFERENTIAL GENE EXPRESSION IN CANCER

(57) Abstract: The invention is directed towards methods for ascertaining gene expression characteristic for cancer, in particular brain cancers such as glioblastoma, and the sequences identified thereby. Compositions, methods and kits encompassing such are provided herein.

INTERNATIONAL SEARCH REPORT

Interr nal Application No
PCT/US 00/31809

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68 G01N33/50

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 G01N

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, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 53319 A (KINZLER KENNETH W ;VOGELSTEIN BERT (US); UNIV JOHNS HOPKINS (US)) 26 November 1998 (1998-11-26) page 81 -page 91; claims 1-52; examples 1-6 ---	1,4-11, 14-18, 21-30
X	DATABASE EBI 'Online! EMBL; 5 January 1998 (1998-01-05) HILLIER ET AL: "WashU-NCI human EST Project" Database accession no. EM_EST:AA705392 XP002174758 SEQ ID NO:1 99,01% abstract --- -/--	1,4-11, 14-18, 21-30

[X] Further documents are listed in the continuation of box C.

[X] 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

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 October 2001	08-11-2001

Name and mailing address of the ISA	Authorized officer
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	Gabriels, J

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	LAL ANITA ET AL: "A public database for gene expression in human cancers." CANCER RESEARCH, vol. 59, no. 21, 1 November 1999 (1999-11-01), pages 5403-5407, XP002174720 ISSN: 0008-5472 page 5404 -page 5407; table 2 ---	1,4-11, 14-18, 21-30
X	WO 99 53062 A (KORENBERG JULIE R ;CHEN XIAO NING (US); CEDARS SINAI HEALTH SYSTEM) 21 October 1999 (1999-10-21) claims 1-57 ---	1,4-11, 14-18, 21-30
X	YAMAGUCHI FUMIO ET AL: "Differential expression of two fibroblast growth factor-receptor genes is associated with malignant progression in human astrocytomas." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 91, no. 2, 1994, pages 484-488, XP002141422 1994 ISSN: 0027-8424 page 485 -page 488 ---	1,4-11, 14-18, 21-30
X	US 5 858 712 A (GOLI SURYA K ET AL) 12 January 1999 (1999-01-12) column 25, line 64 -column 32; claims 1-8 ---	1,4-11, 14-18, 21-30
X	WO 99 23252 A (BAKKENIST CHRISTOPHER JAMES ;MCGEE JAMES O DONNELL (GB); ISIS INNO) 14 May 1999 (1999-05-14) claims 1-26 ---	1,4-11, 14-18, 21-30
P,X	WO 00 28090 A (YAMAMOTO HIROTAKA ;JASTROW AARON (US); KROES ROGER A (US); NYXIS I) 18 May 2000 (2000-05-18) the whole document ---	1,4-11, 14-18, 21-30
X	DATABASE EBI 'Online! EMBL; 27 April 1997 (1997-04-27) ADAMS M.D. ET AL: "Use of a random BAC End Sequence Database for Sequence-Ready Map Building" Database accession no. EM_GSS:AQ005923 XP002181161 99.27 % identical to SEQ ID NO:68 abstract --- -/--	1-30

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EBI 'Online! EMBL; 27 July 1999 (1999-07-27) AGOSTINO M.J. ET AL: "SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM" Database accession no. GSN:AAX60579 XP002181162 98.496 % identical to SEQ ID NO:69 abstract & WO 99 24469 A (GENETICS INST (US)) 20 May 1999 (1999-05-20) ---	1-30
X	WO 99 22243 A (ENDRESS GREGORY A ;FLORENCE KIMBERLY A (US); HUMAN GENOME SCIENCES) 6 May 1999 (1999-05-06) SEQ ID NO:118 of WO9922243 is 98.48 % identical to SEQ ID NO:183 of the present application page 172, line 9 -page 173, line 17 ---	1-30
X	DATABASE EBI 'Online! EMBL; 12 April 1997 (1997-04-12) STRAUSBERG R. ET AL: "National Cancer Institute, Cancer Genome Anatomy Project (CGAP), Tumor gene index" Database accession no. EM_EST:HS1191117 XP002181163 99.789 % identical to SEQ ID NO:183 abstract -----	1-30

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INTERNATIONAL SEARCH REPORT

In ational application No.
PCT/US 00/31809

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 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:

see additional 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.:

Invention 1,68,69, and 183; claims 1-30

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.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 1:

An isolated nucleic acid comprising SEQ ID NO:1, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

2. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 2:

An isolated nucleic acid comprising SEQ ID NO:2, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

Invention 3-67:

Idem for invention 3 to 67 but limited to the sequences comprising SEQ ID NOs 3-67. (SEQ ID NO:3 represents invention number 3,... ,SEQ ID NO:18 represents invention number 18,... , and SEQ ID NO:67 represents invention number 67)

3. Claims: 1-30 (all partially)

Invention 68:

An isolated nucleic acid comprising SEQ ID NO:68, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

4. Claims: 1-30 (all partially)

Invention 69:

An isolated nucleic acid comprising SEQ ID NO:69, or

expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

5. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 70:

An isolated nucleic acid comprising SEQ ID NO:70, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

Invention 71-141:

Idem for invention 71 to 141 but limited to the sequences comprising SEQ ID NOs 71-141. (SEQ ID NO:71 represents invention number 71,... ,SEQ ID NO:100 represents invention number 100,... , and SEQ ID NO:141 represents invention number 141)

6. Claims: 1,2,4-12,14-19,21-30 (all partially)

Invention 142:

An isolated nucleic acid comprising SEQ ID NO:142, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

7. Claims: 1,2,4-12,14-19,21-30 (all partially)

Invention 143:

An isolated nucleic acid comprising SEQ ID NO:143, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. Claims: 1,2,4-12,14-19,21-30 (all partially)

Invention 144:

An isolated nucleic acid comprising SEQ ID NO:144, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

9. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 145:

An isolated nucleic acid comprising SEQ ID NO:145, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

10. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 146:

An isolated nucleic acid comprising SEQ ID NO:146, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

11. Claims: 1,2,4-12,14-19,21-30 (all partially)

Invention 147:

An isolated nucleic acid comprising SEQ ID NO:147, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

12. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 148:

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

An isolated nucleic acid comprising SEQ ID NO:148, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

13. Claims: 1,2,4-12,14-19,21-30 (all partially)

Invention 149:

An isolated nucleic acid comprising SEQ ID NO:149, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

14. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 150:

An isolated nucleic acid comprising SEQ ID NO:150, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

Invention 151-161:

Idem for invention 151 to 161 but limited to the sequences comprising SEQ ID NOs 151-161. (SEQ ID NO:151 represents invention number 151,... ,SEQ ID NO:155 represents invention number 155,... , and SEQ ID NO:161 represents invention number 161)

15. Claims: 1,2,4-12,14-19,21-30 (all partially)

Invention 162:

An isolated nucleic acid comprising SEQ ID NO:162, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

16. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 163:

An isolated nucleic acid comprising SEQ ID NO:163, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

Invention 164-172:

Idem for invention 164 to 172 but limited to the sequences comprising SEQ ID NOs 164-172. (SEQ ID NO:164 represents invention number 164,... ,SEQ ID NO:170 represents invention number 170,... , and SEQ ID NO:172 represents invention number 172)

17. Claims: 1,2,4-12,14-19,21-30 (all partially)

Invention 173:

An isolated nucleic acid comprising SEQ ID NO:173, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

18. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 174:

An isolated nucleic acid comprising SEQ ID NO:174, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

Invention 175-182:

Idem for invention 175 to 182 but limited to the sequences comprising SEQ ID NOs 175-182. (SEQ ID NO:175 represents invention number 175,... ,SEQ ID NO:180 represents invention number 180,... , and SEQ ID NO:182 represents invention number 182)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

19. Claims: 1-30 (all partially)

Invention 183:

An isolated nucleic acid comprising SEQ ID NO:183, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

20. Claims: 1,4-11,14-18,21-30 (all partially)

Invention 184:

An isolated nucleic acid comprising SEQ ID NO:184, or expression vectors, or transformed host cells derived thereof, or therapeutic compound identified thereby or kits thereof for the use in methods for ascertaining the propensity of a cell for malignant phenotype and for ascertaining the suitability of an anti-neoplastic drug candidate for efficacy in treating a malignancy.

INTERNATIONAL SEARCH REPORT

ormation on patent family members

Interr nal Application No
PCT/US 00/31809

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