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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: CANCER-LINKED GENE AS TARGET FOR CHEMOTHERAPY

(57) Abstract: Cancer-linked gene sequences, and derived amino acid sequences, are disclosed along with processes for assaying potential antitumor agents based on their modulation of the expression of these cancer-linked genes. Also disclosed are antibodies that react with the disclosed polypeptides and methods of using the antibodies to treat cancerous conditions, such as by using the antibody to target cancerous cells *in vivo* for purposes of delivering therapeutic agents thereto. Also described are methods of diagnosing using the gene sequences.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/17722

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) : C12Q 1/00, 1/68; G01N 33/53

US CL : 435/7.1, 4, 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)

U.S. : 435/7.1, 4, 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)

Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	OLIE et al A Novel Antisense Oligonucleotide Targeting Survivin Expression Induces Apoptosis and Sensitizes Lung Cancer Cells to Chemotherapy. Cancer Research. June 1, 2000. June 1, 2000. Vol 60, 2805-2809.	1-4
A	WEBB et al. The Geldanamycins Are Potent Inhibitors of the Hepatocyte Growth Factor/Scatter Factor-Met-Urokinase Plasminogen Activator-Plasmin Proteolytic Network. Cancer Research. January 15, 2000. 60, 342-349,	1-4
A	JUNG et al. Flavopiridol Increases Sensitization to Gemcitabine in Human Gastrointestinal Cancer Cell Lines and Correlates with Down-Regulation of Ribonucleotide Reductase M2 Subunit. Clinical Cancer Research. August 2001. Vol. 7, 2527-2536.	1-4
A	CLARKE et al. Gene expression profiling of human colon cancer cells following inhibition of signal transduction by 17-allylamino-17-demethoxygeldanamycin, an inhibitor of the hsp90 molecular chaperone. Oncogene. 2000 Aug 24. Vol. 19, No. 36, pages:4125-33	1-4



Further documents are listed in the continuation of Box C.



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 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

07 February 2006 (07.02.2006)

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Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/17722

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.: 1-4

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

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 inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group 1, Claims 1-4 drawn to a method for identifying an agent that modulates the activity of a cancer-related gene in a cell comprising SEQ ID NO:1.

Group 2, Claims 1, 5-7 drawn to a process for identifying an anti-neoplastic agent comprising contacting a cell, in culture, comprising SEQ ID NO:1 with a modulator identified in the process of claim 1.

Group 3, Claims 1, 8 drawn to a process for identifying an anti-neoplastic agent comprising contacting an animal exhibiting a cancer condition with a modulator identified in the process of claim 1.

Group 4, Claims 9-in-part, 10 drawn to a process for determining the cancerous status of a cell comprising determining an increase in the level of mRNA expression of SEQ ID NO:1 compared to normal control.

Group 5, Claims 9-in-part, 10 drawn to a process for determining the cancerous status of a cell comprising determining an increase in the level of protein expression of SEQ ID NO:1 compared to normal control.

Group 6, Claims 11-12 drawn to a polypeptide comprising SEQ ID NO:2.

Group 7, Claims 13-23 drawn to an antibody that reacts with SEQ ID NO:2/ antibody conjugated to a cytotoxic agent.

Group 8, Claims 24-in-part, 25-26, 29, 32 drawn to a process for treating cancer comprising contacting a cancerous cell with an agent/antibody having activity against a protein expression product encoded by SEQ ID NO:1.

Group 9, Claims 24-in-part, 27-28, 29-31, 32 drawn to a process for treating cancer comprising contacting a cancerous cell with an agent/an immunogenic composition comprising SEQ ID NO:2 or a homologue thereof having activity against a protein expression product encoded by SEQ ID NO:1.

Group 10, Claims 24-in-part, 29, 32 drawn to a process for treating cancer comprising contacting a cancerous cell with an agent having activity against an mRNA expression product encoded by SEQ ID NO:1.

Group 11, Claim 33-in-part, 34-35 drawn to a process for protecting an animal against cancer comprising administering to an animal at risk of developing cancer a therapeutically effective amount of an antibody against SEQ ID NO:2.

Group 12, Claim 33-in-part, 34-35 drawn to a process for protecting an animal against cancer comprising administering to an animal at risk of developing cancer a therapeutically effective amount of immunogenic composition comprising against SEQ ID NO:2 or a homologue thereof.

Group 13, Claim 33-in-part, 34-35 drawn to a process for protecting an animal against cancer comprising administering to an animal at risk of developing cancer a therapeutically effective amount of a composition having activity against the mRNA expression product of SEQ ID NO:1.

Group 14, claim 36 a method for producing test data with respect to the gene modulating activity of a compound.

The inventions listed as Groups 1-14 do not relate to a single general inventive concept under PCT Rule 13.1 because they are not drawn to one of the combinations of categories under PCT article 17(3) (a).

An international stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. When claims to

different categories are present in the application, the claims will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) A product and a process specially adapted for the manufacture of said product; or (2) A product and a process of use of said product; or (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or (4) A process and an apparatus or means specifically designed for carrying out the said process; or (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). Group I will be the main invention. After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d)).

Group 1 is drawn to a method for identifying an agent that modulates the activity of a cancer-related gene in a cell comprising SEQ ID NO:1.

Groups 2-14 are drawn to methods different than the method of Group 1 and the products claimed, that is the protein product claimed, the antibody product claimed are drawn to products not used in a method of modulating the activity of a cancer-related gene in a cell, all of these products and methods are properly broken out as separate groups because Groups 2-14 are not drawn to one of the combinations of categories under PCT article 17(3) (a) and they therefore do not form a single general inventive concept.

Continuation of B. FIELDS SEARCHED Item 3:

MEDLINE, GENBANK

search terms: colon cancer cell, SEQ ID NO:1, modulates activity