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(54) Title: INDUCIBLE SCREEN FOR DRUG DISCOVERY

(57) Abstract: A method for identifying a polynucleotide, the expression of which is modulated in the presence of nitric oxide (NO), which method comprises: (i) providing an mRNA or cDNA population from cells which contain a polynucleotide construct, which construct comprises: (a) a promoter operably linked to a coding sequence, wherein the promoter is responsive to ecdysone or an analog thereof and the coding sequence encodes a nitric oxide synthase (NOS) or a functional variant thereof; or (b) a promoter operably linked to one or more tetracycline operator site sequences and a coding sequence in that order, wherein the coding sequence encodes a nitric oxide synthase (NOS) or a functional variant thereof; (ii) providing an mRNA or cDNA population from cells as defined in step (i), said cells having been contacted with ecdysone or an analog thereof; and (iii) comparing the populations of steps (i) and (ii), thereby to determine which polynucleotides show modulated expression in the presence of NO.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02932

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 C07K14/47 C12N5/10 C12N15/63 A61K38/00

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 C12N

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, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS

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 26066 A (ARIAD GENE THERAPEUTICS INC ; CERASOLI FRANKLIN JR (US)) 18 June 1998 (1998-06-18) claims 1-25	6-16
Y	---	1
Y	US 5 759 836 A (ABRAMSON STEVEN B ET AL) 2 June 1998 (1998-06-02) claims 1,2	1
A	---	6-16
X	WO 99 33971 A (MEDICAL COLLEGE OF GEORGIA RES) 8 July 1999 (1999-07-08) the whole document	2,3
X	US 5 908 756 A (JAFFREY SAMIE R ET AL) 1 June 1999 (1999-06-01) the whole document	2,3
	-/--	

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

9 March 2001

Date of mailing of the international search report

23/03/2001

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02932

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 11620 A (LOWE JOHN ADAMS III ;PFIZER PROD INC (US)) 11 March 1999 (1999-03-11) page 7 -page 8; claims 1-10 ----	17,25,34
X	CHRISTODOULOPOULOS GARYFALLIA ET AL: "Potentiation of chlorambucil cytotoxicity in B-cell chronic lymphocytic leukemia by inhibition of DNA-dependent protein kinase activity using wortmannin." CANCER RESEARCH, vol. 58, no. 9, 1 May 1998 (1998-05-01), pages 1789-1792, XP002161828 ISSN: 0008-5472 page 1790, left-hand column -page 1792, left-hand column ----	18-22, 26-30, 35-39
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 23 November 1998 (1998-11-23) HOSOI YOSHIO ET AL: "A phosphatidylinositol 3-kinase inhibitor wortmannin induces radioresistant DNA synthesis and sensitizes cells to bleomycin and ionizing radiation." Database accession no. PREV199900006904 XP002161830 abstract & INTERNATIONAL JOURNAL OF CANCER, vol. 78, no. 5, 23 November 1998 (1998-11-23), pages 642-647, ISSN: 0020-7136 ----	18-20, 23,24, 26-28, 31-33, 40-42
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 28 May 1998 (1998-05-28) DEL REAL GUSTAVO ET AL: "Suppression of HIV-1 infection in linomide-treated SCID-hu-PBL mice." Database accession no. PREV199800315674 XP002161831 abstract & AIDS (LONDON), vol. 12, no. 8, 28 May 1998 (1998-05-28), pages 865-872, ISSN: 0269-9370 ----- -/--	43
Y		44-51

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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	<p>DANIEL RENE ET AL: "A role for DNA-PK in retroviral DNA integration." SCIENCE (WASHINGTON D C), vol. 284, no. 5414, 23 April 1999 (1999-04-23), pages 644-647, XP002161829 ISSN: 0036-8075 cited in the application the whole document</p>	44-51
A	<p>NO ET AL: "ECDYSONE-INDUCIBLE EXPRESSION IN MAMMALIAN CELLS AND TRANSGENIC MICE" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, INDIA. SECTION A, PHYSICAL SCIENCES, IN, NATIONAL ACADEMY OF SCIENCE, ALLAHABAD, vol. 93, 1996, pages 3346-3351, XP002136440 ISSN: 0369-8203 page 3350, right-hand column -page 3351, left-hand column; figures 1,2</p>	1-16

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

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

1. Claims: 1-3,6-16 (complete)

Invention 1:

A polynucleotide and vector containing an inducible promoter and a nitric oxide synthase coding sequence and methods and uses thereof and cells containing it.

2. Claims: 17,25,43-47 (complete) 51 (partially)

Invention 2:

Products containing NOS inhibitors and uses thereof.

3. Claims: 18-24,26-33 (complete)

Invention 3:

Products containing a DNA repair enzyme inhibitor and a DNA damaging agent and uses thereof.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 4,5

Claims 4, and 5 are directed to compounds identified by the method of claim 3. Claim 3 is again directed to compounds identified by the method of claim 1. However, no such compounds are defined in the application thereby rendering the subject matter of said claims purely speculative and a mere statement of the goals to be achieved. No meaningful search can be carried out for such "read-through claims" whose scope is open-ended and unclear (Article 6 PCT).

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/GB 00/02932

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WO 9826066	A	18-06-1998	AU 7847698 A EP 0948619 A	03-07-1998 13-10-1999
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WO 9933971	A	08-07-1999	AU 2018999 A	19-07-1999
US 5908756	A	01-06-1999	AU 4330197 A EP 0958359 A JP 2001500726 T WO 9808945 A	19-03-1998 24-11-1999 23-01-2001 05-03-1998
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