



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12N 15/12, 15/53, C07K 16/40, 16/18, 14/47, C12N 9/02, A61K 38/17, 38/44, 48/00, G01N 33/50	A3	(11) International Publication Number: WO 00/28031 (43) International Publication Date: 18 May 2000 (18.05.00)
(21) International Application Number: PCT/US99/26592 (22) International Filing Date: 10 November 1999 (10.11.99) (30) Priority Data: 60/107,911 10 November 1998 (10.11.98) US 60/149,332 17 August 1999 (17.08.99) US 60/151,242 27 August 1999 (27.08.99) US (71) Applicant: EMORY UNIVERSITY [US/US]; 2009 Ridgewood Drive, Atlanta, GA 30322 (US). (72) Inventors: LAMBETH, J., David; 461 Emory Drive, Decatur, GA 30207 (US). LASSEGUE, Bernard, P.; 564 Emory Oaks Way, Decatur, GA 30033 (US). GRIENDLING, Kathy, K.; 1819 Kanawha Trail, Stone Mountain, GA 30087 (US). ARNOLD, Rebecca, S.; 4344 Bridle Path Court, Tucker, GA 30084 (US). GUANGJIE, Cheng; Apt 1, 2751 Briarcliff Road, Atlanta, GA 30329 (US). (74) Agents: ELSEVIER, Lisa, C. et al.; Jones & Askew, LLP, 2400 Monarch Tower, 3424 Peachtree Road, N.E., Atlanta, GA 30326 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 23 November 2000 (23.11.00)
(54) Title: MITOGENIC REGULATORS (57) Abstract The present invention relates to new genes encoding for the production of novel proteins involved in generation of reactive oxygen intermediates that affect cell division. The present invention also provides vectors containing these genes, cells transfected with these vectors, antibodies raised against these proteins, kits for detection, localization and measurement of these genes and proteins, and methods to determine the activity of drugs to affect the activity of the proteins of the present invention.		

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INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/12 C12N15/53 C07K16/40 C07K16/18 C07K14/47 C12N9/02 A61K38/17 A61K38/44 A61K48/00 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 C12N C07K A61K 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, STRAND		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LI F ET AL: "CD34+ PERIPHERAL BLOOD PROGENITORS AS A TARGET FOR GENETIC CORRECTION OF THE TWO FLAVOCYTOCHROME B558 DEFECTIVE FORMS OF CHRONIC GRANULOMATOUS DISEASE" BLOOD,US,W.B. SAUNDERS, PHILADELPHIA, VA, vol. 84, no. 1, 1 July 1994 (1994-07-01), pages 53-58, XP000674233 ISSN: 0006-4971	1,3,5,7, 9,11,13
A	page 54, column 2 figures 1,2	2,4,6,8, 10,12,14
X	US 5 593 966 A (MALECH HARRY L ET AL) 14 January 1997 (1997-01-14)	1,3,9,15
A	column 5, line 34 -column 6, line 53; figure 2; table 1 -/--	2,4,10, 16
☒ 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. "&" document member of the same patent family		
Date of the actual completion of the international search 16 August 2000		Date of mailing of the international search report 31.08.00
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 van Klompenburg, W

INTERNATIONAL SEARCH REPORT

In 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.
X	STRAUSBERG ET AL.: "National cancer institute. cancer genome anatomy project (CGAP)" EMBL DATABASE ACC NO: AA493362, 28 June 1997 (1997-06-28), XP002137597 the whole document ---	1-14
X	LLOYD: "Human DNA sequence from clone 146h21 on chromosome Xq22" EMBL DATABASE ACC NO: Z83819, 10 January 1997 (1997-01-10), XP002137598 the whole document ---	1-14
X	ADAMS ET AL.: "Initial assessment of human gene diversity and expression patterns based upon 83 million basepairs of cDNA sequence" EMBL DATABASE ACC NO: AA305700, 18 April 1997 (1997-04-18), XP002137621 cited in the application the whole document ---	1-10
A		11-16
X	PALMER: "Human DNA sequence from clone 257I9 on chromosome 6q25.1-26 contains gene similar to Cytochrome B, CA repeat, GSS" EMBL DATABASE ACC. NO.: AL031773, 29 September 1998 (1998-09-29), XP002144975 the whole document ---	1-14
X	HILLIER ET AL.: "Generation and analysis of 280,000 human expressed sequence tags" EMBL DATABASE ACC. NO.: W52750, 4 June 1996 (1996-06-04), XP002144976 the whole document ---	1-10
X	STRAUSBERG: "National cancer institute, cancer genome anatomy project (CGAP)" EMBL DATABASE ACC. NO.: AA641653, 1 November 1997 (1997-11-01), XP002144977 the whole document ---	1-10
A	WILSON ET AL.: "f53g12.3" EMBL DATABASE ACC. NO.: AF003139, 1 July 1997 (1997-07-01), XP002144978 abstract ---	1-16
P,X	SUH ET AL.: "Cell transformation by the superoxide-generating oxidase Mox1" NATURE, vol. 401, 2 September 1999 (1999-09-02), pages 79-82, XP002137599 figures 1-5 ---	1-8, 11-14

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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.
T	DUPUY ET AL.: "Purification of a novel flavoprotein involved in the thyroid NADPH oxidase" THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 52, 24 December 1999 (1999-12-24), pages 37265-37269, XP002144979 figures 2,3 -& DUPUY ET AL.: EMBL DATABASE ACC. NO.: AF181972, 29 December 1999 (1999-12-29), XP002144980 the whole document -----	1-8

INTERNATIONAL SEARCH REPORT

International application No.
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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:

In so far as claims 11-14 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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.:
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: 1-16 all partially

A protein capable of stimulating superoxide production, wherein the protein comprises a mox1, preferably with the sequence of SEQ ID NO 2, SEQ ID NO 21, SEQ ID NO 42, a fragment thereof or a conservative substitution thereof.
A nucleotide sequence, preferably with the sequence of SEQ ID NO 1, SEQ ID NO 22 or SEQ ID NO 41 encoding for the above mentioned protein, fragment thereof or conservative substitution.

A vector comprising said nucleotide sequence and a cell containing said vector.

An antibody capable of binding the above mentioned protein, fragment or conservative substitution. A method of stimulating superoxide formation, in vitro or in vivo, comprising administration, in vitro or in vivo, of a composition comprising the abovementioned vector or the above mentioned protein or its fragment or its conservative substitution in a pharmaceutically acceptable vector. A method for determining the activity of a drug comprising measuring the activity of the above mentioned protein to stimulate superoxide formation following administration of the drug.

2. Claims: 1-16 all partially

As invention 1, but for a mox2 with SEQ ID NO: 4 and SEQ ID NO: 3

3. Claims: 1-16 all partially

As invention 1, but for a duox1 with SEQ ID NO: 46 and SEQ ID NO: 45 and for a duox2 with SEQ ID NO: 48 and SEQ ID NO: 47

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5593966 A	14-01-1997	US 5585346 A	17-12-1996
		AU 7956791 A	10-12-1991
		WO 9117763 A	28-11-1991