

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
30 June 2005 (30.06.2005)

PCT

(10) International Publication Number  
WO 2005/058028 A3

(51) International Patent Classification:  
A01K 67/027 (2006.01)

(21) International Application Number:  
PCT/US2004/041721

(22) International Filing Date:  
13 December 2004 (13.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/530,043 16 December 2003 (16.12.2003) US

(71) Applicants (for all designated States except US): GENENTECH, INC. [—/US]; MS 49, 1 DNA Way, South San Francisco, California 94080-4990 (US). LEXICON GENETICS INCORPORATED [—/US]; 8800 Technology Forest Place, The Woodlands, Texas 77381 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ANDERSON, Stephen [US/US]; 30 N. Timber Top Drive, The Woodlands, Texas 77380 (US). BRENNAN, Jane [GB/US]; 700 Steiner Street #702, San Francisco, California 94117 (US). DESAUVAGE, Frederic [BE/US]; 187 Shooting Star Isle, Foster City, California 94404 (US). DING, Zhiyong [CN/US]; 3011 Spring Ranch Lane, Spring, Texas 77388 (US). EDWARDS, Joel [US/US]; 62 North Goldenvine Circle, The Woodlands, Texas 77382 (US). FIKES, Nelda [US/US]; 2400 Spring Rain #621, Spring, Texas 77379 (US). HUANG, Wenhui [CN/US]; 10 Shellbark Place, The Woodlands, Texas 77382 (US). OUYANG, Wenjun [CN/US]; 1057 Galley Lane, Foster City, California 94404 (US). RANGEL, Carolina [US/US]; 810 East 24th Street, Houston, Texas 77009 (US). SANGHA, Mamta [CN/US]; 21750 SW 103rd Court, Tualatin, Oregon 97062 (US). SHI, Zheng-Zheng [CN/US]; 53 Silver Crescent Court, The Woodlands, Texas 77382 (US). SPARKS, Mary Jean [US/US]; 7218 Black Forest Drive, Magnolia, Texas 77354 (US). TRACKEY, Joseph [US/US]; 2301 South

Millbend Drive #2414, The Woodlands, Texas 77380 (US). VETTER, Melissa [US/US]; 9110 Huckinston Court, Spring, Texas 77379 (US). WANG, Ching-Yun [CN/US]; 3 White Wing Court, The Woodlands, Texas 77382 (US). WOODINGS, Jessica [US/US]; 6 West Shaker Court, The Woodlands, Texas 77380 (US).

(74) Agents: BARNES, Elizabeth et al.; MS49 1 DNA Way, South San Francisco, California 94080-4990 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, 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, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
18 May 2006

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

(54) Title: NOVEL GENE DISRUPTIONS, COMPOSITIONS AND METHODS RELATING THERETO

(57) Abstract: The present invention relates to transgenic animals, as well as compositions and methods relating to the characterization of gene function. Specifically, the present invention provides transgenic mice comprising disruptions in PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 genes. Such in vivo studies and characterizations may provide valuable identification and discovery of therapeutics and/or treatments useful in the prevention, amelioration or correction of diseases or dysfunctions associated with gene disruptions such as neurological disorders; cardiovascular, endothelial or angiogenic disorders; eye abnormalities; immunological disorders; oncological disorders; bone metabolic abnormalities or disorders; lipid metabolic disorders; or developmental abnormalities.



WO 2005/058028 A3

INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/041721

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> A01K67/027		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) A01K		
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, Sequence Search, WPI Data, PAJ, BIOSIS, EMBASE		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/14328 A (GENENTECH, INC; WOOD, WILLIAM, I; GURNEY, AUSTIN, L; GODDARD, AUDREY;) 25 March 1999 (1999-03-25) the whole document page 20; figures 45,46; example 20	1-149
<input type="checkbox"/> Further documents are listed in the continuation of box C.		
<input checked="" type="checkbox"/> 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 September 2005		Date of mailing of the international search report 07.04.06
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 Sprinks, M

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2004/041721

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 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:  
  
Although claims 103-120 and 144-149 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:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
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 III Observations where unity of invention is lacking (Continuation of item 3 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.:  
  
1-149 (partially)

### 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

## Continuation of Box II.1

Although claims 103-120 and 144-149 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.

-----

## Continuation of Box II.2

Claims 46,47,52,53,63,64,86,87,90,92,93,98,99,102-120,139,140,144-149 encompass compounds defined only by their desired function, contrary to the requirements of clarity of Article 6 PCT, because the result-to-be-achieved type of definition does not allow the scope of the claim to be ascertained. The fact that any compound could be screened does not overcome this objection, as the skilled person would not have knowledge beforehand as to whether it would fall within the scope claimed, except for the compounds disclosed in the description. Undue experimentation would be required to screen compounds randomly. This non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search for said claims

The search of said claims was consequently restricted to antibodies.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

Invention 1: Claims 1-149 partially

A method of identifying a phenotype associated with the disruption of a gene by disrupting said gene in a non-human transgenic animal, wherein said gene encodes PR0224  
---

Inventions 2-16: Claims 1-149 partially

idem Invention 1 for the 15 other genes respectively referred to in claim 1.  
---

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/041721

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9914328	A	25-03-1999	AU 741060 B2	22-11-2001
			CA 2303834 A1	25-03-1999
			JP 2001516580 T	02-10-2001
			JP 2002223786 A	13-08-2002
			JP 2002238586 A	27-08-2002
			JP 2002238587 A	27-08-2002
			JP 2002238588 A	27-08-2002
			JP 2002253280 A	10-09-2002
			NZ 503343 A	27-09-2002

---