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67/027, C12N 15/11, A61K 38/17, 48/00, G01N 33/50

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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,
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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: SPINSTER-LIKE PROTEIN GENES, EXPRESSION PRODUCTS, NON-HUMAN ANIMAL MODEL: USES IN HU-
MAN METABOLIC DISORDERS

(57) Abstract: The present invention relates to a non-human vertebrate animal model displaying an alteration in fat metabolism or in the sensitivity towards leptin or insulin, which model bears a mutation in the gene encoding the spinster like 1 protein (Spin1). The invention also relates to mutant Spin1 proteins and nucleic acid sequences encoding these proteins. Furthermore, the invention relates to the use of the non-human vertebrate animal model for the identification of diagnostic markers, or as a model for studying the molecular and physiological mechanisms associated with an alteration in fat metabolism or an alteration in the sensitivity towards leptin or insulin, or for the identification and testing of agents useful in the prevention, amelioration, or treatment of the above conditions. Agents, pharmaceutical compositions, and methods for treating the above conditions are likewise described, as are methods for identifying said agents.



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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C07K14/47 C12N15/12 C12N5/10 C07K16/18 C12N15/62
 A01K67/027 C12N15/11 A61K38/17 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 C07K 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, BIOSIS, Sequence Search, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/39448 A (HUMAN GENOME SCIENCES INC) 11 September 1998 (1998-09-11) pages 586-587; sequence 389 -----	1-24, 26-52, 54-77, 79-89, 91-114, 121, 125-142, 158-220
X	DATABASE WPI Section Ch, Week 200347 Derwent Publications Ltd., London, GB; Class B04, AN 2003-494229 XP002297580 & CN 1 403 480 A (SHANGHAI XINSHIJIE GENE TECHN DEV CO LTD) 19 March 2003 (2003-03-19) abstract -/--	1-24, 26-52, 54-77, 79-89, 91-114, 121, 125-142, 158-220

Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

<p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p>	<p>*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</p> <p>*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</p> <p>*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.</p> <p>* & * document member of the same patent family</p>
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Date of the actual completion of the international search 23 September 2004	Date of mailing of the international search report 07/10/2004
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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 Giebeler, K
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/003606

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	-& DATABASE EMBL 6 May 2004 (2004-05-06), XP002297578 retrieved from EMBL Database accession no. ADL08448 abstract	1-24, 26-52, 54-77, 79-89, 91-114, 121, 125-142, 158-220
X	SWEENEY SEAN T ET AL: "Unrestricted synaptic growth in spinster: A late endosomal protein implicated in TGF-beta-mediated synaptic growth regulation" October 2002 (2002-10), NEURON, VOL. 36, NR. 3, PAGE(S) 403-416 , XP002297577 ISSN: 0896-6273	1-24, 26-52, 54-77, 79-89, 91-114, 121, 125-142, 158-220
A	the whole document	25,90
X	NAKANO Y ET AL: "MUTATIONS IN THE NOVEL MEMBRANE PROTEIN SPINSTER INTERFERE WITH PROGRAMMED CELL DEATH AND CAUSE NEURAL DEGENERATION IN DROSOPHILA MELANOGASTER" MOLECULAR AND CELLULAR BIOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, US, vol. 21, no. 11, June 2001 (2001-06), pages 3775-3788, XP001016215 ISSN: 0270-7306	1-24, 26-52, 54-77, 79-89, 91-114, 121, 125-142, 158-220
A	see especially Figure 7 the whole document	25,90
X	WO 01/92304 A (INCYTE GENOMICS INC) 6 December 2001 (2001-12-06) pages 180-181; sequence 23	1-24, 26-52, 54-77, 79-89, 91-114, 121, 125-142, 158-220
X	DATABASE EMBL 1 March 2003 (2003-03-01), "Similar to spinster-like protein" XP002297579 retrieved from EMBL Database accession no. Q8IVW8 abstract	1-24, 26-52, 54-77, 79-89, 91-114, 121, 125-142, 158-220

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/003606

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>KIM YOUNG-BUM ET AL: "In vivo administration of leptin activates signal transduction directly in insulin-sensitive tissues: Overlapping but distinct pathways from insulin" ENDOCRINOLOGY, vol. 141, no. 7, July 2000 (2000-07), pages 2328-2339, XP002297575 ISSN: 0013-7227 see especially abstract the whole document</p> <p>-----</p>	197-220
X	<p>MARONI P ET AL: "Early intracellular events induced by in vivo leptin treatment in mouse skeletal muscle." MOLECULAR AND CELLULAR ENDOCRINOLOGY, vol. 201, no. 1-2, 28 March 2003 (2003-03-28), pages 109-121, XP002297576 ISSN: 0303-7207 see especially abstract the whole document</p> <p>-----</p>	197-220

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/003606

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 102-113, 128-136 and 140-151 encompass methods of treatment of the human/animal body by therapy, 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:

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

Continuation of Box II.1

Although claims 102-113, 128-136 and 140-151 encompass methods of treatment of the human/animal body by therapy, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: 53,78,115-120,122-124,143-157,221-223 (all completely);
40-52,54-58,79-87,91-114,121,125-142,158-186,197-220 (all partially)

Claims 40(ii)(iii), 41(ii), 50(ii)(iii), 53, 54(b), 78, 115-120, 122-124, 128(a)(b), 143-157 and 211-223 refer to products which are so unclearly defined that no meaningful search is possible. Claims 40(ii) and 50(ii) relate to a non-coding segment which is not defined by its technical features. Claims 40(iii), 41(ii), 50(iii), 54(b),78 relate to a non-defined protein which affects the expression or activity of mouse or human Spin1 protein. Claim 115 refers to a protein of a human subject known not to have medical condition associated with an alteration in fat metabolism which is effective in treating said medical condition. No such proteins have been disclosed in the application. The same applies to the proteins referred to in claims 116, 117, 122-124, 128-130. Claims 143-145 refer to agents defined as being capable of modulating spin1 activity, without defining the agent by technical features. Claims 221-223 also relate to agents not defined by their technical features. Since it is unclear which kind of substances fall under the definitions of said claims, their scope is ambiguous and undefined. Moreover, it cannot be excluded that even substances known in the art are encompassed by the claims. The claims thus lack clarity under Article 6 PCT. An attempt is made to define the products by reference to a result to be achieved. This lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Independent of the above reasoning, the claims furthermore so lack support (Article 6 PCT), and the application so lacks disclosure (Article 5 PCT), that a meaningful search over the whole of the claimed scope is impossible.

Consequently, no search could be carried out for claims 40(ii)(iii), 41(ii), 50(ii)(iii), 53, 54(b), 78, 115-120, 122-124, 128(a)(b), 143-157 and 211-223, and for claims 42-49, 51, 52, 55-58, 79-87, 91-114, 121, 125-127, 128(d)(e), 131-142, 158-186 and 197-220 when referring back to these claims. The remaining of the claimed subject-matter has been searched completely.

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.
PCT/EP2004/003606

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9839448	A	11-09-1998	AU 6545398	A 22-09-1998
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