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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv))*

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*
— *with sequence listing part of description published separately in electronic form and available upon request from the International Bureau*

(88) Date of publication of the international search report:
8 January 2009

(54) Title: GENETIC VARIANTS ASSOCIATED WITH PERIODIC LIMB MOVEMENTS AND RESTLESS LEGS SYNDROME

(57) Abstract: The present inventions discloses genetic markers and haplotypes that have been found to be associated with risk of Restless Legs Syndrome (RLS), Periodic Limb Movement Disorder (PLMD), and Periodic Limb Movements of Sleep (PLMS). Methods for determination of susceptibility of these disorders are disclosed using such markers, as are kits useful in such determination.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IS2008/000010

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/68

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)
C12Q

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, 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.
A	DESAUTELS ALEX ET AL: "Identification of a major susceptibility locus for restless legs syndrome on chromosome 12q" AMERICAN JOURNAL OF HUMAN GENETICS, vol. 69, no. 6, December 2001 (2001-12), pages 1266-1270, XP002489072 ISSN: 0002-9297 abstract the whole document	1-35, 42-63

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[X] 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 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	Date of mailing of the international search report
4 August 2008	31/10/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Helliot, Bertrand

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DESAUTELS ALEX ET AL: "Restless legs syndrome - Confirmation of linkage to chromosome 12q, genetic heterogeneity, and evidence of complexity" ARCHIVES OF NEUROLOGY, vol. 62, no. 4, April 2005 (2005-04), pages 591-596, XP002489073 ISSN: 0003-9942 abstract the whole document	1-35, 42-63
A	BONATI MARIA TERESA ET AL: "Autosomal dominant restless legs syndrome maps on chromosome 14q." BRAIN, vol. 126, no. 6, June 2003 (2003-06), pages 1485-1492, XP002489074 ISSN: 0006-8950 abstract the whole document	1-35, 42-63
A	LEVCHENKO ANASTASIA ET AL: "The 14q restless legs syndrome locus in the French Canadian population" ANNALS OF NEUROLOGY, vol. 55, no. 6, June 2004 (2004-06), pages 887-891, XP002489075 ISSN: 0364-5134 abstract the whole document	1-35, 42-63
A	CHEN SHENGHAN ET AL: "Genomewide linkage scan identifies a novel susceptibility locus for restless legs syndrome on chromosome 9p" AMERICAN JOURNAL OF HUMAN GENETICS, vol. 74, no. 5, May 2004 (2004-05), pages 876-885, XP002489076 ISSN: 0002-9297 abstract the whole document	1-35, 42-63
A	LEVCHENKO A ET AL: "A novel autosomal dominant restless legs syndrome locus maps to chromosome 20p13." NEUROLOGY 12 SEP 2006, vol. 67, no. 5, 12 September 2006 (2006-09-12), pages 900-901, XP002489077 ISSN: 1526-632X abstract the whole document	1-35, 42-63

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IS2008/000010

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PICHLER I ET AL: "Linkage analysis identifies a novel locus for restless legs syndrome on chromosome 2q in a South Tyrolean population isolate" AMERICAN JOURNAL OF HUMAN GENETICS 200610 US, vol. 79, no. 4, October 2006 (2006-10), pages 716-723, XP002489078 ISSN: 0002-9297 abstract the whole document	1-35, 42-63
A	WINKELMANN ET AL: "Genetics of restless legs syndrome" SLEEP MEDICINE REVIEWS, W.B. SAUNDERS, vol. 10, no. 3, 1 June 2006 (2006-06-01), pages 179-183, XP005475467 ISSN: 1087-0792 abstract the whole document	1-35, 42-63
P,X	STEFANSSON HREINN ET AL: "A genetic risk factor for periodic limb movements in sleep" NEW ENGLAND JOURNAL OF MEDICINE, vol. 357, no. 7, August 2007 (2007-08), pages 639-647, XP002489082 ISSN: 0028-4793 the whole document	1-35, 42-63

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IS2008/000010

Box No. 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:

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 No. 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 allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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.:

1-35 and 42-63 (totally)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ 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: 1-35 and 42-63 (totally)

- Method for determining a susceptibility to a sleep-related movement disorder in a human individual;
- A method of assessing an individual for probability of response to a therapeutic agent used for preventing or ameliorating symptoms associated with a sleep-related movement disorder;
- A method of genotyping a nucleic acid sample obtained from an individual;
- A kit for assessing to a sleep-related movement disorder in a human individual;
- A method for determining the susceptibility to abnormal iron stores in a human individual;

comprising at least one marker selected from the group of markers set forth in Tab. 4, namely markers selected within the C06 LD block, between positions 37,816,141 and 38,797,853 of chromosome 6 (NCBI Build 36).

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2. claims: 36-41 (completely)

- A method for diagnosing a susceptibility to a sleep-related movement disorder in a human individual, wherein the method comprises determining the presence or absence of at least one allele of at least one polymorphic marker associated with the Meis1 gene, namely markers selected within the MeisI LD block, between positions 66,580,000 and 66,660,000 of chromosome 2 (NCBI Build 36).
