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Published:

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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

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18 February 2010

(54) Title: METHODS AND COMPOSITIONS FOR THE DIAGNOSIS AND TREATMENT OF ANGIOGENIC DISORDERS

(57) Abstract: The invention provides methods and compositions for determining whether an individual is at risk of developing, or has, one or more angiogenic disorders. The methods detect the presence and/or amount of one or more genes or gene products in a sample, including a RORA, CRIM1, CXCR4, C5orf26, IGHG3, NALP2, PLA2G4A, IGLJ3, SHQ1, UCHL1, TANC1, PKP2, DNAJC6, C6orf105, NALP1, RGS13, CXCL13, RPS6KA2, MMP7, IL1A, ABCA1, VCAN, KIAA0888, ENPP2, and FAM38B gene or gene product. In addition, the invention provides methods for using one or more of these genes or gene products as a target for preventing or delaying the onset of one or more angiogenic disorders or treating a patient with one or more such disorders. The angiogenic disorder can be, for example, an ocular angiogenic disorder, for example, a disorder associated with choroidal neovascularization, for example, age-related macular degeneration.



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INTERNATIONAL SEARCH REPORT

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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 A61K

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, EMBASE, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DEWAN ANDREW ET AL: "HTRA1 promoter polymorphism in wet age-related macular degeneration" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, WASHINGTON, DC, vol. 314, no. 5801, 1 November 2006 (2006-11-01), pages 989-992, XP002484959 ISSN: 0036-8075 page 990, right-hand column - page 991 ----- -/--	1, 3-29, 35-38



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

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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	JAKOBSDOTTIR JOHANNA ET AL: "Susceptibility genes for age-related maculopathy on chromosome 10q26" AMERICAN JOURNAL OF HUMAN GENETICS, AMERICAN SOCIETY OF HUMAN GENETICS, CHICAGO, IL, US, vol. 77, no. 3, 1 September 2005 (2005-09-01), pages 389-407, XP002419863 ISSN: 0002-9297 pages 399-405	1,3-29, 35-38
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Y	US 2006/281120 A1 (GORIN MICHAEL B [US] ET AL) 14 December 2006 (2006-12-14) claims	1,3-29, 35-38
Y	HADDAD S ET AL: "The Genetics of Age-Related Macular Degeneration: A Review of Progress to Date" SURVEY OF OPHTHALMOLOGY, SURVEY OF OPHTHALMOLOGY INC, XX, vol. 51, no. 4, 1 July 2006 (2006-07-01), pages 316-363, XP025000481 ISSN: 0039-6257 [retrieved on 2006-07-01] table 3	1,3-29, 35-38
X	WO 2005/100605 A (UNIV CALIFORNIA [US]; SLAMON DENNIS J [US]; WILSON CINDY A [US]; DERIN) 27 October 2005 (2005-10-27) claim 21; page 48, lines 1-13; page 65, line 25 - page 66, line 23	30-34
Y	TSAI DER-CHONG ET AL: "Different plasma levels of vascular endothelial growth factor and nitric oxide between patients with choroidal and retinal neovascularization" OPHTHALMOLOGICA, KARGER, BASEL, CH, vol. 220, no. 4, 1 January 2006 (2006-01-01), pages 246-251, XP009122410 ISSN: 0030-3755 page 247, "Materials and Methods"	1,25
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INTERNATIONAL SEARCH REPORT

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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	TEI M ET AL: "MICROARRAY GENE EXPRESSION ANALYSIS OF HUMAN MONOCYTES AND MACROPHAGES" ARVO ANNUAL MEETING ABSTRACT SEARCH AND PROGRAM PLANNER (ANNUAL MEETING OF THE ASSOCIATION FOR RESEARCH IN VISION AND OPHTHALMOLOGY; FORT LAUDERDALE, FL, USA; MAY 04-08, 2003),, 4 May 2003 (2003-05-04), page 1725, XP009122407 "Results" -----	1,25
Y	WO 2007/146957 A (IRM LLC [BM]; WARMUTH MARKUS [US]; FOSTER KARIN [US] IRM LLC; WARMUTH) 21 December 2007 (2007-12-21) claim; page 3, [0014]; page 9, item III -----	25
A	WO 2007/076351 A (ALCON MFG LTD [US]; CHATTERTON JON E [US]; BINGAMAN DAVID P [US]) 5 July 2007 (2007-07-05) claims -----	1,3-39
A	WO 01/58494 A (GENVEC INC [US]; KOVESDI IMRE [US]; BROUGH DOUGLAS E [US]; MCVEY DUNCA) 16 August 2001 (2001-08-16) claims -----	1,3-39

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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 all searchable 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 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, 3-39 (all in part)

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:

Invention 1: Claims 1, 3-39 (all in part)

concerns a method of determining whether a mammal is at risk of developing an ocular angiogenic disorder; a method of preventing, slowing or stopping the development of an ocular angiogenic disorder, a kit or a method of assisting in diagnosing the risk of developing an ocular angiogenic disorder, the methods and kit being characterised in that the amount of a RORA gene or gene product is higher in a sample than in a control.

Inventions 2-16: Claims 1, 3-39 (all in part)

concern a method of determining whether a mammal is at risk of developing an ocular angiogenic disorder; a method of preventing, slowing or stopping the development of an ocular angiogenic disorder, a kit or a method of assisting in diagnosing the risk of developing an ocular angiogenic disorder, the methods and kit being characterised in that the amount of a CRIM1, CXCR4, C5orf26, IGHG3, NALP2, PLA2G4A, IGLJ3, SHQ1, UCHL1, TANC1, PKP2, DNAJC6, C6orf105, NALP1 or RGS13 gene or gene product respectively is higher in a sample than in a control.

Inventions 17-25: Claims 2, 3-39 (all in part)

concern a method of determining whether a mammal is at risk of developing an ocular angiogenic disorder; a method of preventing, slowing or stopping the development of an ocular angiogenic disorder, a kit or a method of assisting in diagnosing the risk of developing an ocular angiogenic disorder, the methods and kit being characterised in that the amount of a CXCL13, RPS6KA2, MMP7, IL1A, ABCA1, VCAN, KIAA0888, ENPP2 or FAM38B gene or gene product respectively is lower in a sample than in a control.

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 2006281120 A1	14-12-2006	NONE	
WO 2005100605 A	27-10-2005	AU 2005233564 A1 CA 2563333 A1 EP 1735461 A1 JP 2007532111 T US 2008318212 A1	27-10-2005 27-10-2005 27-12-2006 15-11-2007 25-12-2008
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