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C12N 15/62, 5/10, C07K 14/47, C12Q 1/68, A01K 67/027, A61P 43/00

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(75) Inventors/Applicants (for US only):

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(54) Title: MACULAR DEGENERATION DIAGNOSTICS AND THERAPEUTICS

(57) Abstract: Therapeutics and diagnostics based on the identification of genetic mutations, which cause Macular Degeneration (MD) are disclosed. In a preferred embodiment, the MD causative mutation results in the following amino acid substitution to the EFEMP1 protein: 345Arg > Trp.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/62 C12N5/10 C07K14/47 C12Q1/68 A61P43/00

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 C12Q C07K

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, WPI Data, PAJ, MEDLINE, BIOSIS, STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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* 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

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

Date of the actual completion of the international search
13 December 2000

Date of mailing of the international search report
14.03.2001

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 epos nl,  
Fax: (+31-70) 340-3018

Authorized officer
REUTER, U
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<tr>
<th>Category</th>
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<tr>
<td>X</td>
<td>WO 99 00410 A (INCYTE PHARMA INC ;CORLEY NEIL C (US); BANDMAN OLGA (US); GUEGLER) 7 January 1999 (1999-01-07) page 2, paragraph 2 page 3-4 page 24 page 28-29; examples 11-13 ---</td>
<td>1-18</td>
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<tr>
<td>A</td>
<td>MONTGOMERY ROBERT A ET AL: &quot;Inhibition of fibrillin 1 expression using U1 snRNA as a vehicle for the presentation of antisense targeting sequence.&quot; HUMAN MOLECULAR GENETICS, vol. 6, no. 4, 1997, pages 519-525, XP002155260 ISSN: 0964-6906 the whole document ---</td>
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<td>A</td>
<td>IKEGAWA SHIRO ET AL: &quot;Structure and chromosomal assignment of the human S1-5 gene (FBNL) that is highly homologous to fibrillin.&quot; GENOMICS, vol. 35, no. 3, 1996, pages 590-592, XP002155261 ISSN: 0888-7543 the whole document ---</td>
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<td>WO 99 47655 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 23 September 1999 (1999-09-23) page 1-5; claims 20,21 page 43; claim 27 page 97; claim 30 ---</td>
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<td>E</td>
<td>WO 00 47752 A (UNIV IOWA RES FOUND ;STONE EDWIN M (US); SHEFFIELD VAL C (US)) 17 August 2000 (2000-08-17) the whole document</td>
<td>1-18</td>
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INTERNATIONAL SEARCH REPORT

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:

2. [X] 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 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. [X] 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.:

   1-18

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)
Continuation of Box I.2

Present claims 15, 16, and 17 relate to a compound defined by reference to a desirable characteristic or property, namely to modulate the EFEMP1 bioactivity, and are lacking any technical feature that would allow the search of the compound.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds an antisense molecule.

The applicant's attention is drawn to the fact that claims, or parts of 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.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-18

   A method for identifying a compound that modulates a EFEMP1 bioactivity, by contacting the compound with a cell or extract, which expresses an EFEMP1 gene and determining the resulting EFEMP1 bioactivity, and compounds isolated by the method.

2. Claims: 19-22

   Methods for identifying a EFEMP1 binding partner, for measuring the strength of an interaction between an EFEMP1 polypeptide and an EFEMP1 binding partner, and identifying a molecule, which is a component of a EFEMP1 biochemical pathway by linking the EFEMP1 polypeptide to a heterologous DNA-binding domain, linking the test molecule to a transcriptional activation domain, and detecting the expression of a reporter gene, which is linked to the binding site of the heterologous DNA-binding domain.

3. Claims: 23-31

   A method for identifying a compound which interacts with a EFEMP1 polypeptide or an EFEMP1 binding partner, by contacting the compound with a FBNL polypeptide and a EFEMP1 binding partner and detecting the extent of EFEMP1 polypeptide/EFEMP1 binding partner complex formation, and compounds isolated by the method.


   Isolated EFEMP1 nucleic acids, which are operably linked to a EFEMP1 transcriptional regulatory sequence, and cell lines and animals comprising these nucleic acids.

5. Claims: 48-52

   A cell in which the biologic activity of one or more EFEMP1 proteins is altered by a chromosomally incorporated transgene, and a transgenic animal comprised of this cell.
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<th>Patent document cited in search report</th>
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<th>Patent family member(s)</th>
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