Title: RCA LOCUS ANALYSIS TO ASSESS SUSCEPTIBILITY TO AMD AND MPGNII

Abstract: The invention relates to gene polymorphisms and genetic profiles associated with an elevated or a reduced risk of alternative complement cascade deregulation disease such as AMD and/or MPGNII. The invention provides methods and reagents for determination of risk, diagnosis and treatment of such diseases. In an embodiment, the present invention provides methods and reagents for determining sequence variants in the genome of an individual which facilitate assessment of risk for developing such diseases.
INTERNATIONAL SEARCH REPORT

A CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12Q 1/68 (2009.01)
USPC - 435/6

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(8) C12Q 1/68 (2009.01)
USPC 435/6

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 practicable, search terms used)

PubWest, Google Scholar, Google Patent dysregulation, polymorphism, screen, genetic profile, regulation, complement, activation, RCA, age-related macular degeneration, AMD, genetic

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>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>US 2007/0020647 A1 (HAGEMAN et al) 25 Jan 2007 (25 01 2007), abstract, para [0010], [0011], [0086], [0055], [0106], [0127], Table 1</td>
<td>1, 2, 7, 9-19, 28</td>
</tr>
</tbody>
</table>

* Further documents are listed in the continuation of Box C

D

- 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 application or patent 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
13 Apr 2009 (13 04 2009)

Date of mailing of the international search report
2 9 APR 2009

Name and mailing address of the ISA/US
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Facsimile No 571-273-3201

Authorized officer
Lee W Young

PCT/ISA/210 (second sheet) (April 2007)
## DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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</tr>
</thead>
</table>
### Observations where certain claims 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. **D 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. **D Claims Nos**
   - because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a)

### 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:

Group I Claims 1, 2, 4-19 and 28 are directed to a method of screening for susceptibility to complement dysregulation in an individual and a method of determining an individual's risk of development or progression of age-related macular degeneration (AMD)

Group II Claims 1, 3-19 and 28 are directed to a method of determining an individual's risk of development or progression of membranoproliferative glomerulonephritis type II (MPGNII)

Group III Claims 20 and 25 are directed to a healthcare method comprising paying for, authorizing payment for or authorizing the practice of claimed methods

-continued on extra sheet—

1. **Claims Nos**
   - As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. **Claims Nos**
   - As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. **Claims Nos**
   - 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. **Claims Nos**
   - 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, 2, 4-19 and 28

### 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.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)
Continuation of Box III

Group IV Claims 21, 23, and 24 are directed to a method for treating or preventing AMD by administering a factor H polypeptide to the individual

Group V Claims 22-24 are directed to a method for treating or preventing MPGNII by administering a factor H polypeptide to the individual

Group VI Claim 26 is directed to an oligonucleotide comprising a nucleotide sequence s of SEQ ID NO 3 and its complement

Group VII Claim 26 is directed to an oligonucleotide comprising a nucleotide sequence s of SEQ ID NO 4 and its complement

Group XIII Claim 27 is directed to an oligonucleotide comprising a nucleotide sequence s of SEQ ID NO 1 and its complement

Group IX Claim 27 is directed to an oligonucleotide comprising a nucleotide sequence s of SEQ ID NO 2 and its complement

Groups I-V have the shared technical feature of screening for susceptibility to complement dysregulation in an individual comprising screening for the presence or absence of a genetic profile characterized by polymorphisms in the genome of the individual associated with complement dysregulation. However, this is not an improvement over the prior art of US 20070020647 A1 to Hageman et al (25 January 2007) that teaches screening for the presence or absence of a genetic profile characterized by polymorphisms in the genome of the individual associated with complement dysregulation (abstract, para [0010]). More specifically, relevant to at least claim 8 of the instant application, rs10922153 is taught in para [0160] and relevant to at least claim 11 of the instant application, rs800292 is taught in para [0055]. Several other polymorphisms are also disclosed by the prior art. In addition, Groups IV and V have the additional shared technical feature of administering a factor H polypeptide to the individual. Hageman discloses administering a factor H polypeptide to the individual (claims 41-44, para [0016]-[0017]). Groups VI-IX do not have a shared technical feature with any of the other groups nor with each other based on the nucleic acid sequences of the claimed inventions. The nucleotides represented by the unique sequences designated SEQ ID NOs 1-4 do not relate to a single general inventive concept because, under PCT Rule 13.2, the different nucleotides represented by the sequences are not common to one another but are different because they are composed of unique nucleic acid sequences.