Title: METHODS OF DETECTING MUTATIONS ASSOCIATED WITH ATAXIA-OCULAR APRAXIA 2 (AOA2)

Abstract: Methods of identifying polymorphisms associated with ataxia-ocular apraxia 2 (AOA2), are described. The polymorphisms associated with AOA2 include specific mutations in the sensori (SETX) gene. Also described are methods of diagnosis of AOA2, as well as methods of assessing an individual for carrier status for AOA2.
**INTERNATIONAL SEARCH REPORT**

**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**

<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>
</table>

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**

3 September 2008

**Date of mailing of the international search report**

25/11/2008

Name and mailing address of the ISA:

- European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk
  Tel. (+31-70) 340-2040;
  Fax (+31-70) 340-3016

Authorized officer

Helliot, Bertrand
<table>
<thead>
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<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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<tbody>
<tr>
<td>A</td>
<td>NICOLAOU PASCHALIS ET AL: &quot;A novel c.5308_5311delGAGA mutation in Senataxin in a Cypriot family with an autosomal recessive cerebellar ataxia&quot; BMC MEDICAL GENETICS, vol. 9, April 2008 (2008-04), page Article No.: 28, XP002494455 ISSN: 1471-2350 the whole document</td>
<td>1-17</td>
</tr>
</tbody>
</table>
INTERNATIONAL SEARCH REPORT

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 fee, 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 (partially), 2-5 (completely), 6 (partially), 7-12 (comp.), 13 (part.) 14-17 (comp.)

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.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)
   - A method of assessing an individual for the presence or absence of a genetic polymorphism associated with ataxia-ocular apraxia 2 (AOA2);
   - A method of diagnosing ataxia-ocular apraxia 2 (AOA2) in an individual;
   - A method of assessing an individual for carrier status for ataxia-ocular apraxia 2 (AOA2);
   - The methods comprising assessing a test sample from the individual for the presence of a 4 base deletion of nucleotide 369-372 in the senataxin (SETX) gene and wherein the presence of the said mutation is indicative of the presence of a genetic polymorphism associated with ataxia-ocular apraxia 2.

2. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)
   Same methods as herein above, wherein the mutation of interest is a 2 base insertion of AT between nucleotides 2747-2748.

3. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)
   Same methods as herein above, wherein the mutation of interest is a single base transition C->T at nucleotide 4234.

4. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)
   Same methods as herein above, wherein the mutation of interest is a single base transition C->T at nucleotide 4816.

5. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)
Same methods as herein above, wherein the mutation of interest is a 6 base deletion of nucleotides 4873-4878 accompanied by an insertion of GG at the same location.

6. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a single base insertion of G between nucleotides 4891-4892.

7. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a 2 base insertion of CA between nucleotides 5301-5302.

8. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a 4 base deletion of nucleotides 5308-5311.

9. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a 2 base deletion of nucleotides 5591-5592.

10. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a single base deletion of nucleotide 5958.

11. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a single base insertion of A between nucleotides 6422-6423.
12. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a single base transition C->T at nucleotide 6292.

13. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a four base deletion of nucleotides 6848-6851.

14. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a single base insertion of T between nucleotides 479-480.

15. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a 4 base deletion of nucleotides 4633-4636.

16. claims: claims 1 (partially), 2-5 (completely), 6 (partially), 7-12 (totally), 13 (partially), 14-17 (completely)

Same methods as herein above, wherein the mutation of interest is a 2 base deletion of nucleotides 6114-6115.