Title: SECRETED POLYPEPTIDE SPECIES INVOLVED IN ALZHEIMER’S DISEASE

Abstract: The invention discloses human secreted polypeptides whose concentrations are specifically altered in the CSF obtained from individuals with Alzheimer’s disease, when compared to the same from individuals free from Alzheimer's disease. The invention also provides methods of using compositions including the polypeptides, polynucleotides encoding them, and antibodies specific for these polypeptides, for diagnosis and prognosis of Alzheimer's disease, and for drug development.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

G01N33/68 C07K14/47 A61K38/00 A61P25/28

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)

G01N

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, Sequence Search, BIOSIS

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>EP 1 408 333 A (PFIZER PRODUCTS INC; OXFORD GLYCOSCIENCES LIMITED) 14 April 2004 (2004-04-14) ADP1 is chromogranin A Seq IDs 159,81,344</td>
<td>1,2,5-13</td>
</tr>
<tr>
<td>X</td>
<td>WO 01/75454 A (OXFORD GLYCOSCIENCES LTD; PFIZER INC; DURHAM, KATHRYN, L; FRIEDMAN, D) 11 October 2001 (2001-10-11) ADP1 is chromogranin A identified by P10645 (AF-2 in this document) sequence 1 on p. 25 is identical with Seq ID 82 pages 2-3,25</td>
<td>1,2,5-13</td>
</tr>
</tbody>
</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: 17 November 2005

Date of mailing of the international search report: 09. 05. 2006

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 epo nl.
Fax (+31-70) 340-3016

Authorized officer: Stolz, B

Form PCT/ISA/210 (second sheet) (April 2005)
<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>
INTERNATIONAL SEARCH REPORT

Box 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 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 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.  □ 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, 5-13 as far as they relate to ADP-1

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 (2)) (January 2004)
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1

Claims 1, 2, 5-13 as far as they relate to ADP-1

2. claims: inventions 2-8

Claims 1 to 13 as far as they relate to ADPs 2 to 8

Invention 9

claims 1, 2, 5-13, 16 and 17 as far as they relate to ADP 9

Inventions 10 to 22

Claims 1 to 13, as far as they relate to ADPs 10 to 21, and 23

Inventions 23-25

claims 1, 2, and 5 to 15 as far as they relate to any of ADPs 22, 24, and 25.
<table>
<thead>
<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
<th>Patent family member(s)</th>
<th>Publication date</th>
</tr>
</thead>
<tbody>
<tr>
<td>EP 1408333</td>
<td>14-04-2004</td>
<td>NONE</td>
<td></td>
</tr>
<tr>
<td>WO 0175454</td>
<td>11-10-2001</td>
<td>AU 4983501 A</td>
<td>15-10-2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 1325338 A2</td>
<td>09-07-2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 2004505609 T</td>
<td>26-02-2004</td>
</tr>
</tbody>
</table>