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accordance with Art. 76 EPC:
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(54) **POLYPEPTIDE BIOMARKERS FOR DIAGNOSING ALZHEIMER'S DISEASE**

(57) A method for assessing the state of Alzheimer's disease in patients is disclosed. A method for monitoring the progression of Alzheimer's disease in patients is also disclosed. The method applies detection of specific markers in body fluids (e.g. CSF), using mass spectrometric

analysis (SELDI-TOF MS). The specific markers are: human cystatin C, human beta-2-microglobulin, human myoglobin neurosecretory protein VGF or fragments of these proteins.

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PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 63 of the European Patent Convention EP 08 00 2793 shall be considered, for the purposes of subsequent proceedings, as the European search report

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | |
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| Y | ----- | 3-8 | |
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| Y | ----- -/-- | 3-8 | |
| | | | TECHNICAL FIELDS SEARCHED (IPC) |
| | | | G01N |
| INCOMPLETE SEARCH | | | |
| <p>The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.</p> <p>Claims searched completely :</p> <p>Claims searched incompletely :</p> <p>Claims not searched :</p> <p>Reason for the limitation of the search: see sheet C</p> | | | |
| Place of search | | Date of completion of the search | Examiner |
| The Hague | | 13 October 2008 | Tuynman, Antonin |
| CATEGORY OF CITED DOCUMENTS | | T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document | |
| X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document | | | |

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EPO FORM 1503 03.82 (P04E07)



PARTIAL EUROPEAN SEARCH REPORT

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EP 08 00 2793

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PARTIAL EUROPEAN SEARCH REPORT

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PARTIAL EUROPEAN SEARCH REPORT

Application Number
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PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 08 00 2793

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | CLASSIFICATION OF THE APPLICATION (IPC) |
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| P,X | WO 03/028543 A (PFIZER PROD INC [US]; OXFORD GLYCOSCIENCES UK LTD [GB]; DURHAM L KATHR) 10 April 2003 (2003-04-10) * claim 1 * * table IV * * sequences 20,273 * | 3,4,7,8 | |
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| | | | TECHNICAL FIELDS SEARCHED (IPC) |
| | | | |

EPO FORM 1503 08.02 (P/AC10)

**INCOMPLETE SEARCH
SHEET C**

Application Number
EP 08 00 2793

Claim(s) searched completely:
3-8,10

Claim(s) not searched:
1,2,9

Reason for the limitation of the search:

Present claims 1,2 and 9 relate to an extremely large number of possible compounds (polypeptides) in methods and kits for the detection of the state of Alzheimer disease, for which a lack of clarity (and conciseness) and support within the meaning of Article 84 EPC arises to such an extent as to render a meaningful search of the claims impossible.

Polypeptide markers that are only characterized by their molecular weight, comprise an enormous amount of polypeptides that have no relation to Alzheimer's disease at all, which can therefore not be distinguishable for Alzheimer's disease. Therefore the claims are not supported (Article 84 EPC) and do not enable (Article 83 EPC) the person skilled in the art over the whole breadth of the claim.

Consequently, the search has been not carried out for these claims.



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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

- Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):
- No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
- None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:
- The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).



**LACK OF UNITY OF INVENTION
SHEET B**

Application Number
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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 7.

2. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 8.

3. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 9.

4. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 10.

5. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 11.

6. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 12.

7. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 13.



**LACK OF UNITY OF INVENTION
SHEET B**

Application Number
EP 08 00 2793

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

8. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 14.

9. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 15.

10. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C or a fragment thereof, comprising the sequence SEQ ID NO: 16.

11. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human cystatin C fragment of

12. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human beta-2-microglobulin or fragments thereof.

13. claims: 3-8,10 (partially)

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is human myoglobin or a fragment thereof.

14. claims: 3-8,10 (partially)



**LACK OF UNITY OF INVENTION
SHEET B**

Application Number
EP 08 00 2793

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Methods and kits for assessing the state of Alzheimer's disease in which the polypeptide marker is neurosecretory protein VGF or a fragment thereof.

ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.

EP 08 00 2793

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 08 00 2793

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

| | | | |
|----------------|--|---------|------------|
| 专利名称(译) | 用于诊断阿尔茨海默病的多肽生物标志物 | | |
| 公开(公告)号 | EP1953556A3 | 公开(公告)日 | 2008-11-26 |
| 申请号 | EP2008002793 | 申请日 | 2003-08-11 |
| [标]申请(专利权)人(译) | 拜尔健康护理有限责任公司 | | |
| 申请(专利权)人(译) | 拜耳医药保健公司 | | |
| 当前申请(专利权)人(译) | 拜耳先灵医药AKTIENGESELLSCHAFT | | |
| [标]发明人 | HOCHSTRASSER DENIS FRANCOIS PROF DR SANCHEZ JEAN CHARLES DR C O BIOMEDICAL PROTEOMICS RES GRP CARRETTE ODILE DR | | |
| 发明人 | YALKINOGLU, ÖZKAN A., DR. KÖNIG, GERHARD, DR. HOCHSTRASSER, DENIS FRANCOIS, PROF. DR. SANCHEZ, JEAN-CHARLES, DR. C/O BIOMEDICAL PROTEOMICS RESEARCH GROUP CARRETTE, ODILE, DR. | | |
| IPC分类号 | G01N33/68 G01N27/62 C07K14/47 C07K14/74 C07K14/805 C07K14/81 C12Q1/37 G01N33/53 | | |
| CPC分类号 | G01N33/6896 C07K14/70539 C07K14/805 C07K14/8139 G01N2800/2821 | | |
| 优先权 | 2002026643 2002-11-29 EP 2002018283 2002-08-23 EP | | |
| 其他公开文献 | EP1953556B1 EP1953556A2 | | |
| 外部链接 | Espacenet | | |

摘要(译)

公开了一种评估患者阿尔茨海默病状态的方法。还公开了一种用于监测患者中阿尔茨海默病进展的方法。该方法应用特定肽标记物的检测，例如，使用质谱分析。



European Patent Office
Office Européen des Brevets
Europäisches Patentamt

PARTIAL EUROPEAN SEARCH REPORT Application Number
which under Rule 63 of the European Patent Convention EP 08 00 2793
shall be considered, for the purposes of subsequent
proceedings, as the European search report

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|---|---|--|---|
| X | WO 00/25138 A (NITSCH ROGER ; GROWDON JOHN (US)) 4 May 2000 (2000-05-04) * the whole document * * example 1 * | 4 | INV G01N33/68 |
| Y | WEI, LIHONG ET AL: "Cystatin C: Icelandic-like mutation in an animal model of cerebrovascular beta-amyloidosis" STROKE, vol. 27, no. 11, 1996, pages 2080-2085, XP00038609 DALLAS * the whole document * * figure 2 * | 3-8 3,4 | |
| Y | ----- ----- /-- | 3-8 | |
| INCOMPLETE SEARCH | | | |
| <p>The Search Division certifies that the present application, in view of none of the claims, demands full search in the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these reasons:</p> <p>Claims searched completely:</p> <p>Claims not searched:</p> <p>Reason for the limitation of the search: see sheet C</p> | | | |
| Place of search The Hague | | Date of completion of the search 13 October 2008 | Examiner Tuyman, Antonin |
| <p>CATEGORY OF OTHER DOCUMENTS</p> <p>AZ particularly relevant if taken into account B particularly relevant if cited with authority C document of the same category D bibliographic reference E non-patent literature F intermediate document</p> <p>T priority documents underlying the invention E other patent documents, not published on, or published on, the date of filing of the application I document cited for other reasons A member of the same patent family, corresponding document</p> | | | |