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- Published:**
- with international search report (Art. 21(3))
 - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- (88) **Date of publication of the international search report:**
16 June 2011



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(54) **Title:** BIOMARKERS AND METHODS FOR DETECTING ALZHEIMER'S DISEASE

(57) **Abstract:** Methods for classifying a test sample as indicative of Alzheimer's disease use protein and peptide biomarkers that are differentially expressed in the cerebral spinal fluid (CSF) of subjects with Alzheimer's disease relative to age-matched controls. The methods also use protein and peptide signatures indicative of Alzheimer's disease. Microarrays and kits for detecting the protein and peptide biomarkers in CSF samples can be used to classify Alzheimer's disease state from test samples.

A. CLASSIFICATION OF SUBJECT MATTER*G01N 33/68(2006.01)i, C40B 40/10(2006.01)i, G06F 19/00(2011.01)i*

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 33/68; C12N; G01N 33/00; G06F 17/30; C07K 16/18; G01N 33/53; G01N 33/50

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & Keywords: Alzheimer's disease, biomarkers, CSF

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Josef Marksteiner et al., 'Cerebrospinal fluid biomarkers for diagnosis of Alzheimer's disease: beta-amyloid (1-42), tau, phospho-tau-181 and total protein', Drugs Today Vol. 43(6) pp. 423-431 (June 2007) See Abstract, Pages 424-427, 428	1-4
X	WO 03-025122 A2 (UNIVERSITY OF KENTUCKY RESEARCH FOUNDATION et al.) 27 March 2003 See Abstract, Claim 1	1-4
X	US 2005-0244890 A1 (HUW DAVIES et al.) 03 November 2005 See Abstract, Claims 1, 13, SEQ ID NO. 18, 20	1-4
A	US 2009-0075395 A1 (LEE KELVIN H. et al.) 19 March 2009 See Abstract, Claims 1,5,9,15,24-25	1-4
A	WO 2007-136614 A2 (MERCK & CO., INC. et al.) 29 November 2007 See Abstract, Claims 1-4	1-4
A	WO 2008-140639 A2 (OLIGOMERIX, INC. et al.) 20 November 2008 See Abstract, Claims 1-3,7	1-4

 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 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 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

29 APRIL 2011 (29.04.2011)

Date of mailing of the international search report

29 APRIL 2011 (29.04.2011)

Name and mailing address of the ISA/KR

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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:

Claims 1-4 (Group 1), Claims 5-10 (Group 2), Claims 11-14 (Group 3), Claim 15 (Group 4), Claim 16 (Group 5), Claims 17-19 (Group 6), Claim 20 (Group 7).

The only common technical feature between Groups 1-7 comprises an amino acid as a biomarker of Alzheimer's disease. However, this feature lacks novelty and/or inventive step with respect to documents of WO 2003/025122 A2 (27 March 2003), US 2005-0244890 A1 (03 November 2005), or Drugs Today Vol. 43(6) pp. 423-431 (June 2007) cited in this ISR.

Thus, there is no technical relationship left over the prior art among the claimed inventions leaving the claims without a single general inventive concept. Hence there is lack of unity "a posteriori" (PCT Rules 13.1 and 13.2).

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.: 1-4

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2010/041257

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		AU 2002-313737 A8	01.04.2003
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		WO 2008-140639 A3	30.12.2009