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- (81) **Designated States** (*unless otherwise indicated, for every  
kind of national protection available*): AE, AG, AL, AM,  
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,  
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,  
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,

HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,  
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,  
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,  
NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU,  
RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ,  
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UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,  
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EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,  
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,  
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17:**

— *of inventorship (Rule 4.17(iv))*

**Published:**

— *with international search report (Art. 21(3))*

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claims and to be republished in the event of receipt of  
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15 May 2014



(54) **Title:** SPECIFIC SALIVARY BIOMARKERS FOR RISK DETECTION, EARLY DIAGNOSIS, PROGNOSIS AND MONITORING OF ALZHEIMER'S AND PARKINSON'S DISEASES

(57) **Abstract:** Methods by which specific biomarkers in saliva are used for risk detection, diagnosis, prognosis and monitoring of Alzheimer's and Parkinson's diseases.

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2013/001407

A. CLASSIFICATION OF SUBJECT MATTER INV. G01N33/68 ADD.		
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 practicable, search terms used) EPO-Internal, BIOSIS, EMBASE, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BERMEJO-PAREJA FELIX ET AL: "Saliva levels of Abeta1-42 as potential biomarker of Alzheimer's disease: a pilot study", BMC NEUROLOGY, BIOMED CENTRAL LTD., LONDON, GB, vol. 10, no. 1, 3 November 2010 (2010-11-03), page 108, XP021074798, ISSN: 1471-2377, DOI: 10.1186/1471-2377-10-108 the whole document ----- -/--	1-9,11, 13,20-22
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
* Special categories of cited documents :		
<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>		<p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p>
Date of the actual completion of the international search	Date of mailing of the international search report	
25 March 2014	02/04/2014	
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  Hoesel, Heidi	

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2013/001407

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PROLO P ET AL: "P3-103 Amyloid-beta, cytokine profiles and natural killer cell activity: supposed markers of Alzheimer's disease", NEUROBIOLOGY OF AGING, TARRYTOWN, NY, US, vol. 25, 1 July 2004 (2004-07-01), page S384, XP027082744, ISSN: 0197-4580 [retrieved on 2004-07-01]	8,9
Y	abstract	1-7
Y	----- GERMAN ET AL: "Serum biomarkers for Alzheimer's disease: Proteomic discovery", BIOMEDICINE AND PHARMACOTHERAPY, ELSEVIER, FR, vol. 61, no. 7, 15 August 2007 (2007-08-15), pages 383-389, XP022201242, ISSN: 0753-3322, DOI: 10.1016/J.BIOPHA.2007.05.009 abstract, p. 383, col. 2, lines 3 - 11, p. 384, item 2.1	1-7
A	----- BOSTON PAUL F ET AL: "Developing a simple laboratory test for Alzheimer's disease: measuring acetylcholinesterase in saliva - a pilot study", INTERNATIONAL JOURNAL OF GERIATRIC PSYCHIATRY, vol. 23, no. 4, April 2008 (2008-04), pages 439-440, XP002715436, ISSN: 0885-6230 the whole document	1-4, 20-22
A	----- SHI MIN ET AL: "Salivary Tau Species are Potential Biomarkers of Alzheimer's Disease", JOURNAL OF ALZHEIMER'S DISEASE, vol. 27, no. 2, 2011, pages 299-305, XP002715437, abstract	20-22
X	----- US 2007/042437 A1 (WANDS JACK R [US] ET AL DE LA MONTE SUZANNE MARIE [US] ET AL) 22 February 2007 (2007-02-22)	17-19
A	par. 0002,0007, 0009, 0068, 0104, claims 1, 6	8-16
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2013/001407

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ALVAREZ ET AL: "Serum TNF-alpha levels are increased and correlate negatively with free IGF-I in Alzheimer disease", NEUROBIOLOGY OF AGING, TARRYTOWN, NY, US, vol. 28, no. 4, 23 February 2007 (2007-02-23), pages 533-536, XP005901141, ISSN: 0197-4580, DOI: 10.1016/J.NEUROBIOLAGING.2006.02.012	17-19
A	abstract, p. 535, col. 2, lines 18 - 23 -----	8-16
T	Singhal R.K, Anand, S.: "Salivary -42, IGF-I, IGF-II, Alpha Amylase, IL-1, and TNF-alpha in Alzheimer's Disease: A Useful diagnostic tool",  3 August 2013 (2013-08-03), XP002721580, Retrieved from the Internet: URL:https://web.archive.org/web/20140228131418/http://wwwhttp://www.webmedcentral.com/wmcpdf/Article_WMC004358.pdf [retrieved on 2014-03-12] the whole document -----	
T	KIM CHANG-BEOM ET AL: "Antibody-based magnetic nanoparticle immunoassay for quantification of Alzheimer's disease pathogenic factor.", JOURNAL OF BIOMEDICAL OPTICS MAY 2014, vol. 19, no. 5, 051205, May 2014 (2014-05), pages 1-7, XP002721581, ISSN: 1560-2281 abstract, items 3.2, 5 -----	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2013/001407

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
US 2007042437	A1	22-02-2007	EP 2001503 A2	17-12-2008
			US 2007042437 A1	22-02-2007
			WO 2007123723 A2	01-11-2007
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**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

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

1. claims: 1-4, 20-22(completely); 5-7(partially)

the inventions listed under subject 1.1 and 1.2 have been searched

1.1. claims: 1-4(completely); 5-7(partially)

screening method for the identification of salivary biomarkers that discriminate between of Alzheimer's disease and Parkinson's disease

1.2. claims: 20-22

diagnosis of Alzheimer's disease by means of assessing the ratio between amyloid beta peptides

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2. claims: 8-19(completely); 5-7(partially)

diagnosis of Alzheimer's disease or Parkinson's disease based on the detection a panel of seven selected markers that discriminate between the said diseases in a saliva sample, test kit for said diagnostic methods

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2013/001407

## 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 fees, 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.:

### 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.