

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
21 December 2007 (21.12.2007)

PCT

(10) International Publication Number  
**WO 2007/144619 A3**

(51) International Patent Classification:  
*C07K 16/28* (2006.01)    *C12N 5/20* (2006.01)  
*A61K 39/395* (2006.01)    *G01N 33/577* (2006.01)

(74) Agents: SZCZUKA, Jan et al.; MARKS & CLERK, 19  
Royal Exchange Square, Glasgow G1 3AE (GB).

(21) International Application Number:  
PCT/GB2007/002205

(22) International Filing Date: 13 June 2007 (13.06.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0611708.9                      14 June 2006 (14.06.2006)    GB

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, 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, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(71) Applicants (for all designated States except US): UNIVERSITY COURT OF THE UNIVERSITY OF EDINBURGH [GB/GB]; Old College, South Bridge, Edinburgh EH8 9YL (GB). UNIVERSITY OF STRATHCLYDE [GB/GB]; McCance Building, 16 Richmond Street, Glasgow G1 1XQ (GB). COMMON SERVICES AGENCY [GB/GB]; Trinity Park House, South Trinity Road, Edinburgh EH5 9SE (GB). INSTITUTE FOR ANIMAL HEALTH [GB/GB]; Compton, Newbury, Berkshire RG20 7NN (GB).

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(72) Inventor; and  
(75) Inventor/Applicant (for US only): HEAD, Mark, William [GB/GB]; University of Edinburgh, National CJD Surveillance Unit, Bryan Matthews Building, Western General Hospital, Edinburgh EH4 2XU (GB).

Published:  
— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
2 May 2008



WO 2007/144619 A3

(54) Title: ANTIBODIES SELECTIVELY BINDING AGGREGATED PRION PROTEIN 106-126 AND USES THEREOF

(57) Abstract: The present invention relates to a novel antibody which selectively binds to the disease associated form of prion protein (PrP<sup>Sc</sup>) under native conditions and the use thereof in methods of prion disease detection, therapy and disease research in general.

## INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2007/002205

A. CLASSIFICATION OF SUBJECT MATTER INV. C07K16/28 A61K39/395 C12N5/20 G01N33/577		
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) C07K		
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, EMBASE, BIOSIS		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 2006/088281 A (PEOPLEBIO INC [KR]; AN SEONG SOO ALEXANDER [US]; LIM KUN TAEK [KR]; OH) 24 August 2006 (2006-08-24) claims 1-45	1-18
A	WO 2006/033974 A (UNIV CASE WESTERN RESERVE [US]; SY MAN-SUN [US]; PAN TAO [US]; LI RULI) 30 March 2006 (2006-03-30) figure 1; example 1	1-18
	----- -/--	
<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 :		
*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  20 February 2008		Date of mailing of the international search report  03/03/2008
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  Bernhardt, Wiebke

## INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2007/002205

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>PAN TAO ET AL: "An aggregation-specific enzyme-linked immunosorbent assay: Detection of conformational differences between recombinant PrP protein dimers and PrPSc aggregates"</p> <p>JOURNAL OF VIROLOGY, vol. 79, no. 19, October 2005 (2005-10), pages 12355-12364, XP009096193 ISSN: 0022-538X abstract; figure 5 page 12362, left-hand column</p>	1-18
A	<p>GU YAPING ET AL: "Prion peptide 106-126 modulates the aggregation of cellular prion protein and induces the synthesis of potentially neurotoxic transmembrane PrP"</p> <p>JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOCHEMICAL BIOLOGISTS, BIRMINGHAM,, US, vol. 277, no. 3, 2002, pages 2275-2286, XP009096116 ISSN: 0021-9258 abstract</p>	1-18
A	<p>SINGH NEENA ET AL: "Prion peptide 106-126 as a model for prion replication and neurotoxicity"</p> <p>FRONTIERS IN BIOSCIENCE, vol. 7, no. Cited May 17, 2002, 1 April 2002 (2002-04-01), pages a60-71 URL, XP009096117 ISSN: 1093-4715 cited in the application abstract page 63, right-hand column</p>	1-18
A	<p>HANAN E ET AL: "ANTIAGGREGATING ANTIBODY RAISED AGAINST HUMAN PRP 106-126 RECOGNIZES PATHOLOGICAL AND NORMAL ISOFORMS OF THE WHOLE PRION PROTEIN"</p> <p>CELLULAR AND MOLECULAR NEUROBIOLOGY, NEW YORK, NY, US, vol. 21, no. 6, December 2001 (2001-12), pages 693-703, XP009017127 abstract</p>	1-18
	----- -/--	

## INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2007/002205

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SERBEC VLADKA CURIN ET AL: "Monoclonal antibody against a peptide of human prion protein discriminates between Creutzfeldt-Jacob's disease-affected and normal brain tissue." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 279, no. 5, 30 January 2004 (2004-01-30), pages 3694-3698, XP009096131 ISSN: 0021-9258 cited in the application abstract	1-18
A	KORTH C ET AL: "PRION (PRPSC)-SPECIFIC EPI TOPE DEFINED BY A MONOCLONAL ANTIBODY" NATURE, NATURE PUBLISHING GROUP, LONDON, GB, vol. 390, no. 6655, 6 November 1997 (1997-11-06), pages 74-77, XP002069611 ISSN: 0028-0836 cited in the application abstract	1-18
A	BIESCHKE J ET AL: "ULTRASENSITIVE DETECTION OF PATHOLOGICAL PRION PROTEIN AGGREGATES BY DUAL-COLOR SCANNING FOR INTENSELY FLUORESCENT TARGETS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 97, no. 10, 9 May 2000 (2000-05-09), pages 5468-5473, XP000999285 ISSN: 0027-8424 abstract	1-18
A	KASCSAK R J ET AL: "MOUSE POLYCLONAL AND MONOCLONAL ANTIBODY TO SCRAPIE-ASSOCIATED FIBRIL PROTEINS" JOURNAL OF VIROLOGY, NEW YORK, US, US, vol. 61, no. 12, December 1987 (1987-12), pages 3688-3693, XP002924865 ISSN: 0022-538X cited in the application abstract	1-18
A	PARAMITHIOTIS E ET AL: "A PRION PROTEIN EPI TOPE SELECTIVE FOR THE PATHOLOGICALLY MISFOLDED CONFORMATION" NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 9, no. 7, July 2003 (2003-07), pages 893-899, XP001180826 ISSN: 1078-8956 figure 1c	1-18

-/--

## INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2007/002205

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SAFAR JIRI G ET AL: "Diagnosis of human prion disease" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 102, no. 9, 1 March 2005 (2005-03-01), pages 3501-3506, XP002432630 ISSN: 0027-8424 page 3501, left-hand column -----	1-18
A	PARCHI P ET AL: "MOLECULAR BASIS OF PHENOTYPIC VARIABILITY IN SPORADIC CREUTZFELDT-JAKOB DISEASE" ANNALS OF NEUROLOGY, BOSTON, US, vol. 39, no. 6, 1996, pages 767-778, XP009006817 ISSN: 0364-5134 abstract; table 1 -----	4

**INTERNATIONAL SEARCH REPORT**

International Application No. PCT/GB2007 /002205

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box II.1

Although claims 1, 6, 7 and 10-16 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

-----

Continuation of Box II.1

Claims Nos.: -

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB2007/002205

## 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:  
see FURTHER INFORMATION sheet PCT/ISA/210
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:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable 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.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2007/002205

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006088281 A	24-08-2006	AU 2005327652 A1	24-08-2006
		CA 2598321 A1	24-08-2006
		EP 1848817 A1	31-10-2007
WO 2006033974 A	30-03-2006	EP 1800125 A2	27-06-2007