

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
16 December 2004 (16.12.2004)

PCT

(10) International Publication Number  
**WO 2004/108895 A3**

(51) International Patent Classification<sup>7</sup>: **C07K 16/00**,  
17/00, C12P 21/08, A61K 39/395, 39/40, 39/42

(21) International Application Number:  
PCT/US2004/017514

(22) International Filing Date: 1 June 2004 (01.06.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/474,654 30 May 2003 (30.05.2003) US

(71) Applicants (for all designated States except US): **NEURALAB LIMITED**; 102 St. James Court, Flatts Smith FL04 (BM). **WYETH** [US/US]; Five Giralda Farms, Madison, NJ 07940 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BASI, Guriq**

[US/US]; 514 Rhodes Drive, Palo Alto, CA 94303 (US). **SALDANHA, Jose, W.** [GB/GB]; 21 Fillebrook Avenue, Enfield, EN1 3BD (GB). **BARD, Frédérique** [US/FR]; 111 Park Pacifica Avenue, Pacifica, CA 94044 (US).

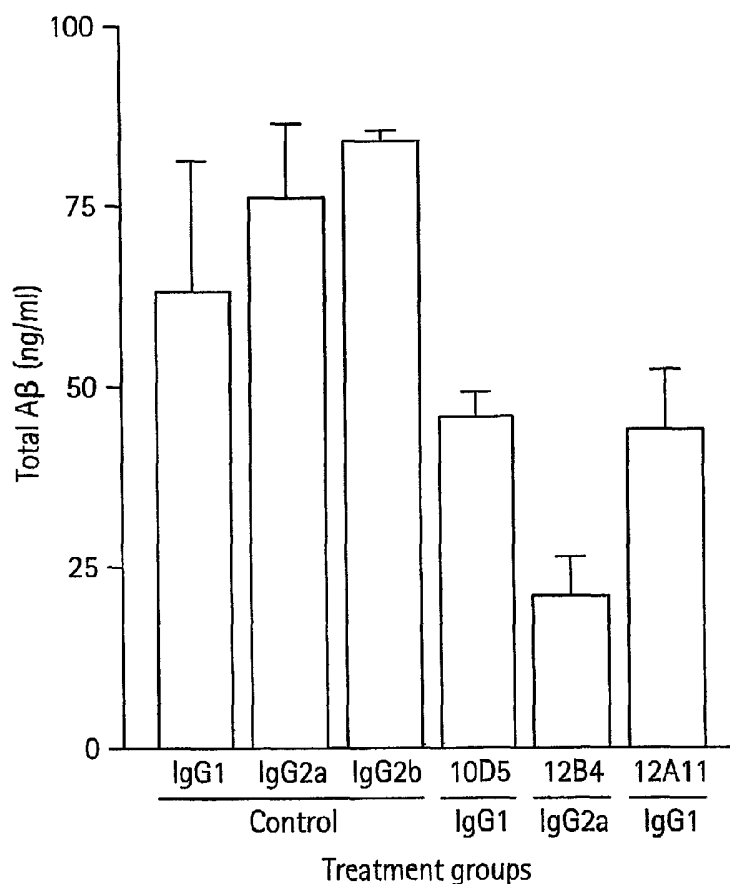
(74) Agents: **MILASINCIC, Debra, J.** et al.; Lahive & Cockfield, LLP, 28 State Street, Boston, MA 02109 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: HUMANIZED ANTIBODIES THAT RECOGNIZE BETA AMYLOID PEPTIDE



(57) Abstract: The invention provides improved agents and methods for treatment of diseases associated with amyloid deposits of Aβ in the brain of a patient. Preferred agents include antibodies, e.g., humanized antibodies.

WO 2004/108895 A3



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, IT, LU, MC, 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).

**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:**

28 July 2005

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/17514

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 16/00, 17/00; C12P 21/08; A61K 39/395, 39/40, 39/42  
US CL : 530/387.1, 387.2, 387.3, 388.1, 388.15; 424/130.1, 141.1, 142.1

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)

U.S. : 530/387.1, 387.2, 387.3, 388.1, 388.15; 424/130.1, 141.1, 142.1

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)

Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,750,324 B1 (SCHENK et al) 15 June 2004 (15.06.2004), entire document.	1-10, 34-44, 121-124
A	US 6,743,427 B1 (SCHENK) 01 June 2004 (01.06.2004), entire document.	1-10, 34-44, 121-124
A	SOLOMON, B. Immunological approaches as therapy for Alzheimer's disease. Expert Opin Biol Ther. December 2002, Vol. 2, No. 8, pages 907-917, entire document.	1-10, 34-44, 121-124
A	HOLTZMAN, D.M. et al. Abeta immunization and anti-Abeta antibodies: potential therapies for the prevention and treatment of Alzheimer's disease. Advanced Drug Delivery Reviews Vol. 54, No. 12, pages 1603-1613, see Figure 1.	1-10, 34-44, 121-124
A	DODEL, R. C. et al. Immunotherapy for Alzheimer's disease. Lancet Neurology April 2003, Vol. 2, No. 4, pages 215-220, see Figure 2.	1-10, 34-44, 121-124



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	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

07 April 2005 (07.04.2005)

Date of mailing of the international search report

26 MAY 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Christopher J. Nichols, Ph.D.

Telephone No. 703-308-0196

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/17514

### 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.: 11-23  
because they relate to subject matter not required to be searched by this Authority, namely:  
Please See Continuation Sheet
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:  
Please See Continuation 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.: 1-10,34-44 and 121-124

#### Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US04/17514

**Box II** Observations where certain claims were found unsearchable 1. because they relate to subject matter not required to be searched by this Authority, namely:

Claims 11-23 and 78-83 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: claims 11-23 require use of "analysis of a three-dimensional model" which is not disclosed or taught in the instant specification. This also represents non-statutory matter as it is a mental step and not the physical manipulation of matter.

### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1 Claim(s) 1-10, 24-49, and 121-124, drawn to humanized antibody 12A11, compositions, and methods of use thereof.

Group 2 Claim(s) 50-65, drawn to an isolated polypeptide and variants thereof.

Group 3 Claim(s) 66-72 and 75, drawn to an isolated nucleic acid, vectors, and host cells comprising same.

Group 4 Claim(s) 73-74, drawn to a transgenic animal.

Group 5 Claim(s) 76-77, drawn to a method of producing an antibody.

Group 6 Claim(s) 84-85, drawn to a method of treating an amyloidogenic disease comprising administering a nucleic acid molecule.

Group 7 Claim(s) 86-120, drawn to a method for reducing neuritic burden comprising administering a humanized immunoglobulin.

The inventions listed as Groups 1-7 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group 1 is drawn to the special technical feature of humanized antibody 12A11, which is not required by any of the other groups.

Group 2 is drawn to the special technical feature of an isolated polypeptide, which is not required by any of the other groups.

Group 3 is drawn to the special technical feature of an isolated nucleic acid, vectors, and host cells comprising same, which is not required by any of the other groups.

Group 4 is drawn to the special technical feature of a transgenic animal, which is not required by any of the other groups.

Group 5 is drawn to the special technical feature of producing an antibody, which is not required by any of the other groups.

Group 6 is drawn to the special technical feature of gene therapy, which is not required by any of the other groups.

Group 7 is drawn to the special technical feature of passive immunization therapy, which is not required by any of the other groups.

Claims 11-23 and 78-83 are unsearchable under PCT Rule 6.4(a).

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US04/17514

Continuation of B. FIELDS SEARCHED Item 3:  
WEST (USPT, PGPUBS, USOCR, JPO, EPO, DERWENT); NCBI (PUBMED); STN (BIOSCIENCE)  
12A11, 10D5, chimeric, humanized, antibody, Abeta, Alzheimers disease, passive immunization