

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
9 November 2006 (09.11.2006)

PCT

(10) International Publication Number
WO 2006/119352 A3

- (51) International Patent Classification:
A61K 35/12 (2006.01)
- (21) International Application Number:
PCT/US2006/016964
- (22) International Filing Date: 3 May 2006 (03.05.2006)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/677,180 3 May 2005 (03.05.2005) US
- (71) Applicant (for all designated States except US): UNIVERSITY OF SOUTH FLORIDA [US/US]; 3702 Spectrum Blvd., Suite 155, Tampa, Florida 33612 (US).

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, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, 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, 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, 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:
11 January 2007

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.



WO 2006/119352 A3

(54) Title: METHOD OF TREATING COGNITIVE DECLINE AND SYNAPTIC LOSS RELATED TO ALZHEIMER'S DISEASE

(57) Abstract: A method treating a subject with Alzheimer's disease wherein Aβ-reactive immune cells, splenocytes and lymphocytes, are generated *in vitro* or *in vivo*, re-stimulated *in vitro*, and then adoptively transferred into the cognitively-impaired subject. The population of immune cells can be derived from a donor with a natural or adaptive immune response to Aβ, stimulated by exposure to Aβ *in vivo*. The donor cells are then collected and re-stimulated by subsequent exposure to Aβ *in vitro* prior to administration to the subject. Alternatively, the population of immune cells can be derived from the subject and then stimulated by exposure to Aβ *in vitro*.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/16964

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: **A61K 35/12(2006.01)**

USPC: 424/93.71
 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. : 424/93.71

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.
X	WO 99/27944 A1 (SCHENK) 10 June 1999 (10.06.1999), especially pages 13-14, 19, and claim 25. NOTE: only relevant pages have been supplied.	1, 2, 4-7, 10, 11, 13, 14, 17, 18
X	US 2002/0072493 A1 (EISENBACH-SCHWARTZ et al.) 13 June 2002 (13.06.2002), especially paragraphs [0014-0023], [0065-0069], [0072], [0100], [0124-0125], and [0137].	1, 2, 4, 5, 7-11, 14-18
---		-----
Y	NOTE: only relevant pages have been supplied.	3, 12
Y	CRIBBS, D.H. et al. Adjuvant-dependent Modulation of Th1 and Th2 Responses to Immunization with beta-Amyloid. Int. Immunol. April 2003, Vol. 15, No. 4, pages 505-514, especially page 513.	3, 12
T	ETHELL, D.W. et al. Abeta-specific T-cells Reverse Cognitive Decline and Synaptic Loss in Alzheimer's Mice. Neurobiology of Disease, August 2006, Vol. 23, pages 351-361.	1-18

<input type="checkbox"/> Further documents are listed in the continuation of Box C.	<input 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	"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 13 October 2006 (13.10.2006)	Date of mailing of the international search report 02 NOV 2006
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. (571) 273-3201	Authorized officer Kimberly A. Ballard <i>J. Roberts for</i> Telephone No. 571-272-0500

Continuation of B. FIELDS SEARCHED Item 3:

EAST, STN (MEDLINE, BIOSIS, LIFESCI, EMBASE, SCISEARCH, CAPLUS)

search terms: amyloid beta, Alzheimer?, (T or Th or T-helper) cells or lymphocytes or leukocytes or splenocytes, adoptive transfer