

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 September 2007 (13.09.2007)

PCT

(10) International Publication Number
WO 2007/103114 A3

(51) International Patent Classification:
A61K 31/16 (2006.01) A61K 31/47 (2006.01)

(21) International Application Number:
PCT/US2007/005267

(22) International Filing Date: 2 March 2007 (02.03.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/779,445 7 March 2006 (07.03.2006) US

(71) Applicant (for all designated States except US): **THE BRIGHAM & WOMEN'S HOSPITAL, INC.** [US/US];
75 Francis Street, Boston, MA 02115 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **AIKAWA, Masanori**
[JP/US]; 79 Willis Road, Chestnut Hill, MA 02467 (US).

(74) Agents: **SANZO, Michael, A.** et al.; Law Office Of
Michael A. Sanzo, 15400 Calhoun Drive, Suite 125,
Rockville, MD 20855 (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, 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.

(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).

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:
29 November 2007

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: NOTCH INHIBITION IN THE TREATMENT OR PREVENTION OF ATHEROSCLEROSIS

(57) Abstract: The present invention is directed to methods of treating or preventing atherosclerosis and other cardiovascular diseases by administering agents that inhibit or modulate the NOTCH signaling pathway. In addition, the invention encompasses methods for assaying compounds for their ability to treat atherosclerosis based upon their effects on NOTCH signaling, and for measuring levels of amount, function, or activity of NOTCH pathway components in biological samples.



WO 2007/103114 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 07/05267

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/16; A61K 31/47 (2007.01)

USPC - 514/613; 514/312

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)

IPC(8): A61K 31/16; A61K 31/47 (2007.01)

USPC: 514/613; 514/312; 514/620; 514/623; 514/602; 514/18; 514/19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Amer J of Path, September 2001, Vol 159, No 3

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

WEST (PGPB,USPT,EPAB,JPAB): notch, cardiovascular, atherosclerosis, gamma, secretase inhibitor

esp@cent: notch, cardiovascular, atherosclerosis

Google Scholar: NOTCH, atherosclerosis, gamma secretase inhibitor

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	WO 2005/008250 A1 (HELLSTROM et al.) 27 January 2005 (27.01.2005), abstract; pg 2, ln 3-18; pg 3, ln 15-20; pg 4, ln 3-14; pg 4, ln 23-30; pg 6, ln 23; pg 10, ln 38 ln 11, ln 5.	1-4, 9, 10, 11, 12 5, 6, 7, 8
X	LINDNER, V. et al. Members of the Jagged/Notch Gene Families Are Expressed in Injured Arteries and Regulate Cell Phenotype via Alterations in Cell Matrix and Cell-Cell Interaction. Amer J of Path. September 2001, Vol 159, No 3, pages 875, 876, ISSN 0002-9440.	20 and 21
X — Y	WO 03/012441 A1 (BODMER et al.) 13 February 2003 (13.02.2003), pg 9, ln 22-26; pg 12, ln 21 pg 13, ln 12; pg 17, ln 6-7; pg 90, ln 27; pg 94, ln 24.	13-16 5, 6, 7, 8, 17-19
Y	US 2005/0025751 A1 (BODMER et al.) 3 February 2005 (03.02.2005), para [0036]	17-19

☐ Further documents are listed in the continuation of Box C.

* 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 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

9 August 2007 (09.08.2007)

Date of mailing of the international search report

01 OCT 2007

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:

Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774