



(43) International Publication Date
6 December 2012 (06.12.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/166630 A3

(51) International Patent Classification:

G01N 33/68 (2006.01) *C12Q 1/68* (2006.01)
G01N 33/15 (2006.01) *G01N 33/53* (2006.01)

(21) International Application Number:

PCT/US2012/039657

(22) International Filing Date:

25 May 2012 (25.05.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/490,931 27 May 2011 (27.05.2011) US

(71) Applicant (for all designated States except US):
XENOTECH LLC [US/US]; 16825 W. 116th Street, Lenexa, Kansas 66219 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CZERWINSKI, Maciej** [US/US]; 5921 Cherokee Drive, Fairway, Kansas 66205 (US). **BUCKLEY, David Benjamin** [US/US]; 23893 W. 124th Court, Olathe, Kansas 66061 (US). **KAZMI, Faraz** [CA/US]; 12221 W. 119th Terrace, Apt. 218, Overland Park, Kansas 66213 (US).

(74) Agent: **COOK, Crissa A.**; Hovey Williams LLP, 10801 Mastin Blvd. Suite 1000, 84 Corporate Woods, Overland Park, Kansas 66210 (US).

(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, 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, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, 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, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, 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).

Published:

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

(88) Date of publication of the international search report:

21 March 2013

(54) Title: IN VITRO TEST SYSTEM TO EVALUATE XENOBIOTICS AS IMMUNE-MODULATORS OF DRUG TRANSPORT AND METABOLISM IN HUMAN HEPATOCYTES

(57) Abstract: A method of evaluating the effect of a xenobiotic on biomarkers, such as drug transporters and drug-metabolizing enzymes in hepatocytes is provided. The method comprises the formation of a xenobiotic-stimulated biological sample, such as whole blood, which contains a plurality of cytokines. A portion of xenobiotic-stimulated biological sample is cultured with hepatocytes. The hepatocytes are then analyzed to evaluate the activity of drug transporters and/or drug-metabolizing enzymes, or other biomarkers to determine the effect of the xenobiotic on drug metabolism in the hepatocytes.



WO 2012/166630 A3

A. CLASSIFICATION OF SUBJECT MATTER*G01N 33/68(2006.01)i, G01N 33/15(2006.01)i, C12Q 1/68(2006.01)i, G01N 33/53(2006.01)i*

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 33/68; C12Q 1/02; C12Q 1/00; C12N 9/02; G01N 33/567; C12Q 1/68

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: effect of xenobiotic, hepatocyte, biomarker, evaluation

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2004-0241714 A1 (BRANCH ROBERT A. et al.) 02 December 2004 See the whole document.	1-36
A	US 2004-0043377 A1 (KAORU SHIMADA et al.) 04 March 2004 See the whole document.	1-36
A	US 2005-0130254 A1 (SUNG-SOO PARK) 16 June 2005 See the whole document.	1-36
A	US 2004-0029153 A1 (JUNZO TAKAHASHI et al.) 12 February 2004 See the whole document.	1-36



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

"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 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

24 DECEMBER 2012 (24.12.2012)

Date of mailing of the international search report

26 DECEMBER 2012 (26.12.2012)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
189 Cheongsu-ro, Seo-gu, Daejeon Metropolitan
City, 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

Kang Yeon Mu

Telephone No. 82-42-481-5516



INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/039657

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004-0241714 A1	02.12.2004	WO 2004-069189 A2 WO 2004-069189 A3	19.08.2004 28.07.2005
US 2004-0043377 A1	04.03.2004	AU 2003-263400 A1 AU 2003-263400 A8 BR 0313960 A CA 2494752 A1 EP 1546713 A1 JP 2004-089085 A MX PA05001402A WO 2004-020998 A1 WO 2004-020998 A8	19.03.2004 19.03.2004 19.07.2005 11.03.2004 29.06.2005 25.03.2004 28.04.2005 11.03.2004 29.12.2004
US 2005-0130254 A1	16.06.2005	AU 2004-303755 A1 AU 2006-282872 A1 AU 2006-282873 A1 AU 2006-284654 A1 CA 2549904 A1 CA 2620215 A1 CA 2620826 A1 CA 2620837 A1 CN 101268364 A0 CN 101268365 A0 CN 101273119 A0 CN 1894396 A CN 1894396 C0 EP 1648994 A2 EP 1697496 A1 EP 1697496 A4 EP 1931987 A1 EP 1931988 A1 EP 1941022 A1 IL 176256D0 JP 2007-513638 A JP 2007-513638 T JP 2009-505661 A JP 2009-505662 A JP 2009-506774 A KR 10-2006-0103818 A KR 10-2006-0127880 A KR 10-2008-0052597 A KR 10-2008-0055854 A KR 10-2008-0056163 A KR20060127880A US 2004-0265997 A1 US 2005-0282152 A1 US 2007-0048732 A1 US 2007-0048733 A1 US 2010-0159503 A1	07.07.2005 01.03.2007 01.03.2007 08.03.2007 07.07.2005 01.03.2007 08.03.2007 01.03.2007 17.09.2008 17.09.2008 24.09.2008 10.01.2007 10.01.2007 26.04.2006 06.09.2006 03.01.2007 18.06.2008 18.06.2008 09.07.2008 05.10.2006 31.05.2007 31.05.2007 12.02.2009 12.02.2009 19.02.2009 04.10.2006 13.12.2006 11.06.2008 19.06.2008 20.06.2008 13.12.2006 30.12.2004 22.12.2005 01.03.2007 01.03.2007 24.06.2010

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/039657

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004-0029153 A1	12.02.2004	US 7829325 B2	09.11.2010
		WO 2005-000376 A2	06.01.2005
		WO 2005-000376 A3	06.01.2005
		WO 2005-061694 A1	07.07.2005
		WO 2007-025153 A1	01.03.2007
		WO 2007-025154 A1	01.03.2007
		WO 2007-027938 A1	08.03.2007
		ZA200605435A	28.11.2007
		AU 1430402 A	27.05.2002
		AU 2002-14304 A1	27.05.2002
		AU 2002-214304 A8	27.05.2002
		EP 1356286 A2	29.10.2003
		JP 2002-233399 A	20.08.2002
		WO 02-40995 A2	23.05.2002
		WO 02-40995 A3	23.05.2002
		WO 02-40995A2	23.05.2002
		WO 02-40995A3	04.09.2003