

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
12 October 2006 (12.10.2006)

PCT

(10) International Publication Number
WO 2006/107846 A3

(51) International Patent Classification:
C12Q 1/68 (2006.01) *C12Q 1/48* (2006.01)
G01N 33/53 (2006.01)

(74) Agent: SALIWANCHKI, LLOYD & SALIWANCHIK;
P.O. Box 142950, Gainesville, FL 32614-2950 (US).

(21) International Application Number:
PCT/US2006/012253

(22) International Filing Date: 31 March 2006 (31.03.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/668,121 1 April 2005 (01.04.2005) US

(71) Applicant (for all designated States except US): **UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INC.** [US/US]; 223 Grinter Hall, Gainesville, Florida 32611 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SVETLOV, Stanislav** [RU/US]; 9710 SW 55 Road, Gainesville, Florida 32608 (US). **HAYES, Ronald, L.** [US/US]; 8032 SW 45th Lane, Gainesville, Florida 32608 (US). **WANG, Kevin K.W.** [US/US]; 9966 SW 19th Lane, Gainesville, Florida 32607 (US). **OLI, Monika** [DE/US]; 3635 NW 31st Terrace, Gainesville, Florida 32605 (US). **OTTENS, Andrew, K.** [US/US]; 4972 SW 91st Drive, Gainesville, Florida 32608 (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, 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

(88) Date of publication of the international search report:
24 January 2008

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.

(54) Title: BIOMAKERS OF LIVER INJURY

(57) Abstract: Novel, sensitive and specific markers for diagnostics and monitoring of liver injuries, including, but not limited to ischemic liver damage, are provided. This includes identification several enzymes of arginine/urea/nitric oxide cycle, sulfuration enzymes and spectrin breakdown related products, among others.



WO 2006/107846 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/12253

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C12Q 1/68(2006.01);G01N 33/53(2006.01)
C12Q 1/48(2006.01)

USPC: 435/7.1,15;530/350,388.8

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. : 435/7.1, 15; 530/350, 388.8

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
ICUBMB DATA BASE FOR ENZYME NOMENCLATURE, REGISTRY IN STN AND CASROLS

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.
Y	WO 03/085083 A2 (PHASE-1 MOLECULAR TOXICOLOGY, INC.) 16 October 2003 (16.10.2003), Entire Document. especially abstract figure, and Page 27, Lines 1-20.	1-24
Y, P	US 2005/0136489 A1 (TSENG et al.) 23 June 2005, (23.06.2005), entire document, especially abstract, Page 5, Column 2, Paragraph 0071, Claims 1, 5, 8-22.	1-24
Y	US 4,702,909 (VILLAREJOS et al.) 27 October 1987 (27.10.1987), entire Document, especially Column 2, Lines 60-66 and Abstract	1-10
Y	KIM, W. et al. Comparison of Proteome Between Hepatitis B Virus and Hepatitis C Virus Associated Hepatocellular Carcinoma. Clinical Cancer Research, 15 November 2003, Volume 9, Pages 5493-5500.	1-24
Y	JAIN, K.K. The Role of Protein-chip Technology in Molecular diagnostics. IVD Technology Archiv, July/August 2002, Pages 1-9. The entire article. and themeline	1-24



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	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search

18 September 2007 (18.09.2007)

Date of mailing of the international search report

16 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

Dr. Kailash C. Srivastava

Telephone No. 571-272-1000

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/12253

Continuation of B. FIELDS SEARCHED Item 3:

WEST: DWPI, EPAB, JPAB, PGPB, USOC, USPT

STN: BIOSIS, BIOTECHABS, BIOTECHNO, CABA, CEABA-VTB, CAPLUS, CEN, CIN, CONFSCI, DISSABS, EMBASE, ESBIODBASE, FRPATFULL, FROSTI, GBPATFULL, IFIPAT, LIFESCI, MEDICONF, MEDLINE, PCTFULL, RDISCLOSURE, SCISEARCH, USPATFULL, WPIDS

Search Strategy:

enzyme, argininosuccinate synthetase, synthetase, enzyme and argino\$, arginino succinate lyase, sulfuration sulfotransferase, squalene synthase, liver glycogen phosphorylase, carbamoyl phosphate synthase, alpha enolase 1, glucose regulated protein, GRP, spectrin breakdown and product, biomarker, biochip, liver disease, ailment, cancer, hepatitis, cirrhosis, injury, malfunction.

GOOGLE SEARCH: liver disease enzymes biochip biomarker