

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
29 January 2004 (29.01.2004)

PCT

(10) International Publication Number
WO 2004/010102 A3

- (51) International Patent Classification⁷: **C12Q 1/02**, C12N 1/00, 13/00, C12M 1/42
- (21) International Application Number: PCT/US2003/022537
- (22) International Filing Date: 18 July 2003 (18.07.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/379,749 20 July 2002 (20.07.2002) US
60/435,400 20 December 2002 (20.12.2002) US
60/469,572 9 May 2003 (09.05.2003) US
- (71) Applicant: **ACEA BIOSCIENCES, INC.** [US/US]; 4108 Sorrento Valley Boulevard, San Diego, CA 92121 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **WANG, Xiaobo** [CN/US]; Acea Biosciences, Inc., 4108 Sorrento Valley Boulevard, San Diego, CA 92121 (US). **XU, Xiao** [US/US]; Acea Biosciences, Inc., 4108 Sorrento Valley Boulevard, San Diego, CA 92121 (US).
- (74) Agents: **DHAND, Sanjeev** et al.; Foley & Lardner, P.O. Box 80278, San Diego, CA 92138-0278 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, 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, 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 (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (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: 22 July 2004
- 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: IMPEDANCE BASED APPARATUSES AND METHODS FOR ANALYZING CELLS AND PARTICLES

(57) Abstract: A device for monitoring the migration or invasion of a biological particle such as a cell is disclosed. The device includes an upper chamber adapted to receive and retain a cell sample, a lower chamber having at least two electrodes, and a bio-compatible porous membrane having a porosity sufficient to allow cells to migrate therethrough. The membrane is disposed in the device so as to separate the upper and lower chambers from one another. Migration of cells through the porous membrane permits contact between the migrating cells and one or more electrodes of the lower chamber. The contact provides a detectable change in impedance between or among the electrodes.

WO 2004/010102 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/22537

A. CLASSIFICATION OF SUBJECT MATTER																				
IPC(7) : C12Q 1/02; C12N 1/00, 13/00; C12M 1/42																				
US CL : 435/29, 173.9, 285.2, 288.5, 817																				
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. : 435/29, 173.9, 285.2, 288.5, 817																				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched none																				
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) BPUB, USPT, EPAB, JPAB, DWPI, HCAPLUS, SCISEARCH, BIOSIS, MEDLINE																				
C. DOCUMENTS CONSIDERED TO BE RELEVANT																				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.																		
A	WO 01/38873 A2 (BIOTRONIC TECHNOLOGIES, INC.) 31 May 2001 (31.05.2001).	1-19																		
A	RISHPON et al. An Amperometric Enzyme-Channeling Immunosensor. Biosens. Bioelectron. 1997, Vol. 12, No. 3, pages 195-204.	1-19																		
A	DUAN et al. Separation-Free Sandwich Enzyme Immunoassays Using Microporous Gold Electrodes and Self-Assembled Monolayer/Immobilized Capture Antibodies. Anal. Chem. 1994, Vol. 66, No. 9, pages 1369-1377.	1-19																		
A	XIAO et al. An In-Depth Analysis of Electric Cell-Substrate Impedance Sensing to Study the Attachment and Spreading of Mammalian Cells. Anal. Chem. 15 March 2002, Vol. 74, No. 6, pages 1333-1339.	1-19																		
A	WO 99/66329 A1 (CENES LIMITED) 23 December 1999(23.12.1999).	1-19																		
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.																				
<table border="0"> <tr> <td>* Special categories of cited documents:</td> <td>"T"</td> <td>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</td> </tr> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"X"</td> <td>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</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"Y"</td> <td>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</td> </tr> <tr> <td>"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)</td> <td>"&"</td> <td>document member of the same patent family</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td></td> <td></td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> <td></td> </tr> </table>			* Special categories of cited documents:	"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	"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent published on or after the international filing date	"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	"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)	"&"	document member of the same patent family	"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		
* Special categories of cited documents:	"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																		
"A" document defining the general state of the art which is not considered to be of particular relevance	"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																		
"E" earlier application or patent published on or after the international filing date	"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																		
"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)	"&"	document member of the same patent family																		
"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																				
Date of the actual completion of the international search		Date of mailing of the international search report																		
01 February 2004 (01.02.2004)		02 JUN 2004																		
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 <i>Susan Hanley</i> Telephone No. 703-308-1235																		