

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
24 October 2002 (24.10.2002)

PCT

(10) International Publication Number  
**WO 02/084285 A3**(51) International Patent Classification<sup>7</sup>: **C12Q 1/68**,  
G01N 33/543, B01J 19/00

(21) International Application Number: PCT/CA02/00543

(22) International Filing Date: 18 April 2002 (18.04.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/284,715 18 April 2001 (18.04.2001) US

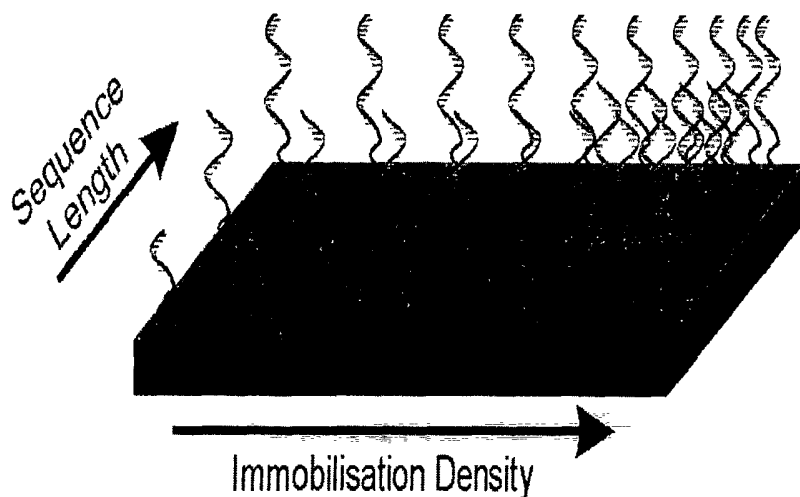
(71) Applicant and

(72) Inventor: **KRULL, Ulrich, J.** [CA/CA]; 1920 Sandown  
Road, Mississauga, Ontario L5M 2Z8 (CA).(74) Agent: **MCKAY-CAREY, Mary, Jane**; McKay-Carey &  
Company, 2590 Commerce Place, 10155-102 Street, Ed-  
monton, Alberta T5J 4G8 (CA).(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, 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, NO, NZ,  
OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
TN, TR, TT, TZ, UA, UG, UZ, 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, CH, CY, DE, DK, ES, FI, FR,  
GB, GR, IE, IT, LU, MC, NL, PT, SE, 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:  
7 August 2003For 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: GRADIENT RESOLVED HYBRIDISATION PLATFORM



(57) **Abstract:** The invention pro-  
vides improved methods and devices  
for the detection and identification  
in a sample of one or more target  
molecules which bind to probe  
molecules, particularly to nucleic  
acid probe molecules. The improved  
method is based on contacting the  
sample with a surface that is coated  
with one or more gradients of probe  
molecules, particularly nucleic  
acid or nucleic acid analog probe  
molecules that serve to bind target  
molecules in the sample, particularly  
nucleic acids having sequences  
that are complementary or partially  
complementary to one or more  
probe molecules. A probe gradient  
generated on the surface is formed

by the variation of a physical, structural or functional property of the probes on the surface. The gradients is generated, e.g., by varying density of probe molecules bound to the surface, by varying probe sequence length, by varying probe sequence, by varying probe sequence type, by varying the orientational structure of probes, and by varying the concentration of label associated with probes. Determination of the location, speed and/or extent of hybridisation of a nucleic acid on such a gradient surface is useful to identify target molecules bound to probes and/or to quantitatively measure the amount of the target in a sample. Hybridisation of target molecules to a gradient of nucleic acid probe can be examined as a function of time and/or hybridisation conditions (e.g., temperature, salt concentration, etc.) The method and devices of this invention employ gradient surfaces to bind to one or more target molecules, particularly nucleic acids (or target sequences) in a sample, detecting their presence in the sample and quantitating the amount of one or more of such targets in a sample.



WO 02/084285 A3

## INTERNATIONAL SEARCH REPORT

Internal application No  
PCT/CA 02/00543

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12Q1/68 G01N33/543 B01J19/00

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 7 B01J G01N C12Q

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 practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 47613 A (SYMYX TECHNOLOGIES INC) 29 October 1998 (1998-10-29) page 3, line 19 -page 5, line 7; claims 29,57,60 paragraph 'VIII! ---	1-84
X	WO 97 33169 A (DUNNINGTON DAMIEN J ;SMITHKLINE BEECHAM CORP (US); YAMASHITA DENNI) 12 September 1997 (1997-09-12) claims 1-5 ---	1-72
X	WO 98 15832 A (BIO MERIEUX ;GINOT FREDERIC (FR)) 16 April 1998 (1998-04-16) page 32, line 14 -page 34, line 5; claims 5,23 --- -/--	1,37-72

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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 document 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

13 May 2003

Date of mailing of the international search report

27/05/2003

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Cuendet, P

## INTERNATIONAL SEARCH REPORT

Intern:      Application No  
PCT/CA 02/00543

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WATTERSON ET AL.: "Effects of oligonucleotide immobilization density on selectivity of quantitative transduction of hybridization of immobilized DNA" LANGMUIR, vol. 16, 2000, pages 4984-4992, XP002240955 abstract page 4992, last paragraph -----</p>	73-83

## INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern

Application No

PCT/CA 02/00543

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9847613	A	29-10-1998	US 6045671 A	04-04-2000
			EP 0917494 A1	26-05-1999
			JP 2000503753 T	28-03-2000
			WO 9847613 A1	29-10-1998
WO 9733169	A	12-09-1997	EP 1025437 A1	09-08-2000
			JP 2000508624 T	11-07-2000
			WO 9733169 A1	12-09-1997
WO 9815832	A	16-04-1998	FR 2754344 A1	10-04-1998
			AT 233404 T	15-03-2003
			CA 2239499 A1	16-04-1998
			DE 69719312 D1	03-04-2003
			EP 0882233 A1	09-12-1998
			WO 9815832 A1	16-04-1998
			JP 2000502458 T	29-02-2000
			US 6218116 B1	17-04-2001