

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
6 May 2005 (06.05.2005)

PCT

(10) International Publication Number
WO 2005/040399 A3

(51) International Patent Classification⁷: **C12Q 1/68**, C12P
19/34, C07H 21/02, 21/04

(21) International Application Number:
PCT/US2004/035177

(22) International Filing Date: 21 October 2004 (21.10.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/513,426 21 October 2003 (21.10.2003) US
60/561,563 12 April 2004 (12.04.2004) US
60/561,721 12 April 2004 (12.04.2004) US

(71) Applicant (for all designated States except US): **ORION
GENOMICS LLC** [US/US]; 4041 Forest Park Avenue, St.
Louis, MO 63108 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **JEDDELOH,
Jeffrey, A.** [US/US]; 6067 Cardinal Creek, Oakville, MO
63129 (US). **LAKEY, Nathan, D.** [US/US]; 2040 Wilson
Ridge Lane, Chesterfield, MO 63005 (US).

(74) Agents: **HINSCH, Matthew, E.** et al.; Townsend and
Townsend and Crew LLP, Two Embarcadero Center, 8th
Floor, San Francisco, CA 94111 (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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, 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 (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, IT, LU, 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).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

Published:

— with international search report

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

21 July 2005

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: METHODS FOR QUANTITATIVE DETERMINATION OF METHYLATION DENSITY IN A DNA LOCUS

(57) Abstract: The present invention is a novel method of determining the average DNA methylation density of a locus of interest within a population of DNA fragments.



WO 2005/040399 A3

INTERNATIONAL SEARCH REPORT

International appli

PCT/US04/35177

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; C12P 19/34; C07H 21/02, 21/04
US CL : 435/6, 91.2; 536/23.1, 24.31, 24.33

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. : 435/6, 91.2; 536/23.1, 24.31, 24.33

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 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.
X	CHU et al. The use of real-time quantitative polymerase chain reaction to detect	1-7, 13, 14, 20-23, 26,
—	hypermethylation of the CpG islands in the promoter region flanking the GSTP1 gene to	27, 29-32, 38, 39, 40,
Y	diagnose prostate carcinoma. The Journal of Urology. April 2002, Vol. 167, pages 1865,	44, 46-48
	especially pages 1855-1856.	-----
		8-12, 15-19, 24-25, 28,
		33-37, 41-43, 45, 49,
		50
Y	FRAGA et al. DNA methylation: A profile of methods and applications. BioTechniques.	15-19, 24-25, 28, 45,
	2002, Vol. 33, No. 3, pages 632-649, especially pages 634, 640 and 641.	49 and 50
Y	US 5,405,760 A (RALEIGH et al) 11 April 1995 (11.04.1995), especially columns 4-6, 8	8-12, 33-37, 41-43
	and 21-22.	

☐ 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

"B" earlier application or patent 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

14 March 2005 (14.03.2005)

Date of mailing of the international search report

18 APR 2005

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

Carla Myers

Telephone No. 571-272-1600

INTERNATIONAL SEARCH REPORT

International application

PCT/US04/35177

Continuation of B. FIELDS SEARCHED Item 3:
DIALOG: MEDLINE, CA, BIOSIS, EMBASE; WEST: US, EP, JP, WO Patents
search terms: methylation, pattern, density, quantity, amount, quantitate