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(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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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[Continued on next page]

(54) Title: METHODS FOR CHARACTERIZING CELL PROXIMITY

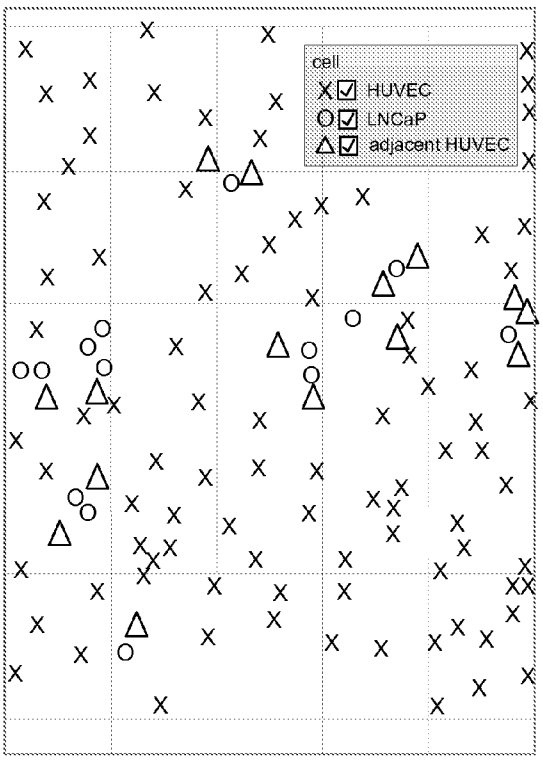

FIG. 5C

(57) Abstract: One aspect of the invention relates to a method of identifying cell adjacency in a coculture of cells. The method includes generating a first set of image data of the coculture of cells, the first set of image data comprising nuclear position data for each imaged cell; generating a second set of image data of at least a subset of the coculture of cells, the second set of image data comprising cell identifier data associated with a first cell type; generating a third set of image data of at least a subset of the coculture of cells, the third set of image data comprising cell identifier data associated with a second cell type; and identifying a group of cells in response to the nuclear position data, wherein each cell having the first cell type in the group is adjacent another cell in the group having the second cell type.

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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/574 G01N33/50 G01N33/68

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

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, BIOSIS, EMBASE, FSTA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93/25713 A (ARCH DEV CORP [US]) 23 December 1993 (1993-12-23) page 6 - page 7; claims 1-31	1-9
X	US 5 264 343 A (KRYSTOSEK ALPHONSE [US] ET AL) 23 November 1993 (1993-11-23) columns 2-4; claims 1-19	1-9
X	EP 1 640 717 A (INST NAT SANTE RECH MED [FR]) 29 March 2006 (2006-03-29) the whole document	1-9
X	WO 98/03873 A (CORNELL RES FOUNDATION INC [US]) 29 January 1998 (1998-01-29) claims 21-37,61-104 page 3, line 30 - page 13, line 25 page 26, line 3 - page 30, line 22	1-9

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[X] Further documents are listed in the continuation of Box C.

[X] 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 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
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 October 2008	12/01/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Fax: (+31–70) 340–3016	Boiangiu, Clara

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/070993

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/33229 A (UNIV AMSTERDAM [NL]; DRIEL ROELAND VAN [NL]) 10 May 2001 (2001-05-10) claims 1-11 page 4, line 29 - page 10, line 20	1-9
X	MEIJER GERRIT A ET AL: "Predicting the risk of metachronous colorectal cancer in patients with rectosigmoid adenomas using quantitative pathological features. A case-control study" JOURNAL OF PATHOLOGY, CHICHESTER, SUSSEX, GB, vol. 184, no. 1, 1 January 1998 (1998-01-01), pages 63-70, XP002417347 ISSN: 0022-3417 the whole document	1-9
X	US 2003/092047 A1 (LAMORTE VICKIE J [US] ET AL) 15 May 2003 (2003-05-15) paragraphs [0015] - [0034]; claims 1-33	1-9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/070993

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-9

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-9

   Method of identifying, in a coculture of cells of differing cell types, cells of a first cell type in contact with cells of a second cell type.

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2. claim: 10

   Method of identifying a cancer epithelial cell.

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3. claims: 11-14

   Method of identifying subpopulations of cells within a population of cells

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4. claims: 15-18

   Method of identifying cell adjacency in a coculture of cells

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/070993

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9325713 A	23-12-1993	US 5487970 A	30-01-1996
US 5264343 A	23-11-1993	NONE	
EP 1640717 A	29-03-2006	WO 2006034881 A1	06-04-2006
WO 9803873 A	29-01-1998	AT 319089 T	15-03-2006
		AU 733544 B2	17-05-2001
		AU 3797697 A	10-02-1998
		BR 9710487 A	17-08-1999
		CA 2261018 A1	29-01-1998
		CN 1244921 A	16-02-2000
		CN 1673744 A	28-09-2005
		DE 69735368 T2	03-08-2006
		EA 4634 B1	24-06-2004
		EP 0956506 A1	17-11-1999
		ES 2255723 T3	01-07-2006
		HK 1025631 A1	20-05-2005
		JP 2002513378 T	08-05-2002
		NZ 333683 A	28-09-2001
		NZ 524036 A	24-12-2004
		PT 956506 T	31-05-2006
WO 0133229 A	10-05-2001	AU 2156501 A	14-05-2001
		CA 2389364 A1	10-05-2001
		HU 0203269 A2	28-02-2003
		JP 2003513282 T	08-04-2003
		NZ 519065 A	26-03-2004
		ZA 200203401 A	29-04-2003
US 2003092047 A1	15-05-2003	NONE	