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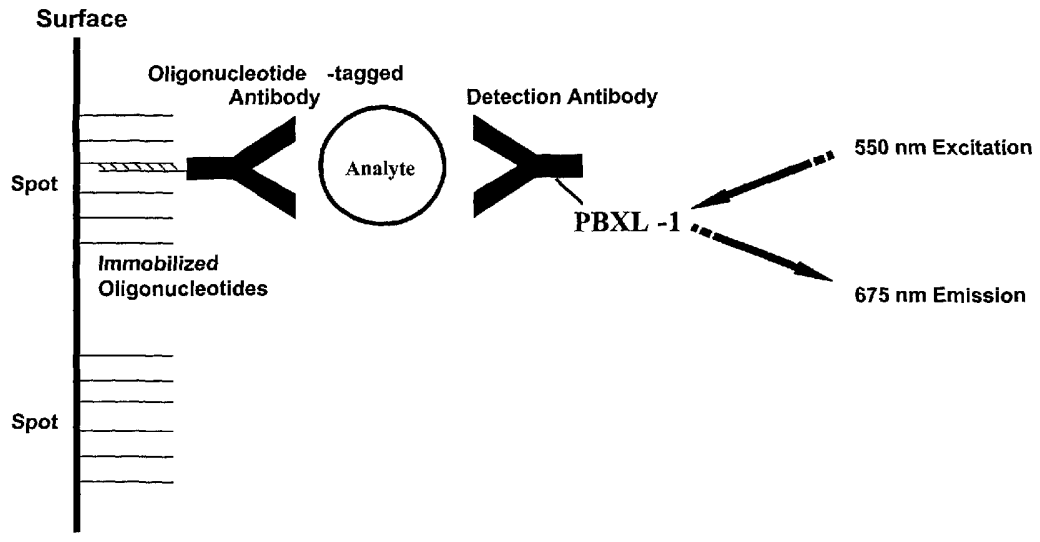
[Continued on next page]

(54) Title: OLIGONUCLEOTIDE PAIRS FOR MULTIPLEXED BINDING ASSAYS



(57) Abstract: The invention is an oligonucleotide-based assay system and kit useful for sorting, detecting, and identifying analytes. The system utilizes complementary oligonucleotide pairs in which one oligonucleotide of each pair is immobilized to a solid substrate and the other oligonucleotide has an analyte binding agent attached to it. The different oligonucleotide pairs hybridize at substantially the same rate, have substantially the same Tm, have nucleotide sequences designed to minimize cross-hybridization between different pairs, and hybridize together relatively rapidly at ambient temperatures without detectable cross-hybridization.

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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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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.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/011885

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

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 C12Q 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, BIOSIS, EMBASE, WPI Data, PAJ, Sequence Search, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GERRY N P ET AL: "Universal DNA microarray method for multiplex detection of low abundance point mutations" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 292, no. 2, 17 September 1999 (1999-09-17), pages 251-262, XP004462280 ISSN: 0022-2836 page 252, column 2, paragraph 2 - page 253, column 2	1-24
X	WO 02/16649 A (ILLUMINA INC) 28 February 2002 (2002-02-28) page 13, line 10 - page 14, line 33	1-24

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

[X] 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	Date of mailing of the international search report
4 October 2004	05.01.2005

Name and mailing address of the ISA	Authorized officer
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Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/US2004/011885

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 96/06948 A (BECKMAN INSTRUMENTS INC) 7 March 1996 (1996-03-07) page 19, line 19 - page 21, line 9; claim 25	24
X	BEN-DOR A ET AL: "UNIVERSAL DNA TAG SYSTEMS: A COMBINATORIAL DESIGN SCHEME" JOURNAL OF COMPUTATIONAL BIOLOGY, MARY ANN LIEBERT INC, US, vol. 7, no. 3/4, 2000, pages 503-519, XP002948494 ISSN: 1066-5277 the whole document	1-24
X	SHOEMAKER D D ET AL: "QUANTITATIVE PHENOTYPIC ANALYSIS OF YEAST DELETION MUTANTS USING A HIGHLY PARALLEL MOLECULAR BAR-CODING STRATEGY" NATURE GENETICS, NEW YORK, NY, US, vol. 14, no. 4, 1 December 1996 (1996-12-01), pages 450-456, XP002043431 ISSN: 1061-4036 page 451, column 2, paragraph 2 - page 452, column 2, paragraph 1 page 455, column 1, paragraph 2	1-24

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/011885

Box 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.: 34,35
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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 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 all searchable claims.

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

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers 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.:
1-24 (all in part)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 34,35

The assay system of claim 34 and the collection of oligonucleotides of claim 35 are defined in reach-through terms, i.e. with respect to oligonucleotides generated by the method of claim 26. Said claims are unclear as they are not defined in terms of technical features of the clamed products per se, and the method does not impart any tangible features on the products which would sufficiently characterize them. Therefore no meaningful search can be carried out for said claims across their entire scope. In view of the fact that the only oligonucleotides identified in the application as having been identified by the method of claim 26 are those defined by SEQ ID Nos 1-188, and the subject-matter of claims 34 and 35 insofar as it relates to said oligonucleotides is encompassed by the other claims, claims 34 and 35 have not been searched and are not included in the grouping of inventions.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

Invention 1. Claims: 1-24 (all in part)

A set of oligonucleotides comprising a nucleic acid having a sequence of 12 or more consecutive oligonucleotides from SEQ ID NO.11 or 12; a set of one or more pairs of complementary oligonucleotides, comprising a pair having a nucleic acid sequence of 12 or more consecutive nucleotides from SEQ ID NOs 11 and 12; an assay system comprising said oligonucleotide pair; a method of detecting an analyte using said oligonucleotide pair.

Inventions 2-15. Claims: 1-24 (all in part)

A set of oligonucleotides comprising a nucleic acid having a sequence of 12 or more consecutive oligonucleotides from respectively SEQ ID NOs 57, 59, 65, 67, 69, 75, 77, 93, 95, 117, 123, 129, 163 and 187, or the complement thereof; a set of one or more pairs of complementary oligonucleotides, comprising a pair having a nucleic acid sequence of 12 or more consecutive nucleotides from respectively SEQ ID NOs 57, 59, 65, 67, 69, 75, 77, 93, 95, 117, 123, 129, 163 and 187, and the complement thereof; an assay system comprising said oligonucleotide pair; a method of detecting an analyte using said oligonucleotide pair.

Inventions 16-94. Claims: 1-8,10-19,22-24 (all in part)

A set of oligonucleotides comprising a nucleic acid having a sequence of 12 or more consecutive oligonucleotides from respectively SEQ ID NOs 1-10, 12-56, 61-64, 71-74, 79-92, 97-116, 119-122, 125-128, 131-162 and 165-186, or the complement thereof; a set of one or more pairs of complementary oligonucleotides, comprising a pair having a nucleic acid sequence of 12 or more consecutive nucleotides from respectively SEQ ID NOs 1-10, 12-56, 61-64, 71-74, 79-92, 97-116, 119-122, 125-128, 131-162 and 165-186, and the complement thereof; a method of detecting an analyte using said oligonucleotide pair.

Invention 95. Claims 25-33 (in full)

A method for generating a collection of unrelated nucleic acid sequences.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2004/011885

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0216649 A	28-02-2002	AU 8839301 A	04-03-2002
		WO 0216649 A2	28-02-2002
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WO 9606948 A	07-03-1996	US 5648213 A	15-07-1997
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		EP 0779934 A1	25-06-1997
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		WO 9606948 A1	07-03-1996