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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.

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(54) Title: DETECTION OF NUCLEIC ACIDS

(57) Abstract: Disclosed are compositions, methods, and kits useful for detection of the presence and/or quantity of one or more chromosomes from single cells, groups of cells, or subcellular compartments. Provided is a lysis buffer for the preparation of substantially accessible nucleic acid molecules from a single cell. Also provided are moderately-repeated highly-conserved nucleic acid sequences, and oligonucleotide primer and probe molecules which hybridize specifically thereto. Methods for the detection of the presence or quantity of one or more chromosomes from a single cell are included, as are methods for the assessment of the reliability of the results of the methods of the invention. Kits for the convenient practice of the invention are also included.

INTERNATIONAL SEARCH REPORT

Inter .onal application No.
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A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/02, 21/04; C12Q 1/68; C12P 19/34
US CL : 536/22.1, 23.1, 24.3, 24.31, 24.33; 435/6, 91.2

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. : 536/22.1, 23.1, 24.3, 24.31, 24.33; 435/6, 91.2

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)

EAST, CAPLUS, MEDLINE, BIOSIS
search terms: molecular, beacon, label, situ, vivo, vitro, repeat, sequence

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,854,033 A (LIZARDI) 29 December 1998, see entire document.	1-24
Y	US 5,876,930 A (LIVAK et al) 02 March 1999, see entire document.	1-24
Y, P	US 5,989,873 A (VINAYAGAMOORTHY et al) 23 November 1999, see entire document.	1-24
Y, P	US 5,994,528 A (VINAYAGMOORTHY et al) 30 November 1999, see entire document.	1-24
Y	MAHAIRAS et al. Sequence tagged connectors: A sequence approach to mapping and scanning the human genome. Proc. Natl. Acad. Sci. August 1999. Vol. 96. pages 9739-9744, see entire document.	1-24

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	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 document 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		

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ARSDELL et al. Human genes for U2 small nuclear RNA are tandemly repeated. Mol. Cell. Biol. March 1984. Vol. 4, No. 3, pages 492-499, see entire document.	1-24
Y	WESTIN et al. Clustered genes for human U2 RNA. Proc. Natl. Acad. Sci. June 1984. Vol. 81. pages 3811-3815, see entire document.	1-24
Y	ARNEMANN et al. Cloning and sequence analysis of a human Y-chromosome-derived testicular DNA, TSPY[1]. Genomics. 1991. Vol. 11. pages 108-114, see entire document.	1-24

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international 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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

Please See Extra 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

Remark on Protest

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

☐ No protest accompanied the payment of additional search fees.

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-24, drawn to nucleic acid sequences.
Group II, claim(s) 25-60, 103 and 104, drawn to methods of detection of nucleic acids.
Group III, claim(s) 61-73, drawn to methods of sample preparation.
Group IV, claim(s) 74-96, drawn to lysis buffers.
Group V, claim(s) 97-102, drawn to methods of preparing gene deleted DNA.
Group VI, claim(s) 105-109, drawn to enhancers.

The inventions listed as Groups I-VI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: First, there is no claimed feature which links the claims together. That is, the method of detection claim of Group II in it's broadest form does not require the nucleic acid Group I, the method of sample preparation of Group III does not require the lysis buffer of Group IV, and none of the methods has a correlative special technical feature. Second, there is no apparent special technical feature with regard to the product components.