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(54) Title: METHODS AND APPARATUS FOR SCREENING AND DETECTING MULTIPLE GENETIC MUTATIONS

(57) Abstract: An assay system and methods are described where patient samples containing genomic DNA are analyzed for the presence of known genetic polymorphisms using a universal reporter strategy. In a preferred embodiment, the amplified DNA is localized at test sites in an array of sites on a microchip followed by a series of hybridization reactions that screen for the presence of a single mutation from among a number of mutations, and allow the identification of specific mutations. In addition to universal reporters, the assay may use blockers and discriminators for screening and identification of known polymorphisms.

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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/23420

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C12Q 1/68  
US CL : 435/6

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, 91.1, 91.2, 183; 436/94; 535/23.1, 24.3, 24.33, 25.3

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 --- Y	US 4,988,617 A (LANDEGREN et al) 29 January 1991, see entire document, especially columns 2, 3, and 13-22, and Figure 1).	1-5, 16, 17, 19, 20, 24, 26, 27, 34,-36, and 40 ----- 18, 25, 28, and 31
X --- Y	US 5,494,810 A (BARANY et al) 27 February, 1996, see entire document, especially Figure 2 and 73-76.	1-5, 9, 10, 15-17, 19, 20, 24, 26, 27, 31, 34-36, 39, and 40 ----- 11-14, 18, 23, 25, 28, and 32
X, P	6,468,742 B2 (NERENBERG et al) 22 October 2002, see entire document, especially sec columns 5-9 and 27-38.	1-40

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	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

19 March 2005 (19.03.2005)

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/23420

## 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.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim 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.  Claim 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 Continuation 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.: 1-40
- Remark on Protest  The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

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

Group I, claims 1-40, drawn to a method for detecting members of a set of polymorphism.

Group II, claims 41-44, drawn to a system for detecting members of a set of polymorphism (claim 41) and a kit for use in a process of detecting members of a set of polymorphism (claims 42 and 44).

The inventions listed as Groups I and II do not relate to a single general 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:

Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because they lack the same or corresponding special technical features. For example, the method recited in claim 1 is known in the art (see US 4,988,617 A, columns 2, 3, and 13-22, and Figure 1).

**Continuation of B. FIELDS SEARCHED Item 3:**

STN and EAST

Search Terms: polymorphism, hybridize or hybridization, blocker, first probe, second probe, and mutation