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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.

(54) Title: METHODS AND COMPOSITIONS FOR GENOTYPING

(57) Abstract: The invention provides compositions and methods for performing primer extension reactions, including employment of amplification primers having 5' tags to incorporate into amplicons variant nucleotides of interest from target nucleic acids at known ratios, with or without sequences surrounding the variant nucleotides of interest. The invention provides identifying the variant nucleotides generated from the target nucleic acid and generated from the 5' tags, comparing the results, evaluating the efficiency of the primer extension reactions, and monitoring the efficacy of such reactions. The invention accounts for DNA sequence and experimental variables that may affect efficiency of incorporation of nucleotides, and provides a reference point for the interpretation of polymorphisms. The invention also provides methods of breeding scrapie-resistant sheep populations.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/24198

A. CLASSIFICATION OF SUBJECT MATTER

IPC:

USPC:

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, 23.1, 91.2; 536/23.1, 24.33, 26.12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

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	US 6,004,744 (GOELET et al.) 21 December 1999 (21, 12, 1999), the abstract and column 5, lines 24-40, column 16, lines 17-18 and column 19, lines 35-37.	48 and 49
Y	US 6,004,744 (GOELET et al.) 21 December 1999 (21, 12, 1999), the abstract, column 5, lines 45-55, column 13, lines 50-53, column 14, lines 40-46, column 26, lines 35-36.	1-47, 50, 53-54
Y	US 6,287,778, (HUNG et al.) 11 September 2001 (11, 09, 2001), the abstract.	19-21 and 41-43

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

11 February 2006 (11.02.2006)

Date of mailing of the international search report

09 MAR 2006

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/24198

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.: 1-50,53 and 54

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, claim(s) 1-50, 53 and 54, drawn to a primer extension reaction performed with a target having at least one variant nucleotide flanked by an invariant nucleotide using a primer with a 5' tag, which is incapable of hybridizing with the target under extension reaction conditions, and containing the at least one variant nucleotide with also utilizing a second primer, which results in the determination of the identity of the at least one variant nucleotide from the target and drawn also to a primer as described above.

Group II, claim(s) 51 and 52, drawn to a method for monitoring the efficiency of incorporation of chain termination into primers in a primer extension reaction utilizing amplicons comprising sequence of known ratio.

Group III, claim(s) 55-59, drawn to a method of screening animals for susceptibility to a disease or disorder via determining the identity of polymorphic nucleotides at three or more alleles at a locus.

Group IV, claim(s) 60-61, drawn to a method of breeding scrapie-resistant sheep via determining the identity of two or more alleles at the PrP locus employing the identities of polymorphic nucleotides to determine whether male and female sheep possess two or more alleles that are not associated with susceptibility to scrapie and breeding male and female sheep that possess two or more alleles that are not associated with susceptibility to scrapie.

The inventions listed as Groups I-IV 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: The special technical features of each of the groups I-IV are described above which are not the same. For Group I, the special technical feature is to perform a primer extension reaction. For Group II, the special technical feature is for monitoring the efficiency of incorporation of chain termination into primers in a primer extension reaction utilizing amplicons comprising sequence of known ratio. For Group III, the special technical feature is for screening animals for susceptibility to a disease or disorder via determining the identity of polymorphic nucleotides at three or more alleles at a locus. For Group IV, the special technical feature is for breeding scrapie-resistant sheep via determining the identity of two or more alleles at the PrP locus employing the identities of polymorphic nucleotides to determine whether male and female sheep possess two or more alleles that are not associated with susceptibility to scrapie and breeding male and female sheep that possess two or more alleles that are not associated with susceptibility to scrapie.

Continuation of B. FIELDS SEARCHED Item 3:

WEST AND STN: medline, caplus, biosis, embase
search terms: tag, amplification, array, incapable of complementary