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- (88) Date of publication of the international search report:
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(54) Title: USE OF NUCLEOTIDE ANALOGS IN THE ANALYSIS OF OLIGONUCLEOTIDE MIXTURES AND IN HIGHLY MULTIPLEXED NUCLEIC ACID SEQUENCING

(57) Abstract: Methods and kits that use nucleotide analogs to confer increased accuracy and improved resolution in the analysis and sequencing of oligonucleotide mixtures are provided.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/19249

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

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)

IPC 7 C12Q

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, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 14362 A (BRAX GENOMICS LTD ; THOMPSON ANDREW HUGIN (GB); SCHMIDT GUENTER (GB) 25 March 1999 (1999-03-25) page 21, paragraph 2	1-49
A	US 5 691 141 A (KOESTER HUBERT) 25 November 1997 (1997-11-25) the whole document	1-49
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Further documents are listed in the continuation of box C.



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

25 October 2002

Date of mailing of the international search report

28. 01. 2003

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/19249

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GROSS J ET AL: "Matrix-assisted laser desorption/ionisation-mass spectrometry applied to biological macromolecules" TRAC, TRENDS IN ANALYTICAL CHEMISTRY, ANALYTICAL CHEMISTRY. CAMBRIDGE, GB, vol. 17, no. 8-9, 9 August 1998 (1998-08-09), pages 470-484, XP004146608 ISSN: 0165-9936 Section 6	1-49
A	--- KOESTER H ET AL: "A STRATEGY FOR RAPID AND EFFICIENT DNA SEQUENCING BY MASS SPECTROMETRY" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 14, 1 September 1996 (1996-09-01), pages 1123-1128, XP000197743 ISSN: 1087-0156 the whole document	1-49
A	--- JACUTIN SWANEE ET AL: "Test of the potential of a dATP surrogate for sequencing via MALDI-MS." NUCLEIC ACIDS RESEARCH, vol. 25, no. 24, 15 December 1997 (1997-12-15), pages 5072-5076, XP002218241 ISSN: 0305-1048 the whole document -----	1-49

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/19249

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 1-49 (all partially)
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 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:

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.:
1-49 (all partially)

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

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

1. Claims: 1-49 (all partially)

Methods and kits for mass spectrometric nucleic acid analysis based on the use of "mass-matched" nucleotide analogues, i.e. wherein each analogue is of identical mass to each of the other analogues. As a consequence, the mass of any single stranded polynucleotide, or extension product, of such analogues will only be dependent on its length, and not on its particular sequence.

2. Claims: 1-49 (all partially)

Methods and kits for mass spectrometric nucleic acid analysis based on the use of "pair-matched" nucleotide analogues, i.e. wherein both Watson-Crick pairs of nucleotides are of identical mass to each other. As a consequence, the mass of any double stranded polynucleotide of such analogues will only be dependent on its length, and not on its particular sequence.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-49 (all partially)

In view of the large number and also the wording of the claims presently on file, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present application fails to comply with the clarity and conciseness requirements of PCT Article 6 (see also PCT Rule 6.1(a)) to such an extent that a meaningful search on the basis of the claims is impossible.

The current set of claims for search comprises a total of 21 independent claims, each one listing a complete list of features or method steps. The scope of most of these claims seems to be, at least, partially overlapping, if not completely coincident or contained in one another. In other words, the claim structure is obscure, and makes extremely difficult to establish the actual distinguishing features between the different methods or products claimed.

Consequently, the search has been carried out for those parts of the application which do appear to be clear and concise, namely the methods explained in the examples 1 and 2, and, based on those examples, a generalisation of their essential features as detailed in the description (especially the following passages: page 4, line 28, to page 9, line 14; page 13, line 10, to page 15, line 22; page 26, line 3, to page 31, line 30): methods and kits for nucleic acid analysis by mass spectrometry based on the use of "mass-matched nucleotides" and "pair-matched nucleotides" as defined in page 14, 2 and 3 respectively.

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 IPEA 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.

The applicant's attention is drawn to the fact that claims, or parts of 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/19249

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9914362	A	25-03-1999	AU 746443 B2	02-05-2002
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			EP 1015632 A1	05-07-2000
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