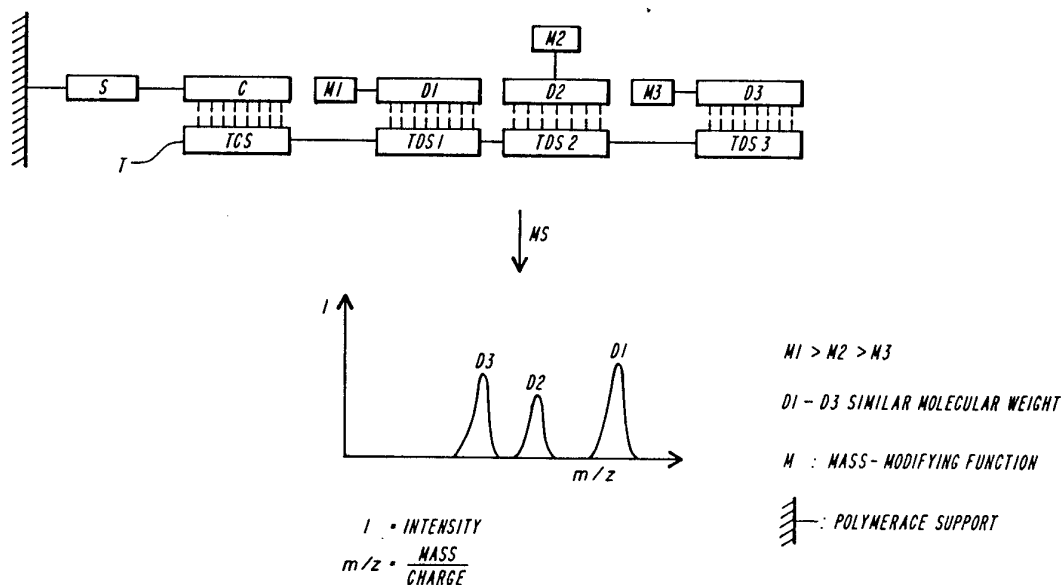




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(54) Title: DNA DIAGNOSTICS BASED ON MASS SPECTROMETRY



(57) Abstract

The invention provides fast and highly accurate mass spectrometer based processes for detecting a particular nucleic acid sequence in a biological sample. Depending on the sequence to be detected, the processes can be used, for example, to diagnose a genetic disease or chromosomal abnormality; a predisposition to a disease or condition, infection by a pathogenic organism, or for determining identity or heredity.

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INTERNATIONAL SEARCH REPORT

International Application No

PC1/US 96/03651

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12Q1/68 C12Q1/70

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 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO,A,94 16101 (KOESTER HUBERT) 21 July 1994 cited in the application see the whole document	1-49
Y	WO,A,93 20236 (APPLIED BIOSYSTEMS) 14 October 1993 see the whole document	1-32, 48, 49
Y	JP,A,06 294 796 (HITACHI LTD) 21 October 1994 see figure 2 & PATENT ABSTRACTS OF JAPAN vol. 94, no. 10 see abstract	1-32
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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- * "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

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* "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

22 October 1996

Date of mailing of the international search report

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Molina Galan, E

INTERNATIONAL SEARCH REPORT

International Application No

PCI/US 96/03651

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SCIENCE, vol. 242, October 1988, LANCASTER, PA US, pages 229-237, XP002016560 LANDEGREN ET AL.: "DNA diagnostics-Molecular techniques and automation" see the whole document ---	1-49
Y	ANALYTICAL BIOCHEMISTRY, vol. 169, 1988, NEW YORK US, page 1-25 XP002016561 MATTHEWS ET AL.: "Analytical strategies for the use of DNA probes" see the whole document ---	1-18, 33-45,48
Y	RAPID COMMUNICATIONS IN MASS SPECTROMETRY, vol. 8, 1994, page 183-186 XP000608266 TANG ET AL.: "MALDI of restriction enzyme digested DNA" cited in the application see the whole document ---	33-45
Y	EP,A,0 412 883 (BERTIN & CIE) 13 February 1991 see claims ---	46,47
Y	WO,A,92 15712 (MOLECULAR TOOL) 17 September 1992 see example 1 ---	46,47
Y	WO,A,91 13075 (ORION) 5 September 1991 see figure 1; example 1 ---	46,47
Y	WO,A,91 15600 (HOPE CITY) 17 October 1991 see the whole document ---	48
A	INTERNATIONAL JOURNAL OF MASS SPECTROMETRY AND ION PROCESSES, vol. 131, no. 1/03, 24 February 1994, pages 335-344, XP000446273 WILLIAMS P: "TIME OF FLIGHT MASS SPECTROMETRY OF DNA LASER-ABLATED FROM FROZEN AQUEOUS SOLUTIONS: APPLICATIONS TO THE HUMAN GENOME PROJECT" see page 341, right-hand column, paragraph 2 - page 342, left-hand column, paragraph 1 --- -/--	1-49

INTERNATIONAL SEARCH REPORT

International Application No

PC1/US 96/03651

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	NUCLEIC ACIDS RESEARCH, vol. 23, no. 16, August 1995, OXFORD GB, pages 3126-3131, XP002016562 TANG ET AL.: "MALDI-MS of immobilised duplex DNA probes" cited in the application see the whole document -----	1-49

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/03651

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.:
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:

1. claims 1-32
2. claims 33-45
3. claims 46-47
4. claims 48-49

* See continuation-sheet PCT/ISA/210 *

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.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 96/ 03651

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Method of detecting a target nucleic acid by determining with mass spectrometry the presence of a detector probe which has hybridised to the (optionally amplified) target nucleic acid sequence.
2. Method of detecting a target nucleic acid by analysing with mass spectrometry the fragments resulting from specific digestion of the target.
3. Method of detecting a target nucleic acid by determining with mass spectrometry the single nucleotide elongation of a target specific primer.
4. Method of detecting a target nucleic acid by analysing with mass spectrometry the target dependent ligation or restriction of a target specific probe.

Taking into consideration the balance between the necessary search effort and the levying of additional fees, the International Searching Authority has decided to search all the inventions present in the application.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PC1/US 96/03651

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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