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(54) Title: MASSIVE PARALLEL METHOD FOR DECODING DNA AND RNA

(57) Abstract: This invention provides methods for attaching a nucleic acid to a solid surface and for sequencing nucleic acid by detecting the identity of each nucleotide analogue after the nucleotide analogue is incorporated into a growing strand of DNA in a polymerase reaction. The invention also provides nucleotide analogues which comprise unique labels attached to the nucleotide analogue through a cleavable linker, and a cleavable chemical group to cap the -OH group at the 3'-position of the deoxyribose.



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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US01/31243

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 19/00, 21/00, 21/02, 21/04; C12Q 1/68; C12P 19/34  
US CL : 435/6, 91.1, 91.2; 536/22.1, 23.1, 24.3, 25.1, 25.3  
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; 536/22.1, 23.1, 24.3, 25.1, 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)

STN  
search terms: nucleic acids, sequencing, PCR, label, terminator, donor, acceptor, solid support, cleavage

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LEE et al. New Energy Transfer Dyes for DNA Sequencing. Nucleic Acids Research. 1997. Vol. 25, No. 14, pages 2816-2822, see entire document.	1-28 and 37-53
Y	ROSENBLUM et al. New Dye-Labeled Terminators for Improved DNA Sequencing Patterns. Nucleic Acids Research. 1997. Vol. 25, No. 22, pages 4500-4504, see entire document.	1-28 and 37-53

☐ 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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13 MARCH 2002

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13 MAY 2002

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US01/31243**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.:  
1-28 and 37-53

**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.  
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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) 1-28, 37-53, drawn to a method of sequencing.

Group II, claim(s) 29-36, drawn to a method of attaching a nucleic acid to a solid support.

Group III, claim(s) 54-60, drawn to a parallel mass spectrometry system.

The inventions listed as Groups I-III 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: they are directed to different methods. The methods of Groups II and III do not use the special technical feature.