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(54) Title: METHODS FOR REPAIRING DEGRADED DNA

(57) Abstract: The present invention provides methods and kits for repair of degraded DNA which may then be used as a template for efficient amplification by a number of different amplification reactions. The method relies upon a series of enzymatic activities provided by DNA repair enzymes.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/24799

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C12Q 1/68(2007.01)

USPC: 435/6,91.1,91.2

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

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)
Medline, STN, Science Direct

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|---------------------------|
| Y | US 2005/0026147 A1 (WALKER et al.) 03 February 2005 (03.02.2005), whole document. | 1, 2, 8, 12, 14 and 16-21 |
| Y | PROMEGA. T4 Polynucleotide Kinase. Promega Technical Bulletin No. 519, July 2002, whole document. | 1, 2, 8, 12, 14 and 16-21 |
| Y | WALLACE et al. The enigma of endonuclease VII. DNA Repair. 2003, Vol. 2, pages 441-453, whole document. | 8 and 14 |
| Y | LIN et al. Oxidative Damage To Mitochondrial Dna In Atrial Muscle Of Patients with Atrial Fibrillation. Free Radical Biology and Medicine. 2003, Vol. 35, No. 10, pages 1310-1318, whole document. | 20 |
| Y | NEW ENGLAND. Biolabs Inc. 1998/1999 CATALOG, p. 79, whole document. | 16 |

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 | | |
| "P" document published prior to the international filing date but later than the priority date claimed | "&" | document member of the same patent family |

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INTERNATIONAL SEARCH REPORT

International application No.

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BOX III. 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) 1-21, drawn to a method for repairing degraded DNA.

Group II, claim(s) 22-29, drawn to a method for amplification of degraded DNA.

Group III, claim(s) 30-32, drawn to a kit.

1. This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below

The inventions listed as Groups I-III 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 method of claim 1 is not joined to the method of at least claim 22 and the kit of at least claim 30. The method requires contacting degraded DNA with an enzyme combination comprising an endonuclease, a DNA N-glycosylase, AP lyase, polymerase, 3'diesterase, polynucleotide kinase and a DNA ligase. This not a special technical feature which joins the claimed inventions because Walker et al. (US 2005/0026147 A1) and Promega (July 2002) teach this method using this enzyme combination. The method of at least claim 1 is not limited in scope so as to require the method of at least claim 22 and the kit of at least claim 30 and so therefore are not joined by special technical feature.

This application contains claims directed to the following patentably distinct species of the claimed invention:

There are several different species elections which are required.

If applicant elected the invention of Group I, applicant is required to elect from the following patentably distinct species of modifications.

Applicant must elect a single modification for initial search and examination

- a. covalent modification
- b. deamination
 - c. intra-strand cross linkage
 - d. inter-strand cross linkage
 - e. nick
 - f. abasic site

Applicant is required to elect from the following patentably distinct species of endonucleases for initial search and examination.

- a. endonuclease VIII
- b. endonuclease IV
- c. ~~endonuclease IV and endonuclease VIII~~

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Applicant is required to elect from the following patentably distinct species of enzymes which provide for DNA N-glycosylase activity for initial search and examination.

- a. endonuclease VIII
- b. uracil DNA glycosylase
- c. 8-oxoguanine DNA glycosylase

Applicant is required to elect from the following patentably distinct species of enzymes which provide for AP lyase activity for initial search and examination.

- a. endonuclease VIII
- b. 8-oxoguanine DNA glycosylase

Applicant is required to elect from the following patentably distinct species of degraded base for initial search and examination.

Claim 21 recites 12 different bases, choose one.

The species are distinct, each from the other, because their structures and modes of action are different. They would also differ in their reactivity and the starting materials from which they are made. Moreover, the above species can be separately classified. Consequently, the species have different issues regarding patentability and represent patentably distinct subject matter. Therefore, this does create an undue search burden, and election for examination purposes as indicated is proper.

If applicant elected the invention of Group II, applicant is required to elect from the following patentably distinct species of amplification types.

Applicant must elect a single amplification type for initial search and examination

- a. polymerase chain reaction
- b. helicase dependent amplification
- c. LATE PCR asymmetric amplification
- d. single primer isothermal linear amplification
- e. multiple displacement amplification

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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 No. III Observations where unity of invention is lacking (Continuation of item 3 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 additional fees, this Authority did not invite payment of any additional fees.
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.: 1,2,8,12,14 and 16-21

- Remark on Protest**
- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
 - The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
 - No protest accompanied the payment of additional search fees.