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Declaration under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

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(54) Title: RIBONUCLEASES AND METHODS OF MAKING THEM RECOMBINANTLY

(57) Abstract: Methods for recombinantly producing new RNases, as well as previously-known RNases, are disclosed. The new RNases are active against human carcinoma cells.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/14844

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: C12N 15/55(2006.01),9/22(2006.01)

USPC: 435/199,320.1
 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. : 435/199, 320.1

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)
 Computer search - CAPLUS. Sequence search.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,239,257 B1 (ARDEL) 29 May 2001.	9
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Y		1-3, 53-54
Y	LEHNINGER, A.L. Biochemistry. New York: Worth Publishers, Inc. 1975, Second Edition, page 962.	1-3, 9 and 53-54
Y	STUDIER, et al. Use Of T7 RNA Polymerase To Direct Expression Of Cloned Genes. Met. Enzymol. 1990, Vol.185, pages 60-89.	1-3, 9 and 53-54
Y	HUANG, H-C., et al. The Rana catesbeiana rcr Gene Encoding a cytotoxic Ribonuclease. J. Biol. Chem. 13 March 1998, Vol.273, No. 11, pages 6395-6401.	1-3, 9 and 53-54
Y	GUERRERO, S.A., et al. His-Tagged Tryparedoxin Peroxidase Of Trypanosome curzi As A Tool For Drug Screening. Appl. Microbiol. Biotechnol. 2000, Vol 53, pages 410-414.	1-3, 9 and 53-54

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

Date of the actual completion of the international search 21 February 2006 (21.02.2006)	Date of mailing of the international search report 10 MAY 2006
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Charles L. Patterson, Jr. Telephone No. 571-273-8300

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/14844

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.: 1-3,9,53 and 54
- 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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/14844

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, claims 1-3, 9 and 53-54, drawn to a vector containing DNA encoding SEQ ID NO:1, a protein of SEQ ID NO:1, a fusion protein comprising SEQ ID NO:1, a targeting moiety and a linker.

Group II, claims 4 and 11, drawn to a vector containing DNA encoding SEQ ID NO:17 and a protein of SEQ ID NO:17.

Group III, claims 5 and 13, drawn to a vector containing DNA encoding SEQ ID NO:34 and a protein of SEQ ID NO:34.

Group IV, claim 6 and 15, drawn to a vector containing DNA encoding SEQ ID NO:51 and a protein of SEQ ID NO:51.

Group V, claims 7 and 48, drawn to a vector containing DNA encoding SEQ ID NO:55 and a protein of SEQ ID NO:55.

Group VI, claims 8, 16-19, drawn to a protein of SEQ ID NO:59 and a gene encoding SEQ ID NO:59.

Group VII, claims 10, 20-23, drawn to a protein of SEQ ID NO:60 and a gene encoding SEQ ID NO:60.

Group VIII, claims 12, 24-27, drawn to a protein of SEQ ID NO:61 and a gene encoding SEQ ID NO:61.

Group IX, claims 14, 33-36, drawn to a protein of SEQ ID NO:68 and a gene encoding SEQ ID NO:68.

Group X, claim 28, drawn to a protein of SEQ ID NO:63.

Group XI, claim 29, drawn to a protein of SEQ ID NO:65.

Group XI, claim 30, drawn to a protein of SEQ ID NO:67.

Group XII, claim 31, drawn to a protein having SEQ ID NO:1 preceded by all or part of SEQ ID NO:64.

Group XIII, claim 32, drawn to a protein having SEQ ID NO:1 preceded by all or part of SEQ ID NO:66.

Group XIV, claims 37-41, drawn to a protein of SEQ ID NO:69, SEQ ID NO:69 conjugated to a targeting moiety and a gene encoding SEQ ID NO:69.

Group XV, claim 42, drawn to a protein having SEQ ID NO:17 preceded by all or part of SEQ ID NO:64.

Group XVI, claim 43, drawn to a protein having SEQ ID NO:17 preceded by all or part of SEQ ID NO:66.

Group XVII, claim 44, drawn to a protein having SEQ ID NO:34 preceded by all or part of SEQ ID NO:64.

Group XVIII, claim 45, drawn to a protein having SEQ ID NO:34 preceded by all or part of SEQ ID NO:66.

Group XIX, claim 46, drawn to a protein having SEQ ID NO:51 preceded by all or part of SEQ ID NO:64.

Group XX, claim 47, drawn to a protein having SEQ ID NO:51 preceded by all or part of SEQ ID NO:66.

Group XXI, claims 49-52 and 55, drawn to a fusion protein of SEQ ID NO:70 and a targeting moiety and a gene encoding a fusion protein of SEQ ID NO:70.

Group, XXII, claim 56, drawn to a vector containing SEQ ID NO:71 and encoding SEQ ID NO:70.

The inventions listed as Groups I-XXII 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:

Groups I-XI, XIV and XXI-XXII are drawn to different proteins and nucleic acids that have different sequences and therefore are structurally different. Groups XII-XIII and XV-XX are different sequences fused together and therefore are structurally different.