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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DOUBLE-STRANDED RNA STRUCTURES AND CONSTRUCTS, AND METHODS FOR GENERATING AND USING THE SAME

(57) Abstract: The present invention relates to novel double-stranded RNA (dsRNA) structures and dsRNA expression constructs, methods for generating them, and methods of utilizing them for silencing genes. Desirably, these methods specifically inhibit the expression of one or more target genes in a cell or animal (*e.g.*, a mammal such as a human) without inducing toxicity. These methods can be used to prevent or treat a disease or infection by silencing a gene associated with the disease or infection. The invention also provides methods for identifying nucleic acid sequences that modulate a detectable phenotype, such as the function of a cell, the expression of a gene, or the biological activity of a target polypeptide.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/33466

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: C07H 21/00(2006.01),21/02(2006.01)

 USPC: 536/23.1,24.1
 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. : 536/23.1,24.1

 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	PADDISON, PJ, et al., Stable suppression of gene expression by RNAi in mammalian cells. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES Vol. 99, No. 3, pages 1443-1448, see Figures 2, 5a, and 6.	1 ----- 4-11, 18-31, 33, 36, 40-43, and 48-51
X --- Y	PADDISON, PJ, et al., Short hairpin RNAs (shRNAs) induce sequence-specific silencing in mammalian cells. Genes and Development 2002 Vol. 16, pages 948-958, see Figures 1a, 3 and 4 and pages 954-956	2 ----- 4-11, 18-31, 33, 36, 40-43, and 48-51
A	PICCIN, A et al., Efficient and heritable functional knock-out of an adult phenotype in Drosophila using a GAL4-driven hairpin RNA incorporating a heterologous spacer. 2001 NUCLEIC ACIDS RESEARCH Vol. 29, No. 12 e55 (5 pages).	1-30, 33, 36, 40-43, 48-51
A	McCAFFREY, AP et al., Gene expression: RNA interference in adult mice. 2002 Nature Vol. 418, pages 38-39.	1-30, 33, 36, 40-43, 48-51

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 application or patent 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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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/33466

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. Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claim 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. Claim Nos.: 31, 32, 34, 37-39, 44-47, 52-107
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. 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.