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Published:
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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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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.

WO 2004/035782 A3

(54) Title: SIRNA MEDIATED GENE SILENCING IN TRANSGENIC ANIMALS

(57) Abstract: The present invention relates to a process that enables constitutive and inducible gene knock down in living organisms using a short hairpin RNA expression vector integrated into the genome of the organism.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/11233

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/11 C12N15/63 C12N5/10 C12Q1/68

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 7 C12N 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)
BIOSIS, MEDLINE, EMBASE, EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DEVROE E & SILVER P A: "Retrovirus-delivered siRNA" BMC TECHNOLOGY, BIOMED CENTRAL, LONDON, GB, 28 August 2002 (2002-08-28), pages 1-5, XP002225637 ISSN: 1472-6750 cited in the application the whole document	1,2,4-7, 11,13
Y		3,8-10, 12

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"P" document published prior to the international filing date but later than the priority date claimed

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 March 2004	14/04/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Mauhin, V

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/11233

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BRUMMELKAMP T R ET AL: "A system for stable expression of short interfering RNAs in mammalian cells" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 296, no. 5567, 2002, pages 550-553, XP002225638 ISSN: 0036-8075 cited in the application the whole document	1,2,4-6, 11-13
X	PAUL C P ET AL: "EFFECTIVE EXPRESSION OF SMALL INTERFERING RNA IN HUMAN CELLS" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 20, no. 5, May 2002 (2002-05), pages 505-508, XP001121066 ISSN: 1087-0156 cited in the application figure 1 table 1 Experimental protocol: Materials	1,2,4-7, 11,13
X	KISTNER ET AL: "Doxycycline-mediated quantitative and tissue-specific control of gene expression in transgenic mice" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 93, no. 20, October 1996 (1996-10), pages 10933-10938, XP002110022 ISSN: 0027-8424 the whole document	1-13
Y	BRONSON SARAH K ET AL: "Single-copy transgenic mice with chosen-site integration" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 93, no. 17, 1996, pages 9067-9072, XP002270939 1996 ISSN: 0027-8424 Introduction last paragraph page 9072	3,8-10, 12

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/11233

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	HASUWA H ET AL: "Small interfering RNA and gene silencing in transgenic mice and rats" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 532, no. 1-2, 4 December 2002 (2002-12-04), pages 227-230, XP004395375 ISSN: 0014-5793 cited in the application the whole document	1,2,4-8, 10-13
X,P	WO 03 057840 A (ALLELE BIOTECHNOLOGY & PHARMAC) 17 July 2003 (2003-07-17) paragraphs '0008!-'0014! paragraph '0021! paragraphs '0023!,'0024! paragraphs '0041!,'0042! paragraphs '0046!-'0048! paragraph '0050! paragraph '0063! paragraph '0065! paragraphs '0069!,'0070! paragraphs '0072!-'0076! paragraph '0079! paragraphs '0112!,'0113! paragraphs '0115!-'0117! paragraph '0129! paragraph '0138! paragraphs '0142!-'0144! paragraph '0155!	1,2,4-8, 10-14
X,P	KAWASAKI H ET AL: "Short hairpin type of dsRNAs that are controlled by tRNA Val promoter significantly induce RNAi-mediated gene silencing in the cytoplasm of human cells" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 31, no. 2, January 2003 (2003-01), pages 700-707, XP002965487 ISSN: 0305-1048 the whole document	1,2,4-7, 11,13
X,P	MATSUKURA SHIRO ET AL: "Establishment of conditional vectors for hairpin siRNA knockdowns." NUCLEIC ACIDS RESEARCH. ENGLAND 1 AUG 2003, vol. 31, no. 15, 1 August 2003 (2003-08-01), pages (e77) 1-5, XP002270940 ISSN: 1362-4962 the whole document	1,2,4-6, 11,13

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/11233

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	VAN DE WETERING MARC ET AL: "Specific inhibition of gene expression using a stably integrated, inducible small-interfering-RNA vector." EMBO REPORTS, vol. 4, no. 6, June 2003 (2003-06), pages 609-615, XP002270941 ISSN: 1469-221X (ISSN print) the whole document	1,2,4-7, 11,13
A	MERLINO G T ET AL: "ACCURATE IN-VITRO TRANSCRIPTIONAL INITIATION OF THE CHICK ALPHA-2 TYPE I COLLAGEN GENE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 256, no. 21, 1981, pages 11251-11258, XP002270942 ISSN: 0021-9258	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/11233

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-10 are partially directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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. [ ] 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

Information on patent family members

International Application No
PCT/EP 03/11233

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03057840 A	17-07-2003	WO 03057840 A2	17-07-2003
		US 2003175772 A1	18-09-2003