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(54) Title: METHOD FOR INHIBITING SMOOTH MUSCLE CELL PROLIFERATION AND OLIGONUCLEOTIDES FOR USE THEREIN

(57) Abstract

The present invention provides multi-G oligonucleotides that are capable of inhibiting smooth muscle cell proliferation. The multi-G oligonucleotides of the present invention can be used as nucleic acid therapeutic compounds to inhibit smooth muscle cell proliferation in arteries *ex vivo*, and more particularly against restenosis. The present invention further provides pharmaceutical compositions containing the multi-G oligonucleotides. A method for screening oligonucleotides for their ability to inhibit smooth muscle cell proliferation *ex vivo* is also provided.

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INTERNATIONAL SEARCH REPORT

Inter onal Application No
PCT/US 95/12770

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/11 C07H21/00 A61K31/70 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 6 C12N C07H A61K 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ANTISENSE RESEARCH AND DEVELOPMENT, vol. 3, no. 1, 1993, US, pages 67-77, XP002015214 YASWEN, P. ET AL.: "Effects of sequence of thioated oligonucleotides on cultured human mammary epithelial cells" cited in the application see page 72, paragraph 2 - page 74, line 2	1-3
Y	see table 1A	13-18, 21-26,29

X	WO,A,93 01286 (MASSACHUSETTS INST TECHNOLOGY) 21 January 1993 cited in the application see page 17, line 1 - line 30	13-16, 21-24,29
Y	see page 21, SEQ IDs 1 and 4	13-18, 21-26,29

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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

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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
10 October 1996	28. 10. 96

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	Andres, S

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Inter onal Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,94 08053 (ISIS PHARMACEUTICALS INC ;HANECAK RONNIE C (US); ANDERSON KEVIN P) 14 April 1994 cited in the application see page 10, line 12 - page 12, line 6 see page 18, line 25 - line 30 see page 19, line 9 - line 26 see tables 2,3 see page 27, line 23	1-3
A	see examples 19,23,24,27	30-33

X	NUCLEIC ACIDS RESEARCH, vol. 21, no. 8, 25 April 1993, OXFORD GB, pages 1853-1856, XP002015215 ECKER, D. ET AL.: "Rational screening of oligonucleotide combinatorial libraries for drug discovery"	1,2
A	see the whole document	30-33

P,X	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 92, no. 9, 25 April 1995, WASHINGTON US, pages 4051-4055, XP002015216 BURGESS, T. ET AL.: "The antiproliferative activity of c-myb and c-myc antisense oligonucleotides in smooth muscle cells is caused by a nonantisense mechanism" see the whole document	13-16, 30-33

T	ANTISENSE RESEARCH AND DEVELOPMENT, vol. 5, 1995, US, pages 175-183, XP002015217 FARRELL, C. ET AL.: "The uptake and distribution of phosphorothioate oligonucleotides into vascular smooth muscle cells in vitro and in rabbit arteries" see the whole document	

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INTERNATIONAL SEARCH REPORT

rnational application No.
PCT/US95/12770

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.: 13-20
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although these claims (as far as in vivo methods are concerned) are directed to a method of treatment of (diagnostic method practised on) 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 searches 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

Inter ɔnal Application No
PCT/US 95/12770

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9301286	21-01-93	AU-B-	659482	18-05-95
		AU-A-	2303292	11-02-93
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		EP-A-	0672193	20-09-95
		FI-A-	951467	28-03-95
		HU-A-	70965	28-11-95
		JP-T-	8500738	30-01-96
		NO-A-	951191	28-03-95
		US-A-	5514577	07-05-96
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