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(54) Title: OLIGONUCLEOTIDES FOR MODULATING TARGET RNA ACTIVITY

(57) Abstract: The present invention describes oligonucleotides that bind to microRNA target sites in target RNAs, such as mRNAs. The oligonucleotides of the invention may mediate RNase H degradation of the target RNA, mediate RNAi of the target RNA or prevent microRNA regulation of the target RNA. The oligonucleotides of the invention are useful e.g. as research tools for studying microRNA:mRNA interactions and for therapeutic development. The present invention also describes methods of identifying microRNA target sites, methods of validating microRNA target sites, methods of identifying oligonucleotides of the invention and methods of modulating the activity of a target RNA using the oligonucleotides of the invention.



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INTERNATIONAL SEARCH REPORT

International application No
PCT/DK2007/050174

A. CLASSIFICATION OF SUBJECT MATTER INV. C12N15/11		
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) C12N		
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) EPO-Internal, CHEM ABS Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2006/027776 A (YISSUM RES DEV CO HEBREW UNIVERSITY OF JERUSALEM [IL]; SOREQ) 16 March 2006 (2006-03-16) the whole document ----- -/--	
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.		
<input checked="" type="checkbox"/> 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 *E* earlier document but published on or after the international filing date *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) *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		
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 *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 *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. *&* document member of the same patent family		
Date of the actual completion of the international search <p align="center">16 September 2008</p>		Date of mailing of the international search report <p align="center">22/12/2008</p>
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer <p align="center">Macchia, Giovanni</p>

INTERNATIONAL SEARCH REPORT

International application No

PCT/DK2007/050174

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>WO 2004/069992 A (SANTARIS PHARMA AS [DK]; HANSEN BO [DK]; THRU CHARLOTTE ALBAEK [DK];) 19 August 2004 (2004-08-19)</p> <p>page 49 ISIS 3603, ISIS, 3667, ISIS 3683, page 53 the whole document</p> <p>-----</p>	<p>1,2,4-7, 11-13, 17, 19-23, 25-28, 32,34, 36,38, 40, 45-49, 51-54, 56,72, 74-78, 84,87-93</p>
X	<p>WO 99/22772 A (ISIS PHARMACEUTICALS, INC. [US]; HARDEE; GEARY; LEVIN; TEMPLIN; HOWARD) 14 May 1999 (1999-05-14)</p> <p>ISIS 6945, ISIS 14692 page 42 - page 43 the whole document</p> <p>-----</p>	<p>1,2,4-7, 11-13, 17, 19-23, 25-28, 32,34, 36,38, 40, 45-49, 51-54, 56,72, 74-78, 84,87-93</p>
X	<p>SORRENTINO R. ET AL.: "Inhibition of MAPK activity, cell proliferation, and anchorage-independent growth by N-Ras antisense in an N-ras-transformed human cell line" ANTISENSE & NUCLEIC ACID DRUG DEVELOPMENT, vol. 11, 2001, pages 349-358, XP002496111</p> <p>Oligonucleotide H8 page 350 the whole document</p> <p>-----</p>	<p>1-14, 16-54, 56-62, 64-66, 68, 70-72, 74-78, 84-93</p>
A	<p>JOHNSON S.M. ET AL.: "RAS is regulated by the let-7 microRNA family" CELL, vol. 120, 2005, pages 635-647, XP002496112 plus 10 pages of Supplemental Data the whole document</p> <p>-----</p>	

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INTERNATIONAL SEARCH REPORT

International application No

PCT/DK2007/050174

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KRÜTZFELDT J. ET AL.: "Strategies to determine the biological function of microRNAs" NATURE GENETICS, vol. 38, 2006, pages S14-S19, XP002496113 the whole document -----</p>	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2007/050174

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:

Although claims 49-53, 56 are 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 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:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of 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.:

1-93, if and where applicable

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Inventions 1-723

Claims 1-93, if and where applicable;
Oligonucleotides, methods, compositions and uses as claimed;
wherein invention 1 refers to subject-matter related to SEQ
ID NO:1, invention 2 refers to subject-matter related to SEQ
ID NO:2, ... , invention 723 refers to subject-matter
related to SEQ ID NO:723.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/DK2007/050174

Patent document cited in search report	A	Publication date		Patent family member(s)	Publication date
WO 2006027776	A	16-03-2006		EP 1791954 A1	06-06-2007
				US 2008306014 A1	11-12-2008
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WO 2004069992	A	19-08-2004		AU 2004209599 A1	19-08-2004
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				US 6083923 A	04-07-2000