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MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
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- with sequence listing part of description (Rule 5.2(a))

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19 February 2015

(54) Title: COMPOSITIONS AND METHODS FOR MODULATION OF TARGET NUCLEIC ACIDS

(57) Abstract: The present disclosure pertains generally to chemically-modified oligonucleotides for use in research, diagnostics, and/or therapeutics. In certain embodiments, the present disclosure describes compounds and methods for the modulation of a target nucleic acid. In certain embodiments, the present disclosure describes compounds and methods for the modulation of Apolipoprotein C-III expression.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2014/043731

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

a. (means)

☐

on paper

☒

in electronic form

b. (time)

☒

in the international application as filed

☐

together with the international application in electronic form

☐

subsequently to this Authority for the purposes of search

2. ☐

In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

SEQ ID NOs:1-14 and 111-133 were searched.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2014/043731

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.: 5-103, 110, 115-209
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:

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 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.:

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/US2014/043731

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12N 15/113 (2014.01)

CPC - C12N 15/113 (2014.11)

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)

IPC(8) - A61K 9/127, 31/713, 31/7088, 31/7105, 38/17, 38/18, 47/44, 48/00; A61P 3/06, 9/10; C07H 21/00, 21/04; C12N 15/113 (2014.01)
USPC - 435/320.1; 514/44A, 44R; 536/24.5Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - C12N 15/113, 15/1136, 15/1137, 2310/14, 2310/315, 2310/321, 2310/3515, 2310/3521 (2014.11) (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PatBase, Google Patents, PubMed

Search terms used: Apolipoprotein C-III APOCIII HALP2 APOC3 sirna% shrna% small interfering rna% small hairpin rna% short hairpin
rna% rna% sirna% rna% micro rna% dsrna% mirna% ssrna% conjugate ligand

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2012/177947 A2 (BETTENCOURT et al) 27 December 2012 (27.12.2012) entire document	1-4
X	WO 2010/083615 A1 (MACDONALD et al) 29 July 2010 (29.07.2010) entire document	111-114
A	US 2012/0122958 A1 (DAWSON et al) 17 May 2012 (17.05.2012) entire document	1-4, 104-109, 111-114
A	CZECH et al. "RNAi-based therapeutic strategies for metabolic disease," Nature Reviews Endocrinology, 19 April 2011 (19.04.2011), Vol. 7, Pgs. 473-484. entire document	1-4, 104-109, 111-114
A	KASSIM et al. "Gene therapy for dyslipidemia: a review of gene replacement and gene inhibition strategies," Clinical Lipidology, 01 December 2010 (01.12.2010), Vol. 5, No. 6, Pgs. 793-809. entire document	1-4, 104-109, 111-114



Further documents are listed in the continuation of Box C.



* 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 application or patent 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

24 November 2014

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Name and mailing address of the ISA/US

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