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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: OLIGOMERIC COMPOUNDS AND COMPOSITIONS FOR USE IN MODULATION OF SMALL NON-CODING RNAS

(57) Abstract: Compounds, compositions and methods are provided for modulating the expression and function of small non-coding RNAs. The compositions comprise oligomeric compounds, targeted to small non-coding RNAs. Methods of using these compounds for modulation of small non-coding RNAs as well as downstream targets of these RNAs and for diagnosis and treatment of disease associated with small non-coding RNAs are also provided.

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INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C07H 21/04; A61K 48/00
US CL : 536/24.5; 514/44
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. : 536/24.5; 514/44

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)
EAST, STN: microRNAs, miRNA, stRNA, mir-10a, modulation, inhibition, hybridization

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/029459 A2 (TUSCHL et al.) 10 April 2003 (10.04.2003), see entire document, especially pages 2-7.	1-13, 15-24

☐ Further documents are listed in the continuation of Box C. ☐ 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 application or patent 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
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Form PCT/ISA/210 (second sheet) (April 2005)

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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.:
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:
Please See Continuation Sheet

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 any 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.: 1-13, 15-24 and species mir10a

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.

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-13 and 15-24, drawn to oligomeric compounds targeted to small non-coding RNA targets.

Groups 2-1871, claim(s) 14, drawn to the sequences recited in the tables of the specification.

Group 1872, claim(s) 25-31 drawn to a method of modulating expression of a small non-coding RNA using the compound of claim 1.

Group 1873, claim(s) 32, 73-75 and 110, drawn to a method of treating an animal with an oligomeric compound that can hybridize to a small non-coding RNA.

Group 1874, claim(s) 33, drawn to a method of treating or preventing a disease associated with CD36.

Group 1875, claim(s) 34-42 and 53-56, drawn to a method of screening an oligomeric compound for an effect on miRNA signaling using a vector that expresses an miRNA precursor.

Group 1876, claim(s) 43-47, 53-56 and 58-62, drawn to a method of screening a miRNA precursor for an effect on miRNA signaling.

Group 1877, claim(s) 48-62, drawn to a method of screening an oligomeric compound for an effect on miRNA signaling wherein the oligomeric compound mimics an miRNA precursor.

Group 1878, claim(s) 63 and 64, drawn to a method of modulating translation using an oligomeric compound that specifically hybridizes to a small non-coding RNA.

Group 1879, claim(s) 65 and 66, drawn to a method of modulating translation using an oligomeric compound that mimics a small non-coding RNA.

Group 1880, claim(s) 67-68, drawn to a method of modulating apoptosis using an oligomeric compound that specifically hybridizes to a small non-coding RNA.

Group 1881, claim(s) 69-70, drawn to a method of modulating apoptosis using an oligomeric compound that mimics a small non-coding RNA.

Group 1882, claim(s) 71 and 72, drawn to a method of modulating conversion of a precursor miRNA into a miRNA.

Group 1883, claim(s) 76 and 77, drawn to a method of identifying an RNA transcript bound to a small non-coding RNA.

Group 1884, claim(s) 78-83, drawn to a method of arresting or delaying entry of a cell at G2/M phase.

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Group 1885, claim(s) 84-86, drawn to a method of detecting a miRNA precursor.

Group 1886, claim(s) 87-88, drawn to a method of identifying miRNA targets.

Group 1887, claim(s) 89-93, drawn to a method of modulating cell differentiation or apoptosis.

Group 1888, claim(s) 94, drawn to a method of treating a condition associated with adipocyte differentiation.

Group 1889, claim(s) 95-99, drawn to a method of treating or preventing a disease associated with aberrant regulation of the cell cycle by miRNAs.

Group 1890, claim(s) 100-102, drawn to a method of maintaining a pluripotent stem cell.

Group 1891, claim(s) 103-105, drawn to a method of identifying a small non-coding RNA binding site.

Group 1892, claim(s) 106-109, drawn to composition comprising two oligomeric compounds.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Claim 3 contains a Markush group containing 91 species of miRNA targeted by the oligomeric compounds of invention 1.

Claim 28 contains a Markush group containing 11 species of diseases or disorders targeted by the method of invention 1872.

Claim 31 contains a Markush group containing 45 species of miRNA targeted by the method of invention 1872.

Claim 51 contains a Markush group containing 4 species of miRNA targeted by the method of invention 1877.

Claim 79 contains a Markush group containing 19 species of miRNA targeted by the method of invention 1884.

Claim 81 contains a Markush group containing 6 species of miRNA targeted by the method of invention 1884.

Claim 83 contains a Markush group containing 7 species of miRNA targeted by the method of invention 1884.

Claim 97 contains a Markush group containing 7 species of diseases or disorders targeted by the method of invention 1889.

Claim 110 contains a Markush group containing 6 species of miRNA targeted by the method of invention 1873.

The inventions listed as Groups 1-1892 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of group 1 is an oligomeric compound comprising a first and second region and at least one modification that is targeted to a small non-coding RNA target or precursor thereof. Such compounds are not a contribution over the prior art. For example, see AGRAWAL et al (WO 94/01550). Agrawal et al. disclose self-stabilized RNAs that have first and second regions that hybridize with mRNA transcripts (a precursor of small non-coding RNAs as per applicant's definition on page 7) and can contain modifications such as phosphorothioates.

Further, this international searching authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed polynucleotide and amino acid sequences, the Markush group shall be regarded as being of similar nature when:
(A) all alternatives have a common property or activity and
(B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant nucleotide sequences are considered to be each separate inventions for the following reasons:

The sequences do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. Each of the different sequences is a nucleotide sequence that is a miRNA or is targeted to a miRNA. Each member of the class cannot be substituted, one for the other.

Further, the instant sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure due to their unique sequence. Accordingly, unity of invention between the sequences of the instant application is lacking and each nucleotide or amino acid sequence claimed is considered to constitute a special technical feature.

For PCT's: If the polynucleotide sequences of the instant invention are recited in the first claimed invention, Applicants will obtain a search of the first sequence listed in the claim. For every other sequence applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

If the sequences are recited in the second or subsequent claimed invention, Applicants will need to elect the group and pay the fee to obtain a search of the first sequence listed in the claims encompassed by the second or subsequent group. For every other sequence in the second/subsequent group that applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.