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20 November 2008

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(54) Title: COMBINED HAIRPIN-ANTISENSE COMPOSITIONS AND METHODS FOR MODULATING EXPRESSION

(57) Abstract: A nucleotide construct comprising a nucleotide sequence that forms a stem and a loop, wherein the loop comprises a nucleotide sequence that modulates expression of a target, wherein the stem comprises a nucleotide sequence that modulates expression of a target, and wherein the target modulated by the nucleotide sequence in the loop and the target modulated by the nucleotide sequence in the stem may be the same or different. Vectors, methods of regulating target expression, methods of providing a cell, and methods of treating conditions comprising the nucleotide sequence are also disclosed.

INTERNATIONAL SEARCH REPORT

International application No

PCT/US08/57704

A CLASSIFICATION OF SUBJECT MATTER

IPC C07H 21/04(2006 01)

USPC 536/24 S

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

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)

C DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
Y	MlYAGISHI et al Stragegies for generation of an siRNA expression library directed against the human genome Oligonucleotides 2003, VoI 13 pages 325-333, especially pages323-327	1-24
Y	STEOUTESDIJK et al hpRNA mediated targeting of the arabidopsis FAD2 gene gives highly efficient and stable silencing Plant Physiology August 2002, VoI 129, pages 1723-173 1, entire document	1-24

☐ Further documents are listed in the continuation of Bo\ 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 claun(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 pnor Io the international filing date but later than the priority date claimed

"T" later document published after the international 6Ung date or priority *date* and not in conQict 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

0 1 September 2008 (01 09 2008)

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INTERNATIONAL SEARCH REPORT

International application No.
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BOX UI. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group 1, claim(s) 1-24. drawn to a nucleotide construct comprising a nucleotide sequence that forms a stem and a loop, wherein the loop comprises a first nucleotide sequence that modulates expression of a target and the stem comprises a second nucleotide sequences that modulates expression of a target.

Group 2, claim(s) 25-42, drawn to a method of regulating expression of a target comprising providing to a cell the a nucleotide construe! comprising a nucleotide sequence that forms a stem and a loop, wherein the loop comprises a first nucleotide sequence that modulates expression of a target and the stem comprises a second nucleotide sequences that modulates expression of a target.

INTERNATIONAL SEARCH REPORT

International application No
PC77US08/57704

Box No. 11 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. HI 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 firsi mentioned in the claims, it is covered by claims Nos 1-24

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