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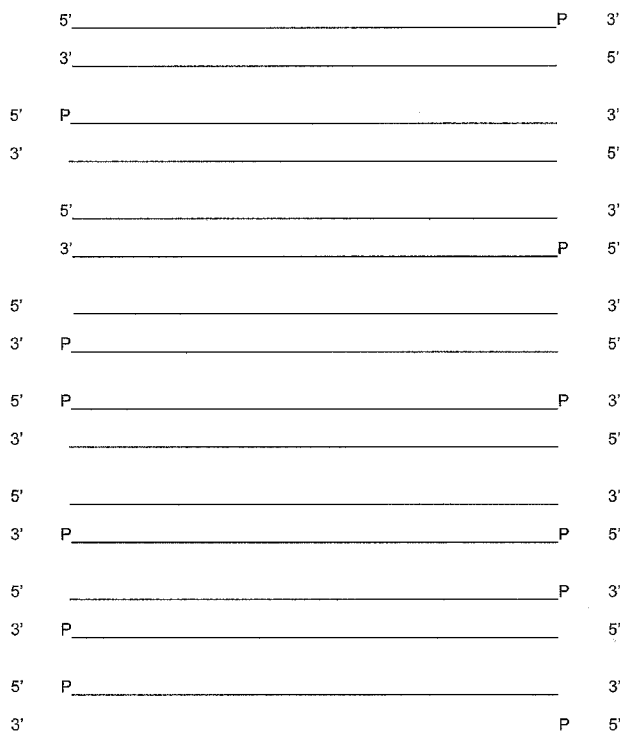
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[Continued on next page]

(54) Title: PEPTIDE DICER SUBSTRATE AGENTS AND METHODS FOR THEIR SPECIFIC INHIBITION OF GENE EX-
PRESSION

FIGURE 1A



(57) Abstract: This invention relates to compounds, com-
positions, and methods useful for reducing a target RNA
and protein levels via use of Dicer substrate siRNA (D
siRN A) -peptide conjugates.

WO 2010/141724 A3



EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))*

Published:

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(88) Date of publication of the international search report:

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/37263

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/713; C07H 21/00 (2010.01)

USPC - 514/44A

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 31/713; C07H 21/00 (2010.01)

USPC - 514/44A

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 514/44A; 514/2; 536/24.5

(Text Search)

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

PubWEST (PGPB, USPT, USOC, EPAB, JPAB); Google Scholar and PubMed.

Search Terms: peptide-dicer substrate, peptide-dsRNA, peptide, dsRNA, neutral, net charge, homobifunctional, heterobifunctional, nucleotide, carbon, linker, linkage, oligonucleotide, internal, internally, conjugat\$, dye, polyaromatic, paclitaxel, metabolic disorder,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	US 2008/0076701 A1 (QUAY et al.) 27 March 2008 (27.03.2008) SEQ ID NO: 1, 3-4, 8-11, 14, 32; table 12, 22; claim 6, 16; para [0005], [0008]-[0012], [0016], [0020], [0026], [0034], [0041], [0043], [0044], [0055], [0074], [0075], [0079], [0081], [0082], [0100], [0119], [0127], [0134],[0141], [0142], [0175], [0240], [0317], [0347]-[0349], [0375], [0376].	1, 3-4, 6-30, 39-43, 57-60, 64-72, 74-77 and 79-86 31-38, 44-56, 61-63, 73 and 78
Y	US 2002/0177150 A1 (MANOHARAN et al.) 28 November 2002 (28.11.2002) para [0013], [0020], [0023], [0024], [0032].	31-35
Y	US 6,316,190 B1 (REIN et al.) 13 November 2001 (13.11.2001) col 21, ln 5-41.	36-38
Y	US 2005/0186591 A1 (BUMCROT et al.) 25 August 2005 (25.08.2005) para [0345].	44-53
Y	US 2006/0167239 A1 (SLATTUM et al.) 27 July 2006 (27.07.2006) para [0004], [0009], [0045].	54-56
Y	US 2005/0255093 A1 (SHONE et al.) 17 November 2005 (17.11.2005) para [0013]-[0020], [0035].	61-63
Y	US 2005/0244858 A1 (ROSSI et al.) 03 November 2005 (03.11.2005) para [0014], [0015].	73
Y	US 2008/0064092 A1 (FOSTER et al.) 13 March 2008 (13.03.2008) SEQ ID NO: 55; para [0018], [0025].	78

 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

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/37263

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.: 87-88
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:

Group I: Claims 1, 3-4, and 6-86, drawn to an isolated double stranded ribonucleic acid composition comprising oligonucleotide strands and a peptide, wherein said peptide has a net charge of about +5 or less, and wherein the peptide has an amino acid sequence of SEQ ID NO: 1 or 45.

Group II+: Claims 1, 3-4, and 6-86, drawn to an isolated double stranded ribonucleic acid composition comprising oligonucleotide strands and a peptide, wherein said peptide has a net charge of about +5 or less, and wherein the peptide has an amino acid sequence selected from the group consisting of SEQ ID NO: 2-44 and 46-89. If Applicant elects to have this group searched, Applicant must specify the specific amino acid sequence to be searched. Each structurally unrelated amino acid sequence constitutes an inventive concept.

---please see continuation on extra 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 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.: Claims 1, 3-4, and 6-86, limited to SEQ ID NOS: 1 and 45

- 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.

Continuation of:

Box No. III Observations where unity of invention is lacking

Group III+: Claims 2 and 6-86, drawn to an isolated double stranded ribonucleic acid composition comprising oligonucleotide strands and a peptide, wherein said peptide has no net charge, and wherein the peptide has an amino acid sequence selected from the group consisting of SEQ ID NO: 1-89. If Applicant elects to have this group searched, Applicant must specify the specific amino acid sequence to be searched. Each structurally unrelated amino acid sequence constitutes an inventive concept.

Group IV+: Claims 5-86, drawn to an isolated double stranded ribonucleic acid composition comprising oligonucleotide strands and a peptide, wherein said peptide has a net charge of about +4 or less, and wherein the peptide has an amino acid sequence selected from the group consisting of SEQ ID NO: 1-89. If Applicant elects to have this group searched, Applicant must specify the specific amino acid sequence to be searched. Each structurally unrelated amino acid sequence constitutes an inventive concept.

The inventions listed as Groups I, II+, III+, and IV+ 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 technical feature shared by the inventions listed as Groups I, II+, III+, and IV+ is an isolated double stranded ribonucleic acid (dsRNA) composition comprising a first oligonucleotide strand having a 5' terminus and a 3' terminus, a second oligonucleotide strand having a 5' terminus and a 3' terminus, and a peptide, wherein said peptide is conjugated to said dsRNA and may have a positive or no net charge. This shared technical feature does not provide a contribution over the prior art, as evidenced by US 2008/0076701 A1 to Quay et al. (published March 27, 2008; hereinafter 'Quay'). Quay teaches an isolated double stranded ribonucleic acid (dsRNA) composition (para [0010]) comprising a first oligonucleotide strand having a 5' terminus and a 3' terminus and a second oligonucleotide strand having a 5' terminus and a 3' terminus (para [0010]), wherein a peptide is conjugated to said dsRNA (para [0010]). Quay further discloses that the peptide comprises a plurality of non-polar (neutrally charged) amino acid residues which may be linked to a plurality of charged amino acid residues (para [0041]), for example at least two positively charged amino acids (claim 16). In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

Another technical feature shared by the inventions listed as Groups I, II+, and III+ is wherein said first strand and said second dsRNA strand have a length that is at least 16 and at most 50 nucleotides in length. This shared technical feature does not provide a contribution over the prior art, because Quay further discloses wherein said first strand and said second strand have a length that is at least 16 and at most 50 nucleotides in length (para [0010] - "double-stranded region of from 25 to 30 base pairs"). In the absence of a contribution over the prior art, the shared technical feature is not a shared special technical feature. Without a shared special technical feature, the inventions lack unity with one another.

A further special technical feature of each of the inventions listed as Groups I, II+, III+, and IV+ is the specific amino acid sequence recited therein. Significant structural similarities cannot readily be ascertained among the sequences. Without significant structural similarities, the sequences do not have a shared special technical feature. In the absence of a shared special technical feature, the inventions lack unity with one another. In this case, the first named structurally related sequences that will be searched without additional fees are SEQ ID NOs: 1 and 45. In order for more sequences to be examined, the appropriate additional examination fees must be paid and the desired sequences to be searched clearly identified.