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Published:

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11 March 2010

(54) Title: SIRNA COMPOUNDS AND METHODS OF USE THEREOF

(57) Abstract: The present invention relates to compounds, pharmaceutical compositions comprising same and methods of use thereof for the inhibition of certain genes, including SOX9, ASPP1, CTSD, CAPNS1, FAS and FAS ligand. The compounds and compositions are useful in the treatment of subjects suffering from diseases or conditions and or symptoms associated with dis-eases or conditions in which gene expression has adverse consequences.



WO 2009/090639 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 09/00053

<p>A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - C12Q 1/68 (2009.01) USPC - 435/6 According to International Patent Classification (IPC) or to both national classification and IPC</p>																													
<p>B. FIELDS SEARCHED</p> <p>Minimum documentation searched (classification system followed by classification symbols) USPC - 435/6</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 435/91.1, 91.3 (see search terms below)</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PubWEST(DB=PGPB,USPT,USOC,EPAB,JPAB; PLUR=YES; OP=ADJ), Google Scholar(Elena FEINSTEIN SOX9, Elena FEINSTEIN FAS, Elena FEINSTEIN siRNA, Hagar KALINSKI siRNA, Hagar KALINSKI SOX9, Hagar KALINSKI FAS, Igor METT SOX9, Igor METT FAS, Igor METT siRNA, EVGENIA ALPERT SOX9, EVGENIA ALPERT FAS, EVGENIA ALPERT siRNA)</p>																													
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>US 2006/0247193 A1 (TAIRA ET AL.) 2 November 2006 (02.11.2006) para [0201], [0208]</td> <td>20, 22</td> </tr> <tr> <td>Y</td> <td></td> <td>21, 23, 25-26</td> </tr> <tr> <td>X</td> <td>US 2006/0115480 A1 (HILLMAN) 1 June 2006 (01.06.2006) para [0031], [0123], [0346], [0390]</td> <td>24</td> </tr> <tr> <td>Y</td> <td>US 2006/2006/0069056 A1 (FEINSTEIN ET AL.) 30 March 2006 930.03.2006) Abstract; para [0028], [0034], [0047]-[0059], [0061]-[0062], [0087]</td> <td>1-19, 25-27</td> </tr> <tr> <td>Y</td> <td>US 6,974,667 B2 (HORNE ET AL.) 13 December 2005 (13.12.2005) SEQ ID NO: 3935; Table 9A, col 179</td> <td>1-19, 21, 25-27</td> </tr> <tr> <td>Y</td> <td>US 2002/0081659 A1 (ROSEN ET AL.) 27 June 2002 (27.06.2002) para [0043], [0601]; Table 1; SEQ ID NO: 68</td> <td>23</td> </tr> <tr> <td>Y</td> <td>US 5,583,032 A (TORRANCE ET AL.) 10 December 1996 (10.12.1996) col 8 ln 6-24</td> <td>16-18</td> </tr> <tr> <td>Y</td> <td>US 2005/0053979 A1 (LIVAK ET AL.), 10 March 2005 (10.03.2005); claim 1, 14</td> <td>18</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	US 2006/0247193 A1 (TAIRA ET AL.) 2 November 2006 (02.11.2006) para [0201], [0208]	20, 22	Y		21, 23, 25-26	X	US 2006/0115480 A1 (HILLMAN) 1 June 2006 (01.06.2006) para [0031], [0123], [0346], [0390]	24	Y	US 2006/2006/0069056 A1 (FEINSTEIN ET AL.) 30 March 2006 930.03.2006) Abstract; para [0028], [0034], [0047]-[0059], [0061]-[0062], [0087]	1-19, 25-27	Y	US 6,974,667 B2 (HORNE ET AL.) 13 December 2005 (13.12.2005) SEQ ID NO: 3935; Table 9A, col 179	1-19, 21, 25-27	Y	US 2002/0081659 A1 (ROSEN ET AL.) 27 June 2002 (27.06.2002) para [0043], [0601]; Table 1; SEQ ID NO: 68	23	Y	US 5,583,032 A (TORRANCE ET AL.) 10 December 1996 (10.12.1996) col 8 ln 6-24	16-18	Y	US 2005/0053979 A1 (LIVAK ET AL.), 10 March 2005 (10.03.2005); claim 1, 14	18
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/></p>																													
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent but published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent but published on or after the international filing date	"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	"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)	"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	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed																		
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<p>Date of the actual completion of the international search</p> <p>1 October 2009 (01.10.2009)</p>	<p>Date of mailing of the international search report</p> <p>13 OCT 2009</p>																												
<p>Name and mailing address of the ISA/US</p> <p>Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201</p>	<p>Authorized officer:</p> <p>Lee W. Young</p> <p>PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774</p>																												

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 09/00053

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:
see 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.:
1-27, limited to SEQ ID No: 1.

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.

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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.

Inventions 1-8525: Nucleic acids having SEQ ID NOS:1-4686 and SEQ ID NOS:37133-40972 (see specification, pg 11, ln 7-8).

The inventions listed as Inventions 1-8525 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:

SEQ ID NOS:1-4686 and SEQ ID NOS:37133-40972 do not share any significant structural element and cannot be considered as having the same or corresponding technical feature.

The inventions listed as Inventions 1-8525 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 feature. According to PCT Rule 13.2, unity of invention exists only when the same or corresponding technical feature is shared by all claimed inventions.

The different physical characteristics of the sequences represent distinct traits that are measured using different techniques and compared using different criteria. The different oligonucleotide sequences represented by the nucleic acid content of the species are different structures that are not common to one another but are different because they are composed of unique nucleic acid sequences.

In this case the first named invention and first named species that will be searched without additional fees is Group I represented by claims 1-27, limited to SEQ ID No: 1.

NOTE: claim 17 is dependent on a claim which is not specified. For purposes of the search and opinion, claim 17 is considered to be dependent on claim 16.