Abstract: The invention relates to saRNA targeting a C/EBPa transcript and therapeutic compositions comprising said saRNA. Methods of using the therapeutic compositions are also provided.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/113 A61K31/7088
ADD.

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)
C12N

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)

EPO-Internal , WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<td>Y</td>
<td>the whole document</td>
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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 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

"S" document member of the same patent family

Date of the actual completion of the international search 19 August 2015

Date of mailing of the international search report 26/08/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2

NL - 2280 HV Rijswijk

Tel. (+31-70) 340-2040;

Fax: (+31-70) 340-3016

Authorized officer

Pi ret, Bernard
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<th>Category*</th>
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<td>Y</td>
<td>LI-LI TAO ET AL: &quot;C/EBP-f+ meliorates CCl-i induced liver fibrosis in mice through promoting apoptosis of hepatic stellate cells with little apoptotic effect on hepatocytes in vitro and in vivo&quot;, APOPTOSIS; AN INTERNATIONAL JOURNAL ON PROGRAMMED CELL DEATH, KLUWER ACADEMIC PUBLISHERS, BO, vol. 17, no. 5, 4 February 2012 (2012-02-04), pages 492-502, XP035040980, ISSN: 1573-675X, DOI: 10.1007/S10495-012-0700-Y</td>
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<td>LOUISE E. 0LOFFSON ET AL: &quot;CCAAT/Enhancer Binding Protein [al pha] (C/EBP [al pha]) in Adipose Tissue Regulates Genes in Lipid and Glucose Metabolism and a Genetic Variant in C/EBP [al pha] Is Associated with Serum Levels of Triglycerides&quot;, JOURNAL OF CLINICAL ENDOCRINOLOGY &amp; METABOLISM, vol. 93, no. 12, 1 December 2008 (2008-12-01), pages 4880-4886, XP055200098, ISSN: 0021-972X, DOI: 10.1210/jc.2008-0574</td>
<td>35-46</td>
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INTERNATIONAL SEARCH REPORT

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 additional 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 an 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.:

   1-23, 35-46, 58-65, 88, 89(completely) ; 74-80(partial ly)

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.
This International Search Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-23, 88, 89 (completely) ; 58-65, 74-80 (partially)
   - Use of a saRNA targeting a C/EBPalpha gene/transcrip for modulating the expression of a tumor suppressor or an oncogene. Uses of these to treat cancer.

1.1. claims: 2-5 (completely) ; 1, 10-23, 58-65, 74-80, 88, 89 (partially)
   - Use of a saRNA targeting a C/EBPalpha gene/transcrip for modulating the expression of an oncogene.

1.2. claims: 6-9 (completely) ; 1, 10-23, 58-65, 74-80, 88, 89 (partially)
   - Use of a saRNA targeting a C/EBPalpha gene/transcrip for modulating the expression of a tumor suppressor.

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2. claims: 24-34 (completely) ; 58-65, 74-80 (partially)
   - Use of a saRNA targeting a C/EBPalpha gene/transcrip for modulating the expression of a microRNA in a cell.

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3. claims: 35-46 (completely) ; 58-65, 74-80 (partially)
   - Use of a saRNA targeting a C/EBPalpha gene/transcrip for treating non-alcoholic fatty acid liver disease, cirrhosis, insulin resistance or obesity.

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4. claims: 47-50 (completely) ; 58-65, 74-80 (partially)
   - Use of a saRNA targeting a C/EBPalpha gene/transcrip for regulating the expression of a pluripotency gene in a cell.

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5. claims: 51-57 (completely) ; 58-65, 74-80 (partially)
   - Use of a saRNA targeting a C/EBPalpha gene/transcrip for regulating epithelial-mesenchymal transition (EMT) in a cell.

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6. claims: 66-73 (completely) ; 74-80 (partially)
   - A double-stranded bimolecular oligonucleotide comprising a saRNA strand and a siRNA strand.

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7. claims: 81-87, 90
Use of a saRNA targeting a C/EBPalpha gene/transcript for treating a white blood cell-related disorder

8. claims: 91-96

Use of a saRNA targeting a C/EBPalpha gene/transcript for regulating the ratio of isoforms of C/EBP in a cell.

9. claim: 97

Use of a saRNA targeting a C/EBPalpha gene/transcript for up-regulating extra coding CEBPA (ecCEBPA) in a cell.

10. claim: 98

Use of a saRNA targeting a C/EBPalpha gene/transcript for increasing liver regeneration after hepatectomy
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