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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ,
CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO,
DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR,
KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
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GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

(54) Title: RNA ENCODING A THERAPEUTIC PROTEIN

(57) Abstract: The present invention relates to an RNA encoding a therapeutic protein. In particular, the present invention relates to RNA suitable for use as a medicament. The present invention concerns such novel RNA as well as compositions and kits comprising the RNA. Furthermore, the present invention relates to the RNA, compositions or kits as disclosed herein for use as a medicament. The present invention also provides the use of the RNA, compositions or kits as disclosed herein for increasing the expression of said encoded protein, in particular in gene therapy.



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A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K48/00 C12N15/85 A61K31/7088 C12N15/67
 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)
 A61K 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, BIOSIS, EMBASE, WPI Data, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2015/138348 A1 (UNIV PENNSYLVANIA [US]) 17 September 2015 (2015-09-17)	1-11, 16, 18, 24, 30-34, 36, 39-50
Y	paragraphs [0023], [0032], [0053], [0056], [0064], [0067], [0072], [0075], [0116] figures 1B-1C -& DATABASE Geneseq [Online] 5 November 2015 (2015-11-05), XP002774408, Database accession no. BCE41300 abstract -/--	1-50

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 26 October 2017	Date of mailing of the international search report 11/01/2018
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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 Barnas, Christoph
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INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-& DATABASE Geneseq [Online] 5 November 2015 (2015-11-05), XP002774409, Database accession no. BCE41289 abstract -----	
Y	WO 02/098443 A2 (VON DER MUELBE FLORIAN [DE]; HOERR INGMAR [DE]; PASCOLO STEVE [DE]) 12 December 2002 (2002-12-12) cited in the application page 6, paragraph 2 - page 9, paragraph 3 page 9, paragraph 2-6 page 10, paragraph 1 page 11, line 31 - page 13, line 9 figures 1A-G figures 2A-D -----	1-50
Y	WO 2009/127230 A1 (CUREVAC GMBH [DE]; THES ANDREAS [DE]; PROBST JOCHEN [DE]; HOERR INGMAR) 22 October 2009 (2009-10-22) page 20, paragraph 2 page 25, line 19 page 52, paragraph 3 page 54, line 31 - page 55, line 6 page 55, paragraph 4 page 56, paragraph 3 claims 13, 14 page 19, lines 9-20 -----	1-50
Y	WO 2015/062738 A1 (CUREVAC GMBH [DE]) 7 May 2015 (2015-05-07) page 7, paragraph 1 - page 8, paragraph 2 page 11, paragraph 2 page 12, line 18 - page 13, line 30 page 16, paragraph 5 - page 17, paragraph 1 page 17, paragraph 4 - page 18, paragraph 1 page 19, lines 8-13 page 20, paragraph 5 - page 21, line 24 page 27, paragraph 3 - page 29, paragraph 2 table 2 -----	1-50
Y	WO 2005/021707 A2 (VICAL INC [US]; VILALTA ADRIAN [US]; EVANS THOMAS G [US]; QUONG MELANI) 10 March 2005 (2005-03-10) paragraphs [0084] - [0085] paragraphs [0119] - [0122] paragraphs [0133] - [0135] paragraph [0262] sequences 2, 24 claims 94, 95, 101, 111, 112, 124 table 4 -----	1-50
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International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>WO 2013/143700 A2 (CUREVAC GMBH [DE]; THES ANDREAS [DE]) 3 October 2013 (2013-10-03) page 4, paragraph 2 - page 5, paragraph 3 page 7, paragraph 2 page 35, paragraph 3 - page 36, paragraph 1 page 53, paragraph 2 - page 54, paragraph 1 page 59, paragraph 2 page 63, paragraph 2-3 page 64, paragraph 3 page 65, line 4 - page 68, line 24 page 74, lines 2-10 page 76, lines 26-28 page 77, lines 19-21 page 84, paragraph 5 -& DATABASE Geneseq [Online]</p> <p>21 November 2013 (2013-11-21), XP002774410, Database accession no. BAV13704 abstract -& DATABASE Geneseq [Online]</p> <p>21 November 2013 (2013-11-21), XP002774411, Database accession no. BAV13703 -& DATABASE Geneseq [Online]</p> <p>21 November 2013 (2013-11-21), XP002774412, Database accession no. BAV13686 abstract -& DATABASE Geneseq [Online]</p> <p>21 November 2013 (2013-11-21), XP002774413, Database accession no. BAV13678 abstract</p>	1-50
A	<p>-----</p> <p>QI M ET AL: "Septin1, a new interaction partner for human serine/threonine kinase aurora-B", 28 October 2005 (2005-10-28), BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ELSEVIER, AMSTERDAM, NL, PAGE(S) 994 - 1000, XP027229954, ISSN: 0006-291X [retrieved on 2005-09-20] page 996, right-hand column, paragraph 2 - left-hand column, paragraph 1 -& DATABASE GenPept [Online]</p> <p>15 March 2015 (2015-03-15), XP002774414, Database accession no. NP_443070 -----</p>	1-50

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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:

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.:

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.:

1-50(partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-50(partially)

An RNA comprising a coding sequence which comprises a nucleic acid sequence selected from the group consisting of nucleic acid sequences according to any one of SEQ ID NO: 34130, 47187, 60244, 21073 and 73301 all of them coding for the enzyme Ornithine Carbonyltransferase (OTC) with SEQ ID NO: 8016 or a fragment or variant of any one of said nucleic acid sequences.

2-8016. claims: 1-50(partially)

Each of invention 2-8016 are RNAs comprising coding sequences which comprise a nucleic acid sequence wherein each group of nucleic acids coding for a specific protein according to Table 1 on p. 105-567 of the description represents one single invention. Invention 2 is represented by the nucleic acid sequences SEQ ID NOs 26115, 39172, 52229, 13058 and 65286 coding for the SEQ ID NO: 1.; invention 3 is represented by the nucleic acid sequences SEQ ID NOs 26116, 39173, 52230, 13059 and 65287 coding for SEQ ID NO: 2;
etc ...
invention 8016 is represented by the nucleic acid sequences SEQ ID NOs 34129, 47186, 60243, 21072, 73300 coding for SEQ ID NO: 8015.

8017-13057. claims: 1-50(partially)

Each of invention 8017-13057 are RNAs comprising coding sequences which comprise a nucleic acid sequence wherein each group of nucleic acids coding for a specific protein according to Table 1 on p. 105-567 of the description represents one single invention. Invention 8017 is represented by the nucleic acid sequences SEQ ID NOs 34131, 47188, 60245, 21074, 73302 coding for SEQ ID NO: 8017 and invention 13057 is represented by the nucleic acid sequences SEQ ID NOs 39171, 52228, 65285, 26114 and 78342 coding for SEQ ID NO: 13057.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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International application No

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