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28 December 2017 (28.12.2017)

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see Notice of 28 December 2017 (28.12.2017)

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(54) Title: INFLUENZA MRNA VACCINES

(57) Abstract: The present invention relates to mRNA sequences usable as mRNA-based vaccines against infections with influenza viruses. Additionally, the present invention relates to a composition comprising the mRNA sequences and the use of the mRNA sequences or the composition for the preparation of a pharmaceutical composition, especially a vaccine, e.g. for use in the prophylaxis or treatment of influenza virus infections. The present invention further describes a method of treatment or prophylaxis of infections with influenza virus using the mRNA sequences.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/12 A61K39/145
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, WPI Data, EMBASE, BIOSIS, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BENJAMIN PETSCH ET AL: "Protective efficacy of in vitro synthesized, specific mRNA vaccines against influenza A virus infection", NATURE BIOTECHNOLOGY, vol. 30, no. 12, 1 January 2012 (2012-01-01), pages 1210-1216, XP055051005, ISSN: 1087-0156, DOI: 10.1038/nbt.2436	1-11, 20-76
Y	page 1211, column 1; figures 1,2 -/--	12,13

[X] Further documents are listed in the continuation of Box C.

[X] 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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 October 2017	15/11/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Saame, Tina

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-& Sook-San Wong ET AL: "An mRNA vaccine for influenza", , 31 December 2012 (2012-12-31), XP055389920, Retrieved from the Internet: URL:http://www.nature.com/nbt/journal/v30/n12/pdf/nbt.2439.pdf [retrieved on 2017-07-11] the whole document	

X	WO 2015/024669 A1 (CUREVAC GMBH [DE]) 26 February 2015 (2015-02-26)	1-11, 20-76
Y	claims 1, 2, 9, 12-14, 16, 33	12,13

Y	DATABASE UniProt [Online] 1 November 1996 (1996-11-01), "RecName: Full=Hemagglutinin {ECO:0000256|SAAS:SAAS00070811};", XP55390955, retrieved from EBI accession no. UNIPROT:Q67043 Database accession no. Q67043 sequence	12,13

Y	DATABASE UniProt [Online] 1 October 2014 (2014-10-01), "RecName: Full=Hemagglutinin {ECO:0000256|SAAS:SAAS00070811};", XP002775008, retrieved from EBI accession no. UNIPROT:A0A068IZQ2 Database accession no. A0A068IZQ2 abstract; sequence	12,13

Y	DATABASE UniProt [Online] 7 January 2015 (2015-01-07), "RecName: Full=Hemagglutinin {ECO:0000256|SAAS:SAAS00070811};", XP002775009, retrieved from EBI accession no. UNIPROT:A0A097PG98 Database accession no. A0A097PG98 sequence	12,13

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/060663

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE UniProt [Online] 20 January 2016 (2016-01-20), "RecName: Full=Hemagglutinin {ECO:0000256|SAAS:SAAS00070811}; Flags: Precursor;", XP002775010, retrieved from EBI accession no. UNIPROT:A0A0N9RU18 Database accession no. A0A0N9RU18 sequence	12,13

A	WO 2012/019630 A1 (CUREVAC GMBH [DE]; THESS ANDREAS [DE]; SCHLAKE THOMAS [DE]; PROBST JOC) 16 February 2012 (2012-02-16) claims 1-5, 12	25-30

A	WO 02/098443 A2 (VON DER MUELBE FLORIAN [DE]; HOERR INGMAR [DE]; PASCOLO STEVE [DE]) 12 December 2002 (2002-12-12) claims 1-3	20-22

A	WO 2010/037408 A1 (CUREVAC GMBH [DE]; FOTIN-MLECZEK MARIOLA [DE]; VOSS SOEHNKE [DE]) 8 April 2010 (2010-04-08) claims 1-4	54,55

A	WO 2015/024665 A1 (CUREVAC GMBH [DE]) 26 February 2015 (2015-02-26) the whole document	1-13, 20-76

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/060663

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.:

1-13, 20-76(all partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-13, 20-76(all partially)

   mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from hemagglutinin (HA) of influenza A virus (or a fragment or variant thereof) according to SEQ ID No 1; compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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2. claims: 1-13, 20-76(all partially)

   mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from hemagglutinin (HA) of influenza A virus (or a fragment or variant thereof) according to SEQ ID No 2; compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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3. claims: 1-13, 20-76(all partially)

   Group of inventions: mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from hemagglutinin (HA) of influenza A virus (or a fragment or variant thereof) selected from SEQ ID Nos 3-14031, 213713, 213787, 213792, 213797 and 213802; compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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4. claims: 14, 15(completely); 1-6, 10, 20-76(partially)

   Group of inventions: mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from hemagglutinin (HA) of influenza B virus (or a fragment or variant thereof) selected from SEQ ID Nos 26398-28576, 214836-214863, 214940-214967; compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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5. claims: 16-19(completely); 1-11, 20-76(partially)

   mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from neuraminidase (NA) of influenza virus (or a fragment or variant thereof); compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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6. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from nucleoprotein (NP) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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7. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from matrix protein 1 (M1) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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8. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from matrix protein 2 (M2) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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9. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from non-structural protein 1 (NS1) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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10. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from non-structural protein 2 (NS2) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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11. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from nuclear export protein (NEP) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and

kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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12. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from polymerase acidic protein (PA) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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13. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from polymerase basic protein (PBI) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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14. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from PB1-F2 of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

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15. claims: 1-3, 6-9, 20-76(all partially)

mRNA sequence comprising at least one coding region, encoding at least one antigenic peptide or protein derived from polymerase basic protein 2 (PB2) of an influenza virus (or a fragment or variant thereof) compositions, vaccines and kits comprising such mRNA sequences; therapeutic use of such mRNA sequences;

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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