Title: Rift Valley Fever Virus Replicon Particles

Abstract: Disclosed herein is a robust system for the reverse genetics generation of a Rift Valley fever (RVF) virus replicon particle (VRPRW), vaccine candidate. VRPRW can actively synthesize viral RNA and proteins, but lack structural glycoprotein genes, preventing spread within immunized individuals and reducing the risk of vaccine-induced pathogenicity. It is disclosed herein that VRPRW immunization is both safe and efficacious, resulting in a robust immune response that is protective against RVF virus challenge within 24 hours of immunization. Provided herein are VRPRW, methods of producing VRPRW, and method of using VRPRW for immunization against RVF virus infection.
INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/046250

A. CLASSIFICATION OF SUBJECT MATTER
IN V. C12N7/00 C12N7/04 A61K39/ 12 A61K35/76 G01N33/50
ADD. A61P37/04 A61P35/00

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<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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<tbody>
<tr>
<td>X</td>
<td>DODD K.A. ET AL. : &quot;Single do se im m unity on with vi rus repl ican parti cles confers rapi d robust protec tion a gainst Rft Val ley Fever Vi rus chal lenge &quot;, J. Vi rol., vol. 86, no. 8, 15 February 2012 (2012-02-15), pages 4204-42 12, XP002711604</td>
<td>1-17, 19-23, 30-32</td>
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<td>Y</td>
<td>the whole document -----</td>
<td>18, 24, 25</td>
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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 invention 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

Date of the actual completion of the international search
13 December 2013

Date of mailing of the international search report
20/12/2013

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentboulevard 2
NL-2280 HV Rijswijk
Tel (31-70) 540-2040, Fax (31-70) 540-3016

Authorized officer
Galli, Ivo

Form PCT/ISA/210 (second sheet) (April 2009)
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<th>Relevant to claim No.</th>
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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 64(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 appellant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of additional fees.

3. [X] 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.:
   1-25, 30-32

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.
- [X] No protest accompanied the payment of additional search fees.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-7
   A RVF virus replicon particle as defined in claims 1-7

1.1. claims: 8-16
   A method for producing it through viral rescue from plasmids.

1.2. claim: 17
   An immunogenic composition thereof.

1.3. claims: 19-23
   Medical use of the replicon particles or of the composition thereof, in raising an immune response against RVF.

1.4. claims: 30-32
   A method of differentiating subjects vaccinated with the replicon particle from subjects infected with RVFV.

2. claims: 18, 24, 25
   A composition of the RVF replicon particle and an immunogenic protein from a heterologous virus. Medical uses thereof.

3. claims: 26-29
   Medical use of the replicon particle of subject 1 in the treatment of cancer.
<table>
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<th>Patent family member(s)</th>
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<tr>
<td></td>
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<td>ZA 200610012 A</td>
<td>25-03-2009</td>
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