



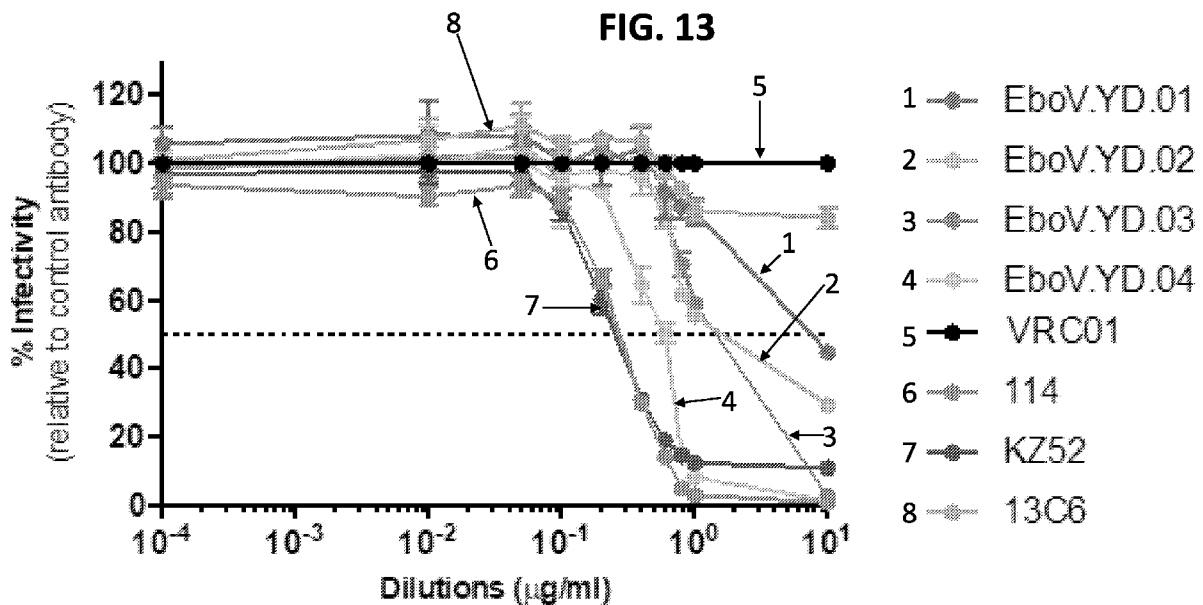
- (51) International Patent Classification:  
A61K 39/42 (2006.01) C07K 16/08 (2006.01)
- (21) International Application Number:  
PCT/US2019/067423
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62/782,809 20 December 2018 (20.12.2018) US
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(81) 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, JO, 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,

(54) Title: EBOLA VIRUS GLYCOPROTEIN-SPECIFIC MONOCLONAL ANTIBODIES AND USES THEREOF



(57) Abstract: Human monoclonal antibodies that specifically bind Ebola virus glycoprotein with nanomolar affinity are described. The monoclonal antibodies were isolated by bulk sorting of plasmablasts from a human Ebola virus vaccinee and pairing of the immunoglobulin heavy and light chain genes using emulsion PCR. The paired immunoglobulin genes were expressed using Fab yeast display to screen and characterize the antibodies. The Ebola virus-specific monoclonal antibodies can be used, for example, to diagnose and treat Ebola virus infection or Ebola virus disease in a subject.



SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,  
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

- (84) Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, 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:**

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
- *of inventorship (Rule 4.17(iv))*

**Published:**

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
- *with sequence listing part of description (Rule 5.2(a))*

**(88) Date of publication of the international search report:**

20 August 2020 (20.08.2020)

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/067423

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
  - a.  forming part of the international application as filed:
    - in the form of an Annex C/ST.25 text file.
    - on paper or in the form of an image file.
  - b.  furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
  - c.  furnished subsequent to the international filing date for the purposes of international search only:
    - in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
    - on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
2.  In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2019/067423

## 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.:

1-34(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.

INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2019/067423

A. CLASSIFICATION OF SUBJECT MATTER  
INV. A61K39/42 C07K16/08  
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 C07K 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

| Category* | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|-----------|--|-----------------------|
| X         | D. CORTI ET AL: "Protective monotherapy against lethal Ebola virus infection by a potently neutralizing antibody", SCIENCE, vol. 351, no. 6279, 18 March 2016 (2016-03-18), pages 1339-1342, XP055651508, US ISSN: 0036-8075, DOI: 10.1126/science.aad5224 the whole document<br>-----<br>-/-- | 1-34                  |

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

"&" document member of the same patent family

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| Date of the actual completion of the international search<br>24 March 2020   | Date of mailing of the international search report<br>08/07/2020 |
| Name and mailing address of the ISA/<br>European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016 | Authorized officer<br>Galli, Ivo                                 |

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2019/067423

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT |   |                       |
|--|---|-----------------------|
| Category*  | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
| A  | <p>A. A Panina ET AL: "Recombinant Antibodies to the Ebola Virus Glycoprotein", Acta Naturae, vol. 9, no. 4, December 2017 (2017-12), pages 84-91, XP055677231, DOI: 10.32607/2075-8251-2017-9-4-84-91 Retrieved from the Internet: URL:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5762832/pdf/AN20758251-09-04-084.pdf [retrieved on 2020-03-17] the whole document</p> <p style="text-align: center;">-----</p> | 1-34                  |
| A  | <p>EP 3 339 439 A1 (UNIV HOKKAIDO NAT UNIV CORP [JP]) 27 June 2018 (2018-06-27) the whole document</p> <p style="text-align: center;">-----</p>   | 1-34                  |
| A  | <p>ZHEN-YONG KECK ET AL: "Macaque Monoclonal Antibodies Targeting Novel Conserved Epitopes within Filovirus Glycoprotein", JOURNAL OF VIROLOGY., vol. 90, no. 1, 1 January 2016 (2016-01-01), pages 279-291, XP055317321, US ISSN: 0022-538X, DOI: 10.1128/JVI.02172-15 the whole document</p> <p style="text-align: center;">-----</p>   | 1-34                  |
| A  | <p>PANINA A A ET AL: "Chimeric fab fragments of antibodies to recombinant Ebola virus glycoprotein", RUSSIAN JOURNAL OF BIOORGANIC CHEMISTRY, M A I K NAUKA - INTERPERIODICA, RU, vol. 43, no. 4, 2 August 2017 (2017-08-02), pages 409-420, XP036289629, ISSN: 1068-1620, DOI: 10.1134/S1068162017040069 [retrieved on 2017-08-02] the whole document</p> <p style="text-align: center;">-----</p>                 | 1-34                  |
| A  | <p>WANG B. ET AL: "Facile Discovery of a Diverse Panel of Anti-Ebola Virus Antibodies by Immune Repertoire Mining", SCIENTIFIC REPORTS, vol. 5, 13926, 10 September 2015 (2015-09-10), XP055238413, the whole document</p> <p style="text-align: center;">-----</p>   | 1-34                  |
|  | -/--  |                       |

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2019/067423

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT |   |                       |
|--|---|-----------------------|
| Category*  | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
| A  | WENDELIEN B. O. ET AL: "Neutralizing Antibody Fails to Impact the Course of Ebola Virus Infection in Monkeys", THE JOURNAL OF INFECTIOUS DISEASES, vol. 3, no. 1, E9, 1 January 2007 (2007-01-01), XP055263524, the whole document<br>----- | 1-34                  |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/067423

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|--|------------------|-------------------------|------------------|
| EP 3339439                             | A1               | 27-06-2018              |                  |
|  |                  | CA 2995922 A1           | 23-02-2017       |
|  |                  | CN 107922939 A          | 17-04-2018       |
|  |                  | EP 3339439 A1           | 27-06-2018       |
|  |                  | JP W02017030172 A1      | 07-06-2018       |
|  |                  | US 2018237503 A1        | 23-08-2018       |
|  |                  | WO 2017030172 A1        | 23-02-2017       |
| -----                                  |                  |                         |                  |

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

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

1. claims: 1-34(partially)

A monoclonal antibody against the Ebola GP, characterized by the CDRs of YD01.

Coding nucleic acids, vectors, pharmaceutical compositions, methods of detecting, medical uses, methods of producing the antibody.

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2-8. claims: 1-34(partially)

A monoclonal antibody against the Ebola GP, characterized by the CDRs of YD02, YD03, YD04, YD05, YD06, YD07, YD08, respectively.

Coding nucleic acids, vectors, pharmaceutical compositions, methods of detecting, medical uses, methods of producing the antibody.

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