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Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *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:
22 March 2018 (22.03.2018)

(54) Title: EBOLA VIRUS ANTIBODIES AND BINDING AGENTS DERIVED THEREFROM

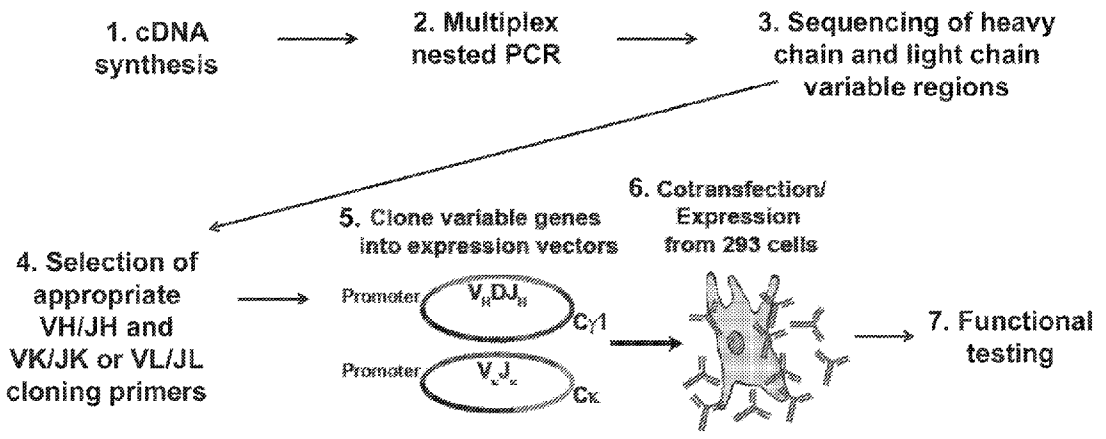

FIG. 1

(57) Abstract: This disclosure relates to antibodies and antigen binding fragments that specifically bind Ebola virus particles. In certain embodiments, the antibodies and fragments are capable of treating or preventing an Ebola viral infection. In certain embodiments, the antibodies and antigen binding fragments are also contemplated for diagnostic methods and compositions related thereto.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 38/18, A61K 39/395 (2018.01)
CPC - C07K 2317/76, A61K 39/39558

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)
See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2016/075546 A2 (LANZAVECCHIA et al.) 19 May 2016 (19.05.2016) claims 1-3 and 10.	1-5, 7, 8
A	US 2015/0125455 A1 (MEDIMMUNE LIMITED) 07 May 2015 (07.05.2015) para [0100]; SEQ ID NO: 335;	1-5, 7, 8
A	US 2008/0069822 A1 (JENSEN et al.) 20 March 2008 (20.03.2008) claim 17; SEQ ID NO: 367.	1-5, 7, 8
X,P	US 2016/0215040 A1 (REGENERON PHARMA) 28 July 2016 (28.07.2016) abstract; claims 1-10.	1-5, 7, 8

☐ 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

Date of the actual completion of the international search	Date of mailing of the international search report
01 February 2018	13 FEB 2018
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

--continued from Box III: Observations where unity of invention is lacking--

Group I+: Claims 1-5, 7, 8 and 11-18, directed to a non-naturally occurring chimeric antibody (or antigen binding fragment) comprising six complementarity determining regions (CDRs), a nucleic acid encoding the antibody, or a pharmaceutical composition comprising the antibody. The antibody, nucleic acid and composition will be searched to the extent that the antibody encompasses CDRs of 5.1.10B3 (Note, 5.1.10B3 LC is SEQ ID NO: 1 that comprises LCDR1, LCDR2, LCDR3 corresponding to SEQ ID Nos: 11, 12, 13, and 5.1.10B3 HC is SEQ ID NO: 2 that comprises HCDR1, HCDR2, HCDR3 corresponding to SEQ ID Nos: 14, 15, 16; see applicant specification p. 2 ln 19-28), and the Fc mutation G236A (the first claimed Fc mutation in claim 3; Note, the mutations in claim 3 are in reference to SEQ ID NO: 50). It is believed that claims 1-5, 7 and 8 encompass this first named invention, and thus these claims will be searched without fee to the extent that the antibody encompasses CDRs of 5.1.10B3, and Fc mutation G236A. Additional antibodies will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected antibodies. Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. An exemplary election would be CDRs of antibody 5.6.1A02 and Fc mutation S239D (Note, 5.6.1A02 LC is SEQ ID NO: 3 that comprises LCDR1, LCDR2, LCDR3 corresponding to SEQ ID Nos: 17, 18, 19, and 5.6.1A02 HC is SEQ ID NO: 4 that comprises HCDR1, HCDR2, HCDR3 corresponding to SEQ ID Nos: 20, 21, 22; see applicant specification p. 2, ln 30 to p. 3, ln 8) (claims 1-5, 7 and 8).

Group II, claims 9, 10, 19 and 20, directed to a method of detecting, preventing or treating Ebola virus infection comprising use of an Ebola binding antibody or antigen binding fragment thereof.

The inventions listed as Group I+ and II do not relate to a single special technical feature under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I+ has the special technical feature of a non-naturally occurring chimeric antibody (or antigen binding fragment) comprising six CDRs of a specific sequence, that is not required by Group II.

Group II has the special technical feature of assaying the expression of an Ebola virus epitope or administering an antibody, that is not required by Group I+.

No technical features are shared between the amino acid sequences encoding anti-Ebola antibody or Fc varaints of Groups I+, and accordingly, these groups lack unity a priori.

Additionally, even if Groups I+ were considered to share the technical features of including: a non-naturally occurring chimeric antibody or antigen binding fragment comprising six CDRs, wherein the CDRs comprise the three light and three heavy chain CDRs, wherein the antibody or antigen binding fragment thereof binds to an epitope expressed in an Ebola virus particle, a nucleic acid encoding the antibody, or a pharmaceutical composition comprising the antibody and a physiologically acceptable carrier or excipient, these shared technical features are previously disclosed by WO 2016/075546 A2 to LANZAVECCHIA et al., (hereinafter Lanzavecchia).

Lanzavecchia teaches a non-naturally occurring chimeric antibody or antigen binding fragment (claim 1 "An isolated or purified human antibody or a recombinant antibody, or an antigen binding fragment thereof, that specifically binds the Ebola virus GP protein") comprising six CDRs, wherein the CDRs comprise the three light and three heavy chain CDRs (claims 2 and 3 "wherein the antibody or antigen binding fragment comprises a heavy chain comprising CDRI, CDR2 and CDR3 and a light chain comprising CDRI, CDR2 and CDR3"), wherein the antibody or antigen binding fragment thereof binds to an epitope expressed in an Ebola virus particle (claim 1 "An isolated or purified human antibody or a recombinant antibody, or an antigen binding fragment thereof, that specifically binds the Ebola virus GP protein"; claim 10 "An antibody, or an antigen binding fragment thereof, that binds to the same epitope as the antibody of any one of the previous claims"; the Ebola virus GP protein is expressed in an Ebola virus particle), a nucleic acid encoding the antibody in a vector (claims 12-14 "A nucleic acid molecule comprising a polynucleotide encoding the antibody...vector comprising the nucleic acid molecule"), and a pharmaceutical composition comprising the antibody and a physiologically acceptable carrier or excipient (claim 17 "pharmaceutical composition comprising the antibody of any one of claims 1-11, or an antigen binding fragment thereof, the nucleic acid of claim 12 or claim 13, the vector of claim 14, the cell of claim 15, or the immunogenic polypeptide of claim 16, and a pharmaceutically acceptable excipient, diluent or carrier").

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

Therefore, Group I+ and II inventions lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.

NOTE, claim 6 is held unsearchable because it is a dependent claim and is not drafted in accordance with the second and third sentences of Rule 6.4(a).

NOTE, Claim 15 depends from claim 1, as drafted, is objected to, because it does not appear to be the intent of the applicant. For this International Search and Opinion, claim 15 is reconstrued as dependent claim of claim 11.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 17/43305

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 13*ter*.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 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.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/US 17/43305

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.: 6
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:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

--continued on first extra 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 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.:
1-5, 7, 8 limited to 5.1.10B3 antibody (SEQ ID NOs: 1, 2, 11-16) and Fc G236A

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.