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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, 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, KN, KP, KR, 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, 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.

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[Continued on next page]

(54) Title: SYNTHETIC PEPTIDE COMPOUNDS AND METHODS OF USE

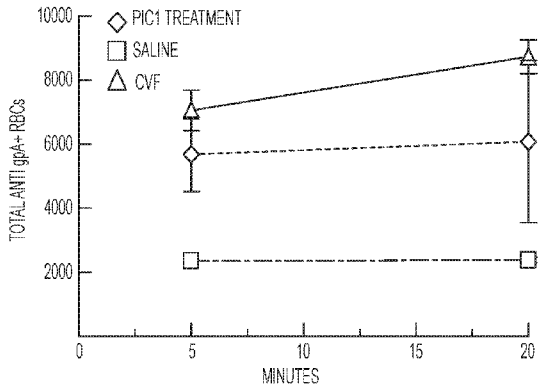

FIG. 26C

(57) Abstract: The present invention provides synthetic peptide compounds and uses thereof for therapy and diagnostics of complement-mediated diseases, such as inflammatory diseases, autoimmune diseases, and microbial and bacterial infections; and non-complement-mediated diseases, such cystic fibrosis and various acute diseases. The invention is directed to modifications of a synthetic peptide of 15 amino acids from the Polar Assortant (PA) peptide, which is a scrambled peptide derived from human Astrovirus protein. In some embodiments, the invention is directed to peptide compounds that are peptide mimetics, peptide analogs and/or synthetic derivatives of PA (e.g., sarcosine derivatives) having, for example, internal peptide substitutions, and modifications, including PEGylation at the N-terminus and C-terminus. The invention further provides methods of selecting at least one synthetic peptide for treating various conditions.

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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))*

(88) Date of publication of the international search report:
23 February 2017

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/39421

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 14/08; A61K 45/06, 38/16 (2016.01)
CPC - C07K 14/005, 7/08, 14/08; A61K 38/162, 38/03
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)
IPC(8) Classifications: C07K 14/08; A61K 45/06, 38/16; CPC Classifications: C07K 14/005, 7/08, 14/08; A61K 38/162, 38/03

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)
PatSeer (US, EP, WO); USPTO Web Page; Google Scholar; EBSCO: Entrez Pubmed; NCBI BLAST; Lens.org; ENA; Search terms -- hemolysis, 'synthetic peptide', 'C1 inhibitor', 'polar assortant', transfusion, PEG, sarcosine, 'acute intravascular hemolytic transfusion reaction'

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X – Y	US 2013/0244924 A1 (KRISHNA, NK et al.) September 19, 2013; abstract; paragraphs [0017], [0061], [0068], [0069], [0024], [0108]; figure 7; SEQ ID NO: 9	1-2, 26/1-2, 27-28, 30/27-28 --- 3-4, 18-19, 26/3-4, 26/18-20
Y	(SHARP, JA et al.) Peptide Inhibitor of Complement C1, a Novel Suppressor of Classical Pathway Activation: Mechanistic Studies and Clinical Potential. 22 August 2014, Vol. 5; pages 1-9; abstract; page 1, second column, first paragraph; page 2, second column, third paragraph; page 5, first column, second paragraph; second column, first paragraph; DOI: 10.3389/fimmu.2014.00406	3-4, 18-19, 26/3-4, 26/18-20
Y	US 2015/0031599 A1 (PROLONG PHARMACEUTICALS LLC) January 29, 2015; paragraphs [0073], [0353]	20, 26/20
A	US 2014/0309175 A1 (BELROSE PHARMA, INC.) October 16, 2014; paragraphs [0097], [0111], [0112]	29, 30/29
A	US 2015/0064176 A1 (OMEROS CORPORATION) March 5, 2015; entire document	1-4, 18-20, 26/1-4, 26/18-20 27-29, 30/27-29

☐ 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
2 December 2016 (02.12.2016)	09 JAN 2017
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/39421

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/US16/39421

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:

-***-Continued Within the Next Supplemental Box-***-

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.:
1-4, 18-20, 26-30

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
Information on patent family members

International application No.
PCT/US16/39421

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

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.

Group I, Claims 1-4, 18-20, 26 (in-part) and 27-30 are directed toward a method of treating and/or preventing a hemolytic reaction, including autoimmune hemolytic anemia, in a subject in need thereof comprising: administering to the subject in need thereof a composition comprising a therapeutically effective amount of a synthetic peptide comprising at least about 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 3-47; peptides for said methods; and a pharmaceutical composition for said methods.

Group II, Claims 5, 6 and 26 (in-part) are directed toward a method of treating hypoxic ischemic encephalopathy in a subject.

Group III, Claims 7, 8 and 26 (in-part) are directed toward a method of treating cystic fibrosis in a subject.

Group IV, Claims 9-12 and 26 (in-part) are directed toward a method of treating a bacterial infection in a subject.

Group V, Claims 13, 14 and 26 (in-part) are directed toward a method of enhancing Lactobacillus growth in a subject.

Group VI, Claims 15-17 and 26 (in-part) are directed toward a method of treating a viral infection in a subject.

Group VII, Claims 21-23 and 26 (in-part) are directed toward a method of treating birth asphyxia in a subject.

Group VIII, Claims 24, 25 and 26 (in-part) are directed toward a method of treating acute kidney injury in a subject.

The inventions listed as Groups I - VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features of Group I include hemolysis, not present in any other Groups; the special technical features of Group II include hypoxic ischemic encephalopathy, not present in any other Groups the special technical features of Group III include cystic fibrosis, not present in any other Groups; the special technical features of Group IV include a bacterial infection, not present in any other Groups; the special technical features of Group V include enhancing Lactobacillus growth, not present in any other Groups; the special technical features of Group VI include a viral infection, not present in any other Groups; the special technical features of Group VII include birth asphyxia, not present in any other Groups; the special technical features of Group VIII include acute kidney injury, not present in any other Groups.

Groups I - VIII share the technical features including: a method of producing an effect or result, comprising administering to a subject in need thereof a composition comprising a therapeutically effective amount of a synthetic peptide comprising at least about 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 3-47, wherein the composition comprises at least one pharmaceutically acceptable carrier, diluent, or excipient. Groups I - IV and VI - VIII share the technical features including: treating a disorder or condition; Groups VI and VI share the technical features including treating an infection.

However, these shared technical features are previously disclosed by US 2013/0244924 A1 to Krishna et al. (hereinafter 'Krishna').

Krishna discloses a method of producing an effect or result (a method of treating a disease (producing an effect or result); paragraph [0017]), comprising administering to a subject in need thereof (comprising administering to a subject in need thereof; paragraph [0017]) a composition comprising a therapeutically effective amount (a composition comprising a therapeutically effective amount; paragraph [0015]) of a synthetic peptide (of a synthetic peptide; paragraph [0012]) comprising SEQ ID NO: 3 (comprising SEQ ID NO: 9 (SEQ ID NO: 3); Table 1, paragraph [0059]; wherein SEQ ID NO: 9 is 100% identical to applicants' SEQ ID NO: 3), wherein the composition comprises at least one pharmaceutically acceptable carrier, diluent, or excipient (wherein the composition comprises at least one pharmaceutically acceptable carrier, diluent, or excipient; abstract, paragraph [0015]); treating a disorder or condition (treating a disease (disorder or condition); paragraph [0017]). Krishna further discloses wherein complement is vital for host defense against pathogens including bacteria and viruses (wherein complement is vital for host defense against pathogens including bacteria and viruses; paragraph [0068]); and wherein humans with alternative pathway defects suffer from severe bacterial infections (wherein humans with alternative pathway defects suffer from severe bacterial infections; paragraph [0070]).

Krishna does not disclose treating an infection. However, it would have been obvious to a person of ordinary skill in the art at the time of the invention was made to have modified the disclosure of Krishna to have used the peptides and compositions disclosed by Krishna for the treatment of bacterial and/or viral infections, based on the disclosure of Krishna, in order to provide effective treatment for said infections by modulating the complement system, as disclosed by Krishna.

Since none of the special technical features of the Groups I-VIII inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Krishna reference, unity of invention is lacking.