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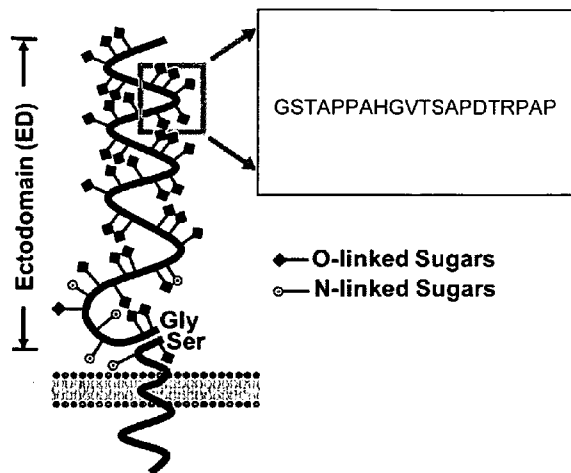
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[Continued on next page]

(54) Title: MUC1 DECOY PEPTIDES FOR TREATMENT AND PREVENTION OF BACTERIAL INFECTIONS

Fig. 1

A.



(57) Abstract: Pseudomonas aeruginosa flagellin protein recruits the mammalian host sialidase enzyme neuraminidase- 1 (NEU1) to remove sialic acid residues from the extracellular domain of the mammalian cell-surface protein MUC 1 (MUC 1 -ED), thereby exposing a cryptic binding site on the MUC 1 -ED protein backbone for flagellin binding. NEU1 -driven MUC 1 -ED desialylation rapidly increases P. aeruginosa adhesion to the airway epithelium. MUC1 -ED desialylation also increases MUC 1 -ED cleavage and shedding from the cell surface, where desialylated, shed MUC1 -ED competitively blocks P. aeruginosa adhesion to cell-associated MUC1 -ED. Presented herein are data showing that exogenously-administered, deglycosylated MUC1 -ED peptides reduced adhesion of P. aeruginosa to airway epithelial cells. Also presented are data showing that administration of P. aeruginosa to mice in combination with deglycosylated MUC 1 -ED decreased P. aeruginosa recovered from the lungs at 48 hr and 72 hr post-infection. Such findings are extended to the methods of treatment and prevention of bacterial infections defined herein.

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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))*

— *with sequence listing part of description (Rule 5.2(a))*

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

11 May 2017

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US15/00313

Box No. 1 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/US15/00313

**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.: 5-11, 15, 19  
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:

-\*\*\*-Please see supplemental page-\*\*\*-

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.:  
Group I, Claims 1-4 and 20-22

- 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/US15/00313

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(8) - A61K 39/00, 38/16, 38/17; C12P 21/02; C07K 14/435 (2017.01) CPC - A61K 38/1735, 38/1703, 38/1709, 38/02, 39/00; C07K 14/4727, 14/435 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC(8) Classifications: A61K 39/00, 38/16, 38/17; C12P 21/02; C07K 14/435 (2017.01) CPC Classifications: A61K 38/1735, 38/1703, 38/1709, 38/02, 39/00; C07K 14/4727, 14/435 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, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC, RU, AT, CH, TH, BR, PH); Lens.org; ENA; Pubmed; NCBI Blast; EBSCO; Google Scholar: Terms: MUC1, tandem, repeat, peptide, decoy, prevent, treat, bacteria, infect, ectodomain, desialyated, deglycosylated, GSTAPPAHGVTSPDTRPAP		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/033667 A2 (DEPARTMENT OF VETERANS AFFAIRS, REHABILITATION R & D SERVICE) 22 April 2004; page 29, lines 14-18	20, 22/20
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Y		1, 3/1, 4/1
Y	(MCAULEY, JL et al.) MUC1 cell surface mucin is a critical element of the mucosal barrier to infection. The Journal of Clinical Investigation. August 2007, Vol. 117, No. 8; pages 2319-2324; page 2313, 2nd column, 2nd paragraph; page 2317, 1st column, 3rd paragraph	1, 3/1, 4/1
A	WO 2013/025972 A1 (GLOBEIMMUNE, INC., et al.) 21 February 2013; paragraph [0066]	2, 3/2, 4/2, 21, 22/21
A	US 2004/0157278 A1 (ASTLE, JH et al.) 12 August 2004; paragraph [0008]; Claim 7	2, 3/2, 4/2, 21, 22/21
A	(LINDEN, SK et al.) MUC1 Limits Helicobacter pylori Infection both by Steric Hindrance and by Acting as a Releasable Decoy. PLoS Pathogens. 1 October 2009, Vol. 5, No. 10; e1000617; DOI: 10.1371/journal.ppat.1000617	1-2, 3/1-2, 4/1-2, 20-21, 22/20-21
A	US 2014/0107189 (BANCEL, S et al.) 17 April 2014; entire document	1-2, 3/1-2, 4/1-2, 20-21, 22/20-21
A	WO 2008/147405 A1 (OKLAHOMA MEDICAL RESEARCH FOUNDATION) 4 December 2008; entire document	1-2, 3/1-2, 4/1-2, 20-21, 22/20-21
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> 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	"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
"E"	earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"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		Date of mailing of the international search report
21 February 2017 (21.02.2017)		24 MAR 2017
Name and mailing address of the ISA/US		Authorized officer
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300		Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT  
Information on patent family members

International application No.

PCT/US15/00313

-\*\*\*-Continued from Box No. 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 and 20-22 are directed toward a decoy peptide and method of treating or preventing a bacterial infection in a subject therewith.

Group II, Claims 12-14, 16-18 are directed toward methods of determining whether a subject has an infection, or has been colonized, by a selected bacteria.

The inventions listed as Groups I and II 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 SEQ ID NO: 1, not present in Group II; the special technical features of Group II include detection of a shed MUC1 ectodomain, not present in Group I.

Groups I and II share the technical features including: a method, wherein a subject has an infection of a selected bacteria; and a MUC1 fragment.

However, these shared technical features are previously disclosed by the article 'Muc1 Limits Helicobacter felis Binding to Gastric Epithelial Cells but Does not Limit Colonization and Gastric Pathology Following Infection' by Every et al. (hereinafter 'Every').

Every discloses a method, wherein a subject has an infection of a selected bacteria (detection of a releasable MUC1 decoy by gastric epithelial cells upon infection with H. pylori (a method, wherein a subject has an infection of a selected bacteria); page 489, first column, first paragraph); and a MUC1 fragment (a releasable MUC1 decoy (a MUC1 fragment); page 489, first column, first paragraph).

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