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(54) **LYSIN-ANTIMICROBIAL PEPTIDE (AMP) POLYPEPTIDE CONSTRUCTS, LYSINS, ISOLATED POLYNUCLEOTIDES ENCODING SAME AND USES THEREOF**

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CPC ***C07K 14/4723*** (2013.01); ***C12N 15/64*** (2013.01); ***A61P 31/04*** (2018.01); *A61K 9/0073* (2013.01)

(57) **ABSTRACT**

The present disclosure is directed to a lysin-AMP polypeptide construct comprising: (a) a first component comprising the polypeptide sequence of: (i) SEQ ID NO: 118 (GN202); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of SEQ ID NO: 118 (GN202); or (iii) an active fragment of SEQ ID NO: 118 (GN202); and (b) a second component comprising the polypeptide sequence of at least one antimicrobial peptide (AMP), wherein the at least one AMP comprises SEQ ID NO: 114 (FIRL). Exemplary lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44) as well as methods of treating bacterial infections using the present lysin-AMP polypeptide constructs are also disclosed.

Specification includes a Sequence Listing.

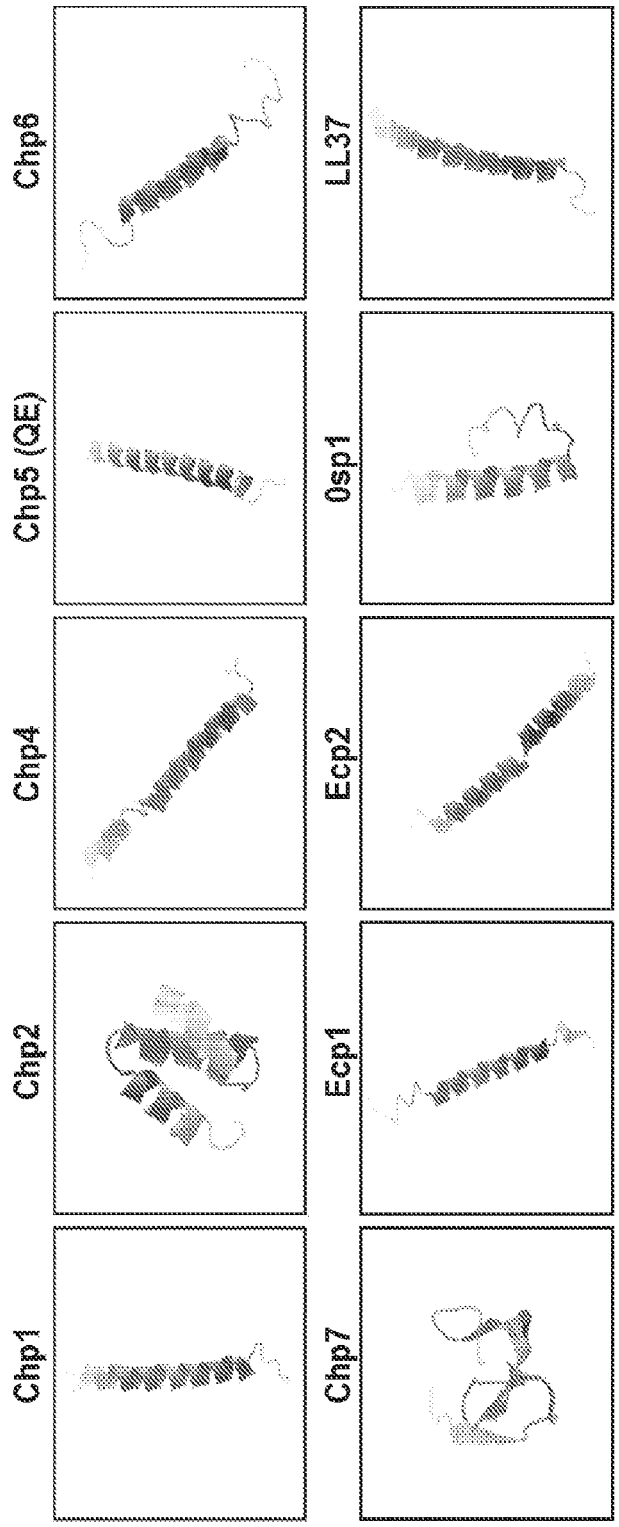

FIG. 1

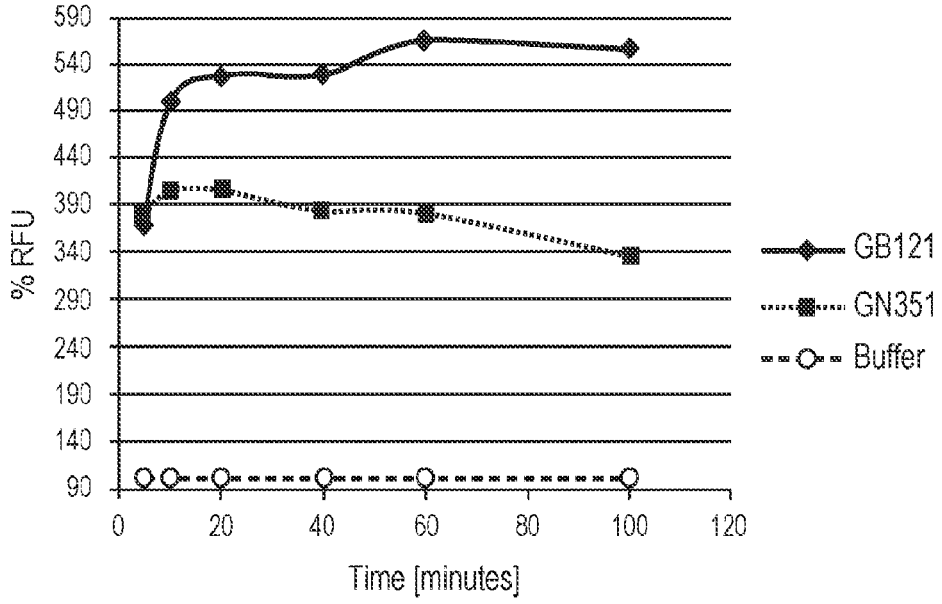
590
540
490
440
390
340
290
240
190
140
90
% RFU
0
20
40
60
80
100
120
Time [minutes]
GB121
GN351
Buffer

FIG. 2A

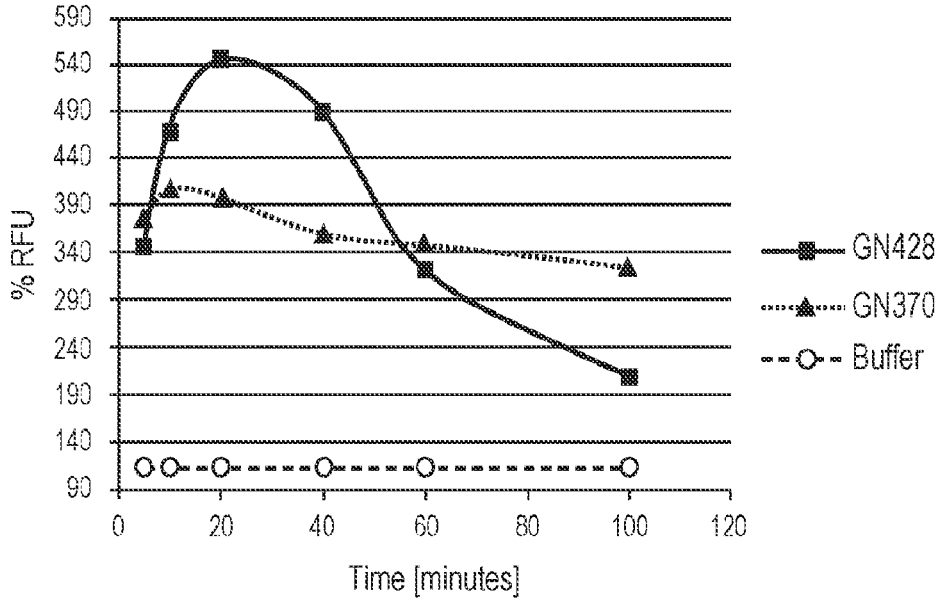
590
540
490
440
390
340
290
240
190
140
90
% RFU
0
20
40
60
80
100
120
Time [minutes]
GN428
GN370
Buffer

FIG. 2B

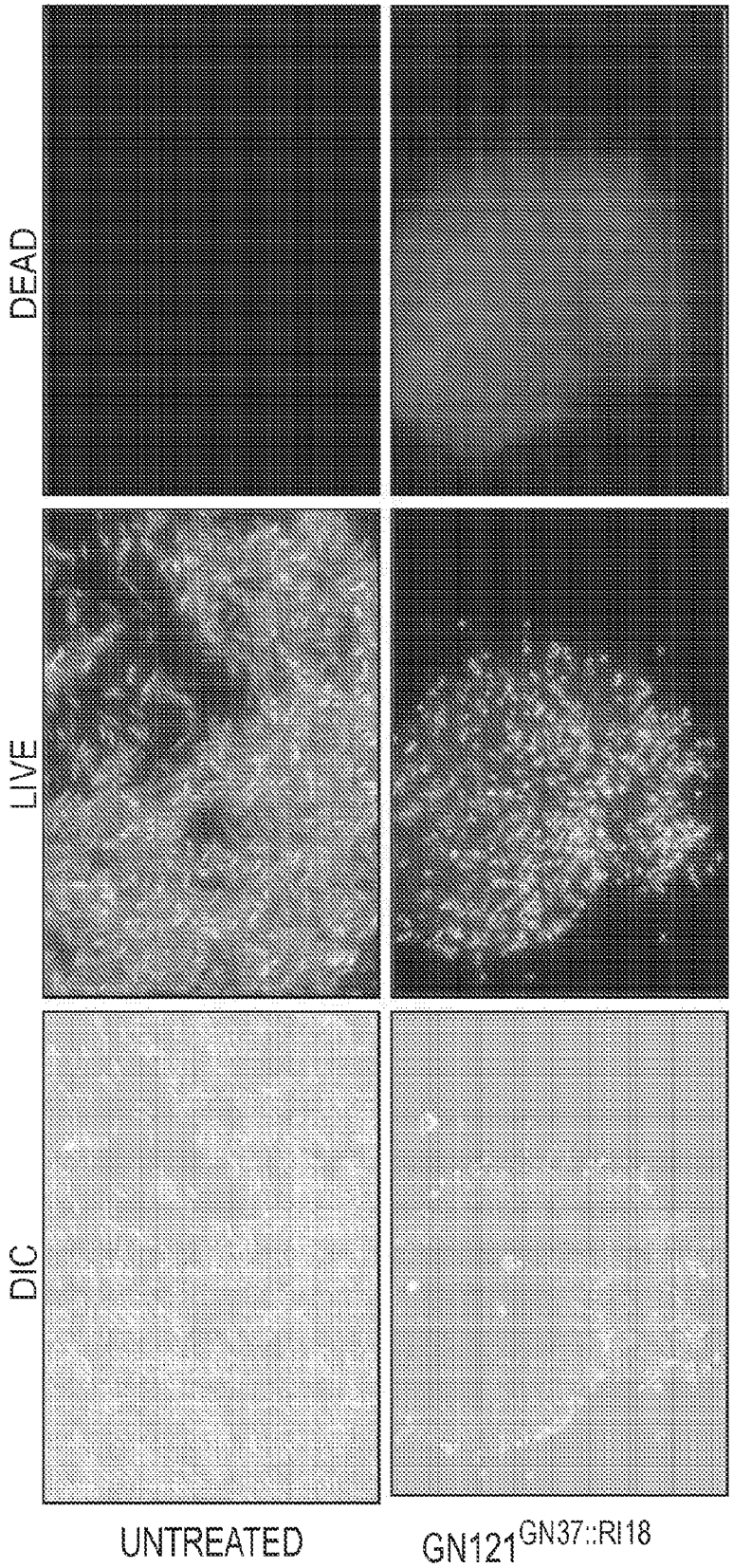

FIG. 3

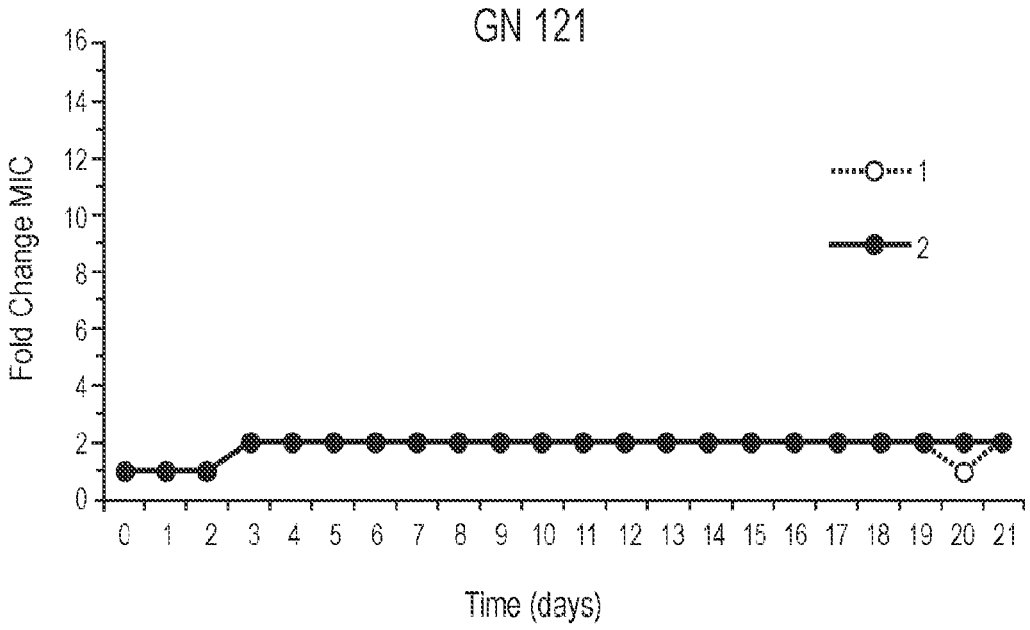
GN 121
Fold Change MIC
16
14
12
10
8
6
4
2
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Time (days)
1
2

FIG. 4A

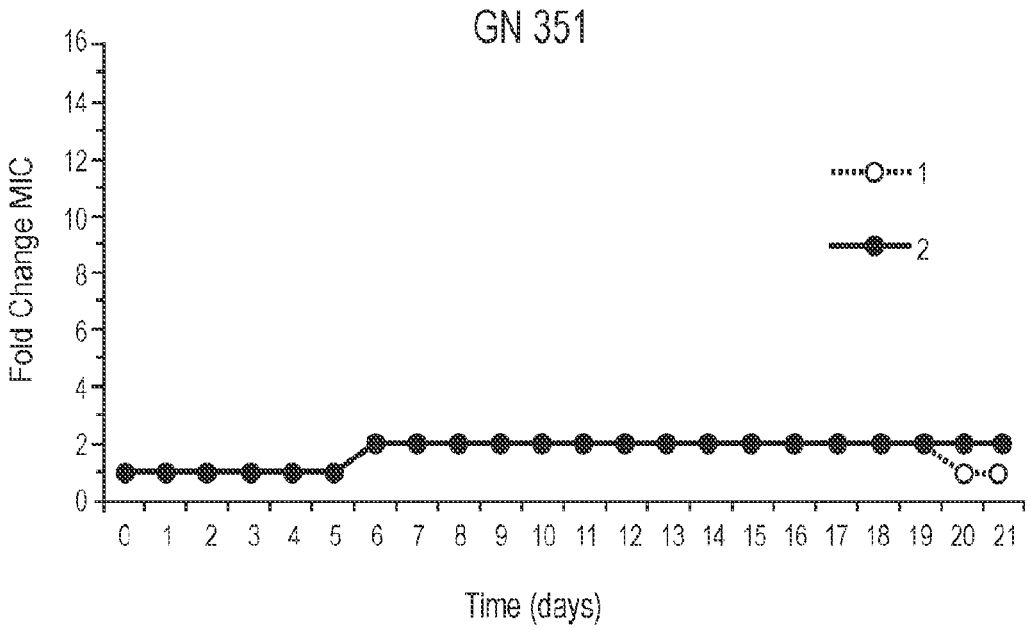
GN 351
Fold Change MIC
16
14
12
10
8
6
4
2
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Time (days)
1
2

FIG. 4B

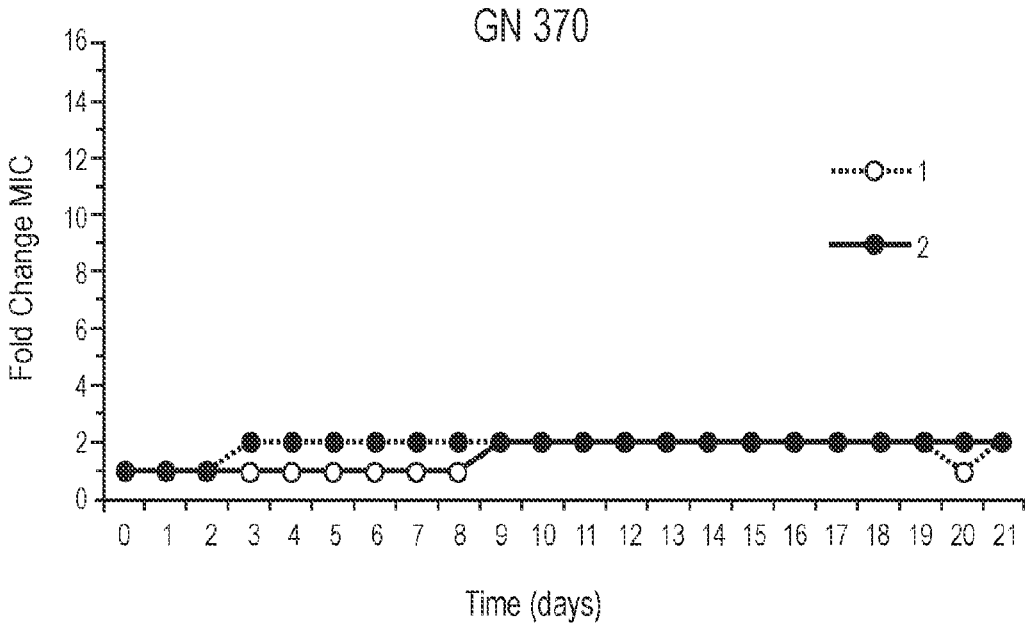
GN 370
Fold Change MIC
16
14
12
10
8
6
4
2
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Time (days)
1
2

FIG. 4C

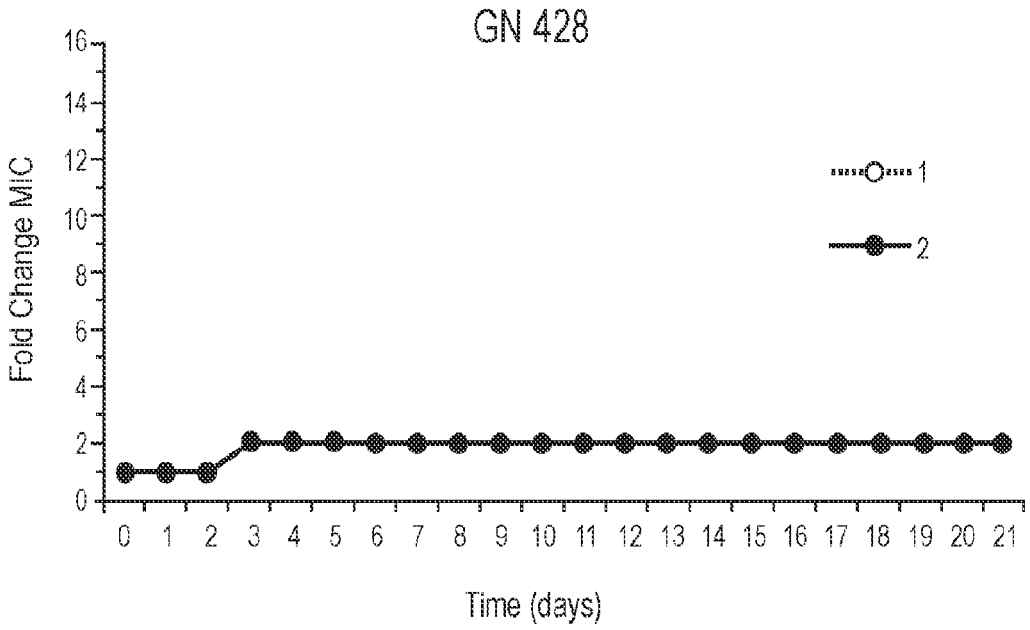
GN 428
Fold Change MIC
16
14
12
10
8
6
4
2
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Time (days)
1
2

FIG. 4D

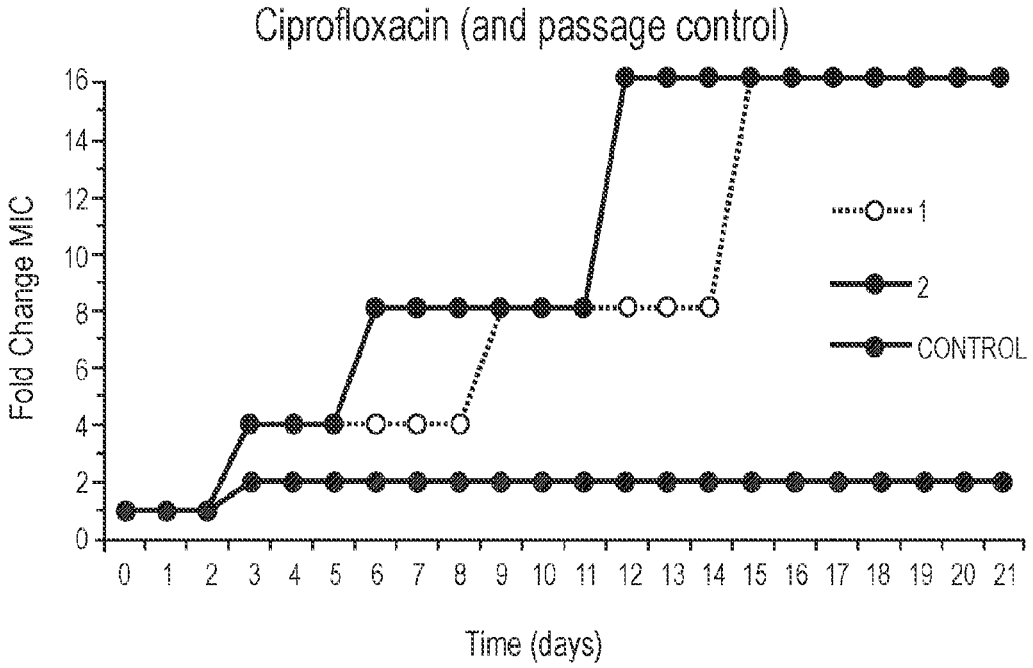
Ciprofloxacin (and passage control)
Fold Change MIC
0
2
4
6
8
10
12
14
16
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Time (days)
1
2
CONTROL

FIG. 4E

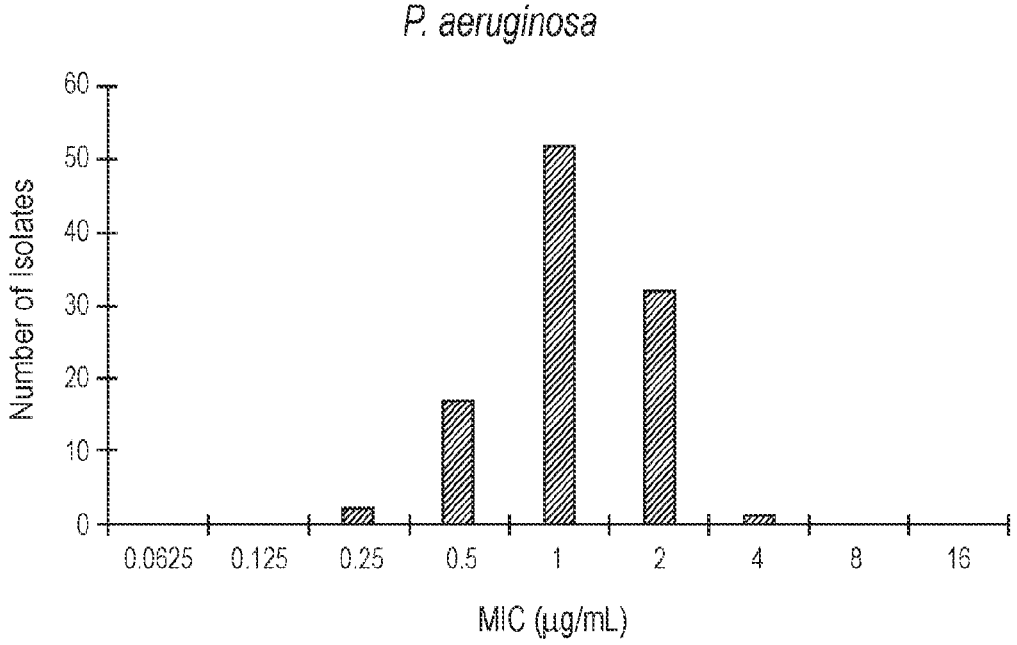
P. aeruginosa
Number of Isolates
0
10
20
30
40
50
60
0.0625 0.125 0.25 0.5 1 2 4 8 16
MIC (µg/mL)

FIG. 5

LYSIN-ANTIMICROBIAL PEPTIDE (AMP) POLYPEPTIDE CONSTRUCTS, LYSINS, ISOLATED POLYNUCLEOTIDES ENCODING SAME AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of, and relies on the filing date of, U.S. patent application Ser. No. 16/777,154, filed 30 Jan. 2020, which application is a continuation-in-part and claims the benefit of, and relies on the filing date of PCT Application No. PCT/US2019/047916, filed on 23 Aug. 2019, which claims the benefit of priority of PCT/US2019/024912, filed on 29 Mar. 2019, which claims the benefit of priority of U.S. provisional Application No. 62/722,793, filed 24 Aug. 2018, U.S. Provisional Application No. 62/650,235, filed on 29 Mar. 2018, and U.S. Provisional Application No. 62/721,969, filed on 23 Aug. 2018, and also relies on the filing date of U.S. Provisional Application No. 62/849,320 filed on 17 May 2019, U.S. Provisional Application No. 62/860,836 filed 13 Jun. 2019 and U.S. Provisional Application No. 62/935,479 filed 14 Nov. 2019, each of which is herein incorporated by reference in its entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on 27 Jan. 2021, is named 2020-01-30_0341_0021-00-CIP_ST25 txt and is 286,955 bytes in size.

FIELD OF THE DISCLOSURE

[0003] The present disclosure relates to the field of antibacterial agents and more specifically to polypeptides having lysin activity against Gram-negative bacteria and the use of these agents in killing Gram-negative bacteria and combating bacterial infection and contamination.

BACKGROUND

[0004] Gram-negative bacteria, in particular, members of the genus *Pseudomonas* and the emerging multi-drug resistant pathogen *Acinetobacter baumannii*, are an important cause of serious and potentially life-threatening invasive infections. *Pseudomonas* infection presents a major problem in burn wounds, chronic wounds, chronic obstructive pulmonary disorder (COPD), cystic fibrosis, surface growth on implanted biomaterials, and within hospital surfaces and water supplies where it poses a host of threats to vulnerable patients.

[0005] Once established in a patient, *P. aeruginosa* can be especially difficult to treat. The genome encodes a host of resistance genes, including multidrug efflux pumps and enzymes conferring resistance to beta-lactam and aminoglycoside antibiotics, making therapy against this Gram-negative pathogen particularly challenging due to the lack of novel antimicrobial therapeutics. This challenge is compounded by the ability of *P. aeruginosa* to grow in a biofilm, which may enhance its ability to cause infections by protecting bacteria from host defenses and chemotherapy.

[0006] In the healthcare setting, the incidence of drug-resistant strains of *Pseudomonas aeruginosa* is increasing. In an observational study of health care-associated bloodstream infections (BSIs) in community hospitals, *P. aeruginosa* was one of the top four Multiple Drug Resistant (MDR) pathogens, contributing to an overall hospital mortality of 18%. Additionally, outbreaks of MDR *P. aeruginosa* are well-documented. Poor outcomes are associated with MDR stains of *P. aeruginosa* that frequently require treatment with drugs of last resort, such as colistin.

[0007] Moreover, reduced effectiveness of certain antibiotics is observed in combating both Gram-negative and Gram-positive infections due to factors in the environment of the infection, such as the pulmonary surfactant, rather than to antibiotic resistance developments. Certain antibiotics, such as daptomycin, for example, have failed to meet criteria in a clinical trial for severe community-acquired pneumonia. This deficiency has been shown to be due to an interaction between daptomycin and pulmonary surfactant, which inhibits the activity of this antibiotic against Gram-positive organisms, specifically in the lung environment and more generally in the airway environment wherein pulmonary surfactant is present. Silverman, J. A. et al., "Surfactant Inhibition of Daptomycin," *JID,* 191: 2149-2152 (2005). Thus, daptomycin is not indicated for treatment of lung and more generally airway (especially lower respiratory tract) infections and those of skill in the art would not employ a treatment regimen including daptomycin to treat such infections. The inability of daptomycin to combat infection in the presence of pulmonary surfactants has been shown dramatically in, for example, Koplowicz, Y. B. et al., "Development of daptomycin-susceptible methicillin-resistant *Staphylococcus aureus* Pneumonia during high-dose daptomycin therapy", *Clin Infect Dis.* 49(8):1286-7 (2009). Recent studies have focused on overcoming daptomycin inactivity in the presence of surfactant by testing and evaluating antibacterial activity of hybrid molecules of the structurally related lipopeptide A54145. Nguyen, K. T. et al., "Genetically engineered lipopeptide antibiotics related to A54145 and daptomycin with improved properties", *Antimicrob. Agents Chemother.* 2010 April; 54(4):1404-1413.

[0008] Pulmonary surfactant, a primary component of epithelial lining fluid, is a complex lipid-and-protein mixture that coats the interior surface of the airway, reducing surface tension within the alveoli. Surfactant is composed primarily of dipalmitoylphosphatidylcholine (~80% in all mammalian species), along with significant amounts of phosphatidylglycerol (PG) and smaller amounts of minor phospholipids, neutral lipids, and cholesterol. There are 4 protein components: hydrophilic proteins SP-A and SP-D and hydrophobic proteins SP-B and SP-C. Goerke, J., "Pulmonary Surfactant: functions and molecular composition", *Biochim. Biophys. Acta.* 1998; 1408:79-89. Daptomycin is inserted into artificial membrane vesicles composed of phosphatidylcholine (PC) and PC/PG. Lakey J. H. et al., "Fluorescence indicates a calcium-dependent interaction between the lipopeptide antibiotic LY146032 and phospholipid membranes," *Biochemistry* 1988; 27:4639-45; Jung, D. et al., "Structural transitions as determinants of the action of the calcium-dependent antibiotic daptomycin", *Chem. Biol.* 2004; 11:949-57.

[0009] Thus, to the extent that otherwise effective antibiotics are inhibited by factors present in the organ or tissue that is the site of the infection, such as pulmonary surfactant in the case of infections of the lungs or other airways and more generally of the respiratory tract, a treatment regimen

that would restore and even augment activity of such antibiotics would be of commercial and public health value.

[0010] In addition to daptomycin discussed above, other antibiotics that are known to be inhibited by pulmonary surfactant include without limitation: tobramycin, an aminoglycoside used to treat infections caused by the gram-negative bacterium *Pseudomonas aeruginosa*, a common cause of pneumonia (van't Veen, A. et al., "Influence of pulmonary surfactant on in vitro bactericidal activities of amoxicillin, ceftazidime, and tobramycin", *Antimicrob. Agents Chemother.* 39:329-333 (1995)), and colistin, a cyclic lipopeptide (polymyxin) broadly active against gram-negative bacteria, including *P. aeruginosa*. Schwameis, R. et al., "Effect of Pulmonary surfactant on antimicrobial activity in vitro", *Antimicrob. Agents Chemother.* 57(10):5151-54 (2013).

[0011] To address the need for new antimicrobials with novel mechanisms, researchers are investigating a variety of drugs and biologics. One such class of antimicrobial agents includes lysins. Lysins are cell wall peptidoglycan hydrolases, which act as "molecular scissors" to degrade the peptidoglycan meshwork responsible for maintaining cell shape and for withstanding internal osmotic pressure. Degradation of peptidoglycan results in osmotic lysis. However, lysins, typically, have not been effective against Gram-negative bacteria, at least in part, due to the presence of an outer membrane (OM), which is absent in Gram-positive bacteria and which limits access to subjacent peptidoglycan. Modified lysins ("artilysins") have also been developed. These agents, which contain lysins fused to specific α-helical domains with polycationic, amphipathic, and hydrophobic features, are capable of translocating across the OM. However, artilysins typically exhibit low in vivo activity.

[0012] Although recent publications have described novel lysins that may be used against Gram-negative bacteria with varying levels of efficacy in vivo, there remains a continuing medical need for additional antibacterials that retain activity in human blood matrices or pulmonary surfactant to target MDR *P. aeruginosa* and other Gram-negative bacteria for the treatment of invasive infections.

SUMMARY

[0013] The present application is directed to novel polypeptide constructs comprising lysins and antimicrobial peptides (AMP) that can be used, for example, to treat bacterial infections, including infections caused by Gram-negative bacteria, particularly multi-drug resistant Gram-negative bacteria, including, but not limited to *Pseudomonas aeruginosa*. Newly identified lysins and variants thereof, as well as variants of other lysins are also provided. As described herein, the lysin-AMP polypeptide constructs, newly obtained lysins and variant lysins may be included in pharmaceutical compositions that can be used, for example, to treat bacterial infections. Also provided herein, inter alia, are methods for using the lysin-AMP polypeptide constructs, newly identified lysins and variant lysins for treating bacterial infections, augmenting the efficacy of antibiotics and, generally, inhibiting the growth, reducing the population, or killing Gram-negative bacteria, such as *P. aeruginosa*. Lysin variant polypeptides and polynucleotides encoding the constructs and lysin variants are also provided. In certain embodiments, the lysin-AMP polypeptide constructs, newly obtained lysins and variant lysins may be used to treat bacterial infections in an organ or tissue in which pulmonary surfactant is present, such as, for example, pneumonia (including hospital acquired pneumonia) and cystic fibrosis. In other embodiments, the lysin-AMP polypeptide constructs, newly obtained lysins and variant lysins may be used to treat Gram-negative bacterial infections that are associated with biofilms.

[0014] In one aspect, the present disclosure is directed to a lysin-AMP polypeptide construct comprising: (a) a first component comprising the polypeptide sequence of: (i) SEQ ID NO: 118 (GN202); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of SEQ ID NO: 118; or (iii) an active fragment of SEQ ID NO: 118 (GN202); and (b) a second component comprising the polypeptide sequence of: (i) at least one antimicrobial peptide (AMP), wherein the at least one AMP comprises the polypeptide sequence of SEQ ID NO: 114 (FIRL).

[0015] The present disclosure also provides an isolated polynucleotide comprising a nucleic acid molecule encoding a lysin-antimicrobial peptide (AMP) polypeptide construct, the nucleic acid molecule comprising: (a) a first nucleic acid encoding the polypeptide sequence of: (i) SEQ ID NO: 118 (GN202); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of SEQ ID NO: 118; or (iii) an active fragment of SEQ ID NO: 118 (GN202); and (b) a second nucleic acid encoding the polypeptide sequence of: (i) at least one antimicrobial peptide (AMP), wherein the at least one AMP comprises the polypeptide sequence of SEQ ID NO: 114 (FIRL).

[0016] In another aspect, the present disclosure is directed to a method of treating a bacterial infection caused by a Gram-negative bacteria, which method comprises: administering to a subject diagnosed with, at risk for, or exhibiting symptoms of a bacterial infection, a pharmaceutical composition comprising a lysin-antimicrobial peptide (AMP) polypeptide construct and a pharmaceutically acceptable carrier, wherein the lysin-AMP polypeptide construct comprises: (a) a first component comprising the polypeptide sequence of: (i) SEQ ID NO: 118 (GN202); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of SEQ ID NO: 118; or (iii) an active fragment of SEQ ID NO: 118 (GN202); and (b) a second component comprising the polypeptide sequence of: (i) at least one antimicrobial peptide (AMP), wherein the at least one AMP comprises the polypeptide sequence of SEQ ID NO: 114 (FIRL).

[0017] The present disclosure also provides a method of preventing, disrupting or eradicating a Gram-negative bacterial biofilm comprising: administering a lysin-AMP polypeptide construct in an amount effective to kill Gram-negative bacteria in a biofilm to a subject in need thereof, wherein the lysin-AMP polypeptide construct comprises (a) a first component comprising the polypeptide sequence of: (i) SEQ ID NO: 118 (GN202); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of SEQ ID NO: 118; or (iii) an active fragment of SEQ ID NO: 118 (GN202); and (b) a second component comprising the polypeptide sequence of: (i) at least one antimicrobial peptide (AMP), wherein the at least one AMP comprises the polypeptide sequence of SEQ ID NO: 114 (FIRL).

[0018] In another aspect, the present disclosure is directed to a lysin-AMP polypeptide construct comprising: (a) a first

component comprising the polypeptide sequence of: (i) a lysin selected from the group consisting of GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN76 (SEQ ID NO: 203), GN4 (SEQ ID NO: 74), GN146 (SEQ ID NO: 78), GN14 (SEQ ID NO: 124), GN37 (SEQ ID NO: 84) optionally with a single pI-increasing mutation, GN316 (SEQ ID NO: 22) optionally with a single point mutation, lysin Pap2_gp17 (SEQ ID NO: 96), GN329 (SEQ ID NO: 26), GN424 (SEQ ID NO: 56), GN202 (SEQ ID NO: 118), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN333 (SEQ ID NO: 28), GN485 (SEQ ID NO: 68), GN123 (SEQ ID NO: 173) and GN121 (SEQ ID NO: 175); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 203, 74, 78, 124, 84, 22, 96, 26, 56, 118, 58, 60, 64, 66, 28, 68, 173 or 175; or (iii) an active fragment of the lysin; and (b) a second component comprising the polypeptide sequence of: (i) at least one antimicrobial peptide (AMP) selected from the group consisting of Chp1 (SEQ ID NO: 133), Chp2 (SEQ ID NO: 70), CPAR39 (SEQ ID NO: 135), Chp3 (SEQ ID NO: 137), Chp4 (SEQ ID NO: 102), Chp6 (SEQ ID NO: 106), Chp7 (SEQ ID NO: 139), Chp8 (SEQ ID NO: 141), Chp9 (SEQ ID NO: 143), Chp10 (SEQ ID NO: 145), Chp11 (SEQ ID NO: 147), Chp12 (SEQ ID NO: 149), Gkh1 (SEQ ID NO: 151), Gkh2 (SEQ ID NO: 90), Unp1 (SEQ ID NO: 153), Ecp1 (SEQ ID NO: 155), Ecp2 (SEQ ID NO: 104), Tma1 (SEQ ID NO: 157), Osp1 (SEQ ID NO: 108), Unp2 (SEQ ID NO: 159), Unp3 (SEQ ID NO: 161), Gkh3 (SEQ ID NO: 163), Unp5 (SEQ ID NO: 165), Unp6 (SEQ ID NO: 167), Spi1 (SEQ ID NO: 169), Spi2 (SEQ ID NO: 171), Ecp3 (SEQ ID NO: 177), Ecp4 (SEQ ID NO: 179), ALCES1 (SEQ ID NO: 181), AVQ206 (SEQ ID NO: 183), AVQ244 (SEQ ID NO: 185), CDL907 (SEQ ID NO: 187), AGT915 (SEQ ID NO: 189), HH3930 (SEQ ID NO: 191), Fen7875 (SEQ ID NO: 193), SBR77 (SEQ ID NO: 195), Bdp1 (SEQ ID NO: 197), LVP1 (SEQ ID NO: 199), Lvp2 (SEQ ID NO: 201), an esculentin fragment (SEQ ID NO: 80), RI12 (SEQ ID NO: 88), TI15 (SEQ ID NO: 94), RI18 (SEQ ID NO: 92), FIRL (SEQ ID NO: 114), a fragment of LPS binding protein (SEQ ID NO: 76), RR12whydro (SEQ ID NO: 110), RI18 peptide derivative (SEQ ID NO: 131) and cationic peptide (SEQ ID NO: 120) or (ii) a polypeptide having AMP activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 133, 70, 135, 137, 102, 106, 139, 141, 143, 145, 147, 149, 151, 90, 153, 155, 104, 157, 108, 159, 161, 163, 165, 167, 169, 171, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 80, 88, 94, 92, 114, 76, 110, 131 and 120, wherein the lysin-AMP polypeptide construct comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0019] In another aspect, the present disclosure is directed to an isolated polypeptide comprising a lysin selected from the group consisting of GN121 (SEQ ID NO: 175), GN217 lysin (SEQ ID NO: 8), GN394 lysin (SEQ ID NO: 48), GN396 lysin (SEQ ID NO: 50), GN408 lysin (SEQ ID NO: 52), GN418 lysin (SEQ ID NO: 54), GN428 (SEQ ID NO: 60), and GN486 (SEQ ID NO: 66) or an active fragment thereof, wherein the lysin or active fragment thereof inhibits *P. aeruginosa* bacterial growth, reduces a *P. aeruginosa* bacterial population and/or kills *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0020] In another aspect, the present disclosure is directed to (i) a lysin-AMP polypeptide construct comprising GN75 (SEQ ID NO: 212), GN83 (SEQ ID NO: 216) or a dispersin-like molecule, such as GN80 (SEQ ID NO: 214) or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of SEQ ID NOS: 212, 216 or 214 (iii) an active fragment thereof, wherein the lysin or active fragment thereof inhibits *P. aeruginosa* bacterial growth, reduces a *P. aeruginosa* bacterial population and/or kills *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0021] The present disclosure is also directed to an isolated polynucleotide comprising a nucleic acid molecule encoding a lysin-antimicrobial peptide (AMP) polypeptide construct, the nucleic acid molecule comprising:

(a) a first nucleic acid molecule encoding a first component comprising: (i) a lysin selected from the group consisting of GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN76 (SEQ ID NO: 203), GN4 (SEQ ID NO: 74), GN146 (SEQ ID NO: 78), GN14 (SEQ ID NO: 124), GN37 (SEQ ID NO: 84) optionally with a single pI-increasing mutation, GN316 (SEQ ID NO: 22) optionally with a single point mutation, lysin Pap2_gp17 (SEQ ID NO: 96), GN329 (SEQ ID NO: 26), GN424 (SEQ ID NO: 56), GN202 (SEQ ID NO: 118), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN333 (SEQ ID NO: 28), GN485 (SEQ ID NO: 68), GN123 (SEQ ID NO: 173) and GN121 (SEQ ID NO: 175); or (ii) a polypeptide having lysin activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 203, 74, 78, 124, 84, 22, 96, 26, 56, 118, 58, 60, 64, 66, 28, 68, 173 or 175; or (iii) an active fragment of the lysin; and

(b) a second nucleic acid molecule encoding a second component comprising: (i) at least one antimicrobial peptide (AMP) selected from the group consisting of Chp1 (SEQ ID NO: 133), Chp2 (SEQ ID NO: 70), CPAR39 (SEQ ID NO: 135), Chp3 (SEQ ID NO: 137), Chp4 (SEQ ID NO: 102), Chp6 (SEQ ID NO: 106), Chp7 (SEQ ID NO: 139), Chp8 (SEQ ID NO: 141), Chp9 (SEQ ID NO: 143), Chp10 (SEQ ID NO: 145), Chp11 (SEQ ID NO: 147), Chp12 (SEQ ID NO: 149), Gkh1 (SEQ ID NO: 151), Gkh2 (SEQ ID NO: 90), Unp1 (SEQ ID NO: 153), Ecp1 (SEQ ID NO: 155), Ecp2 (SEQ ID NO: 104), Tma1 (SEQ ID NO: 157), Osp1 (SEQ ID NO: 108), Unp2 (SEQ ID NO: 159), Unp3 (SEQ ID NO: 161), Gkh3 (SEQ ID NO: 163), Unp5 (SEQ ID NO: 165), Unp6 (SEQ ID NO: 167), Spi1 (SEQ ID NO: 169), Spi2 (SEQ ID NO: 171), Ecp3 (SEQ ID NO: 177), Ecp4 (SEQ ID NO: 179), ALCES1 (SEQ ID NO: 181), AVQ206 (SEQ ID NO: 183), AVQ244 (SEQ ID NO: 185), CDL907 (SEQ ID NO: 187), AGT915 (SEQ ID NO: 189), HEI3930 (SEQ ID NO: 191), Fen7875 (SEQ ID NO: 193), SBR77 (SEQ ID NO: 195), Bdp1 (SEQ ID NO: 197), LVP1 (SEQ ID NO: 199), Lvp2 (SEQ ID NO: 201), an esculentin fragment (SEQ ID NO: 80), RI12 (SEQ ID NO: 88), TI15 (SEQ ID NO: 94), RI18 (SEQ ID NO: 92), FIRL (SEQ ID NO: 114), a fragment of LPS binding protein (SEQ ID NO: 76), RR12whydro (SEQ ID NO: 110), RI18 peptide deriva-

tive (SEQ ID NO: 131) and cationic peptide (SEQ ID NO: 120) or (ii) a polypeptide having AMP activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 133, 70, 135, 137, 102, 106, 139, 141, 143, 145, 147, 149, 151, 90, 153, 155, 104, 157, 108, 159, 161, 163, 165, 167, 169, 171, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 80, 88, 94, 92, 114, 76, 110, 131 and 120, wherein the lysin-AMP polypeptide construct comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0022] In yet another aspect, the present disclosure is directed to an isolated polynucleotide sequence comprising a nucleic acid molecule encoding a lysin selected from the group consisting of GN121 (SEQ ID NO: 175), GN217 lysin (SEQ ID NO: 8), GN394 lysin (SEQ ID NO: 48), GN396 lysin (SEQ ID NO: 50), GN408 lysin (SEQ ID NO: 52), GN418 lysin (SEQ ID NO: 54), GN428 (SEQ ID NO: 60), and GN486 (SEQ ID NO: 66) or an active fragment thereof, wherein the lysin or active fragment thereof inhibits *P. aeruginosa* bacterial growth, reduces a *P. aeruginosa* bacterial population and/or kills *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0023] In another aspect, the present disclosure is directed to (i) an isolated polynucleotide comprising a nucleic acid molecule encoding a lysin-AMP polypeptide construct comprising GN75 (SEQ ID NO: 212), GN83 (SEQ ID NO: 216) or a dispersin-like molecule, such as GN80 (SEQ ID NO: 214) or (ii) a polypeptide having lysin activity and having at least 80% identity to SEQ ID NOS: 212, 216 or 214 or (iii) an active fragment of SEQ ID NOS: 212, 216 or 214, wherein the lysin-AMP polypeptide construct comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0024] In one aspect, the present disclosure is directed to a pharmaceutical composition comprising an isolated lysin and/or a lysin-antimicrobial peptide (AMP) polypeptide construct and a pharmaceutically acceptable carrier,

[0025] wherein the isolated lysin comprises at least one of: (i) GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN121 (SEQ ID NO: 175), GN123 (SEQ ID NO: 173), GN217 (SEQ ID NO: 8), GN316 variant (SEQ ID NO: 24), GN316 (SEQ ID NO: 22), GN329 (SEQ ID NO: 26), GN333 (SEQ ID NO: 28), GN394 (SEQ ID NO: 48), GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52), GN418 (SEQ ID NO: 54), GN424 (SEQ ID NO: 56), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN485 (SEQ ID NO: 68), Lysin PaP2_gp17 (SEQ ID NO: 96), (ii) an active fragment thereof, or (iii) a polypeptide having lysin activity and at least 80% sequence identity with the polypeptide sequence of at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 212, 216, 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

[0026] wherein the lysin-AMP polypeptide construct comprises: (a) a first component comprising the polypeptide sequence of: (i) a lysin selected from the group consisting of GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN76 (SEQ ID NO: 203), GN4 (SEQ ID NO: 74), GN146 (SEQ ID NO: 78), GN14 (SEQ ID NO: 124), GN37 (SEQ ID NO: 84) optionally with a single pI-increasing mutation, GN316 (SEQ ID NO: 22) optionally with a single point mutation, lysin Pap2_gp17 (SEQ ID NO: 96), GN329 (SEQ ID NO: 26), GN424 (SEQ ID NO: 56), GN202 (SEQ ID NO: 118), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN333 (SEQ ID NO: 28), GN485 (SEQ ID NO: 68), GN123 (SEQ ID NO: 173) and GN121 (SEQ ID NO: 175); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 203, 74, 78, 124, 84, 22, 96, 26, 56, 118, 58, 60, 64, 66, 28, 68, 173 or 175; or (iii) an active fragment of the lysin; and (b) a second component comprising the polypeptide sequence of: (i) at least one antimicrobial peptide (AMP) selected from the group consisting of Chp1 (SEQ ID NO: 133), Chp2 (SEQ ID NO: 70), CPAR39 (SEQ ID NO: 135), Chp3 (SEQ ID NO: 137), Chp4 (SEQ ID NO: 102), Chp6 (SEQ ID NO: 106), Chp7 (SEQ ID NO: 139), Chp8 (SEQ ID NO: 141), Chp9 (SEQ ID NO: 143), Chp10 (SEQ ID NO: 145), Chp11 (SEQ ID NO: 147), Chp12 (SEQ ID NO: 149), Gkh1 (SEQ ID NO: 151), Gkh2 (SEQ ID NO: 90), Unp1 (SEQ ID NO: 153), Ecp1 (SEQ ID NO: 155), Ecp2 (SEQ ID NO: 104), Tma1 (SEQ ID NO: 157), Osp1 (SEQ ID NO: 108), Unp2 (SEQ ID NO: 159), Unp3 (SEQ ID NO: 161), Gkh3 (SEQ ID NO: 163), Unp5 (SEQ ID NO: 165), Unp6 (SEQ ID NO: 167), Spi1 (SEQ ID NO: 169), Spi2 (SEQ ID NO: 171), Ecp3 (SEQ ID NO: 177), Ecp4 (SEQ ID NO: 179), ALCES1 (SEQ ID NO: 181), AVQ206 (SEQ ID NO: 183), AVQ244 (SEQ ID NO: 185), CDL907 (SEQ ID NO: 187), AGT915 (SEQ ID NO: 189), HH3930 (SEQ ID NO: 191), Fen7875 (SEQ ID NO: 193), SBR77 (SEQ ID NO: 195), Bdp1 (SEQ ID NO: 197), LVP1 (SEQ ID NO: 199), Lvp2 (SEQ ID NO: 201), an esculentin fragment (SEQ ID NO: 80), RI12 (SEQ ID NO: 88), TI15 (SEQ ID NO: 94), RI18 (SEQ ID NO: 92), FIRL (SEQ ID NO: 114), a fragment of LPS binding protein (SEQ ID NO: 76), RR12whydro (SEQ ID NO: 110), RI18 peptide derivative (SEQ ID NO: 131) and cationic peptide (SEQ ID NO: 120) or (ii) a polypeptide having AMP activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 133, 70, 135, 137, 102, 106, 139, 141, 143, 145, 147, 149, 151, 90, 153, 155, 104, 157, 108, 159, 161, 163, 165, 167, 169, 171, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 80, 88, 94, 92, 114, 76, 110, 131 and 120, wherein the pharmaceutical composition comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0027] In another aspect, the present disclosure is directed to a pharmaceutical composition comprising (i) a lysin-AMP polypeptide construct comprising GN75 (SEQ ID NO: 212), GN83 (SEQ ID NO: 216) or a dispersin-like molecule, such as GN80 (SEQ ID NO: 214) or (ii) a polypeptide having lysin activity and having at least 80% identity to SEQ ID NOS: 212, 216 or 214 or (iii) an active fragment of SEQ ID NOS: 212, 216 or 214, wherein the lysin-AMP polypeptide construct comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P.*

aeruginosa bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0028] In yet another aspect, the present disclosure is directed to a method of treating a bacterial infection caused by a Gram-negative bacteria, wherein the Gram-negative bacteria comprises *P. aeruginosa* and optionally one or more additional species of Gram-negative bacteria, which method comprises: administering to a subject diagnosed with, at risk for, or exhibiting symptoms of a bacterial infection, a pharmaceutical composition as described herein. In certain embodiments, the bacterial infection is in an organ or tissue in which pulmonary surfactant is present, such as in the lungs or the airways.

[0029] In yet another aspect, the present disclosure is directed to a method of preventing or treating a bacterial infection comprising: co-administering to a subject diagnosed with, at risk for, or exhibiting symptoms of a bacterial infection, a combination of a first effective amount of a pharmaceutical composition as described herein, and a second effective amount of an antibiotic suitable for the treatment of a Gram-negative bacterial infection.

[0030] In one aspect, the present disclosure is directed to a method for augmenting the efficacy of an antibiotic suitable for the treatment of a Gram-negative bacterial infection, comprising: co-administering the antibiotic in combination with a composition containing an effective amount of an isolated lysin and/or a lysin-antimicrobial peptide (AMP) polypeptide construct,

[0031] wherein the isolated lysin comprises at least one of: (i) GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN121 (SEQ ID NO 175), GN123 (SEQ ID NO: 173), GN217 (SEQ ID NO: 8), GN316 variant (SEQ ID NO: 24), GN316 (SEQ ID NO: 22), GN329 (SEQ ID NO: 26), GN333 (SEQ ID NO: 28), GN394 (SEQ ID NO: 48), GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52), GN418 (SEQ ID NO: 54), GN424 (SEQ ID NO: 56), GN425 (SEQ ID NO:58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN485 (SEQ ID NO: 68), Lysin PaP2_gp17 (SEQ ID NO: 96), or (ii) an active fragment thereof, or (iii) a polypeptide having lysin activity and at least 80% sequence identity with the polypeptide sequence of at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

[0032] wherein the lysin-AMP polypeptide construct comprises: (a) a first component comprising the polypeptide sequence of: (i) a lysin selected from the group consisting of GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN76 (SEQ ID NO: 203), GN4 (SEQ ID NO: 74), GN146 (SEQ ID NO: 78), GN14 (SEQ ID NO: 124), GN37 (SEQ ID NO: 84) optionally with a single pI-increasing mutation, GN316 (SEQ ID NO: 22) optionally with a single point mutation, lysin Pap2_gp17 (SEQ ID NO: 96), GN329 (SEQ ID NO: 26), GN424 (SEQ ID NO: 56), GN202 (SEQ ID NO: 118), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN333 (SEQ ID NO: 28), GN485 (SEQ ID NO: 68), GN123 (SEQ ID NO: 173) and GN121 (SEQ ID NO: 175); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 203, 74, 78, 124, 84, 22, 26; 56, 118, 58, 60, 64, 66, 28, 68, 173 or 175; or (iii) an active fragment of the lysin; and (b) a second component comprising the polypeptide sequence of: (i) at least one antimicrobial peptide (AMP) selected from the group consisting of Chp1 (SEQ ID NO: 133), Chp2 (SEQ ID NO: 70), CPAR39 (SEQ ID NO: 135), Chp3 (SEQ ID NO: 137), Chp4 (SEQ ID NO: 102), Chp6 (SEQ ID NO: 106), Chp7 (SEQ ID NO: 139), Chp8 (SEQ ID NO: 141), Chp9 (SEQ ID NO: 143), Chp10 (SEQ ID NO: 145), Chp11 (SEQ ID NO: 147), Chp12 (SEQ ID NO: 149), Gkh1 (SEQ ID NO: 151), Gkh2 (SEQ ID NO: 90), Unp1 (SEQ ID NO: 153), Ecp1 (SEQ ID NO: 155), Ecp2 (SEQ ID NO: 104), Tma1 (SEQ ID NO: 157), Osp1 (SEQ ID NO: 108), Unp2 (SEQ ID NO: 159), Unp3 (SEQ ID NO: 161), Gkh3 (SEQ ID NO: 163), Unp5 (SEQ ID NO: 165), Unp6 (SEQ ID NO: 167), Spi1 (SEQ ID NO: 169), Spi2 (SEQ ID NO: 171), Ecp3 (SEQ ID NO: 177), Ecp4 (SEQ ID NO: 179), ALCES1 (SEQ ID NO: 181), AVQ206 (SEQ ID NO: 183), AVQ244 (SEQ ID NO: 185), CDL907 (SEQ ID NO: 187), AGT915 (SEQ ID NO: 189), HH3930 (SEQ ID NO: 191), Fen7875 (SEQ ID NO: 193), SBR77 (SEQ ID NO: 195), Bdp1 (SEQ ID NO: 197), LVP1 (SEQ ID NO: 199), Lvp2 (SEQ ID NO: 201), an esculentin fragment (SEQ ID NO: 80), RI12 (SEQ ID NO: 88), TI15 (SEQ ID NO: 94), RI18 (SEQ ID NO: 92), FIRL (SEQ ID NO: 114), a fragment of LPS binding protein (SEQ ID NO: 76), RR12whydro (SEQ ID NO: 110), RI18 peptide derivative (SEQ ID NO: 131) and cationic peptide (SEQ ID NO: 120) or (ii) a polypeptide having AMP activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 133, 70, 135, 137, 102, 106, 139, 141, 143, 145, 147, 149, 151, 90, 153, 155, 104, 157, 108, 159, 161, 163, 165, 167, 169, 171, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 80, 88, 94, 92, 114, 76, 110, 131 and 120, wherein the composition comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant, and wherein administration of the combination is more effective in inhibiting the growth, or reducing the population, or killing the Gram-negative bacteria in the presence or absence or both in the presence and absence of human serum or in the presence of pulmonary surfactant than administration of either the antibiotic or the lysin or lysin-AMP polypeptide construct individually.

[0033] In another aspect, the present disclosure is directed to a method for augmenting the efficacy of an antibiotic suitable for the treatment of a Gram-negative bacterial infection, comprising: co-administering the antibiotic in combination with a composition containing an effective amount of (i) a lysin-AMP polypeptide construct comprising GN75 (SEQ ID NO: 212), GN83 (SEQ ID NO: 216) or a dispersin-like molecule, such as GN80 (SEQ ID NO: 214) or (ii) a polypeptide having lysin activity and having at least 80% identity to SEQ ID NOS: 212, 216 or 214 or (iii) an active fragment of SEQ ID NOS: 212, 216 or 214, wherein the lysin-AMP polypeptide construct comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant,

[0034] and wherein administration of the combination is more effective in inhibiting the growth, or reducing the

population, or killing the Gram-negative bacteria in the presence or absence or both in the presence and absence of human serum or in the presence of pulmonary surfactant than administration of either the antibiotic or the lysin or lysin-AMP polypeptide construct individually.

[0035] In another aspect, the present disclosure is directed to a method of inhibiting the growth, or reducing the population, or killing of at least one species of Gram-negative bacteria, wherein the at least one species of Gram-negative bacteria is *P. aeruginosa* and optionally one or more additional species of Gram-negative bacteria, which method comprises: contacting the bacteria with a composition containing an effective amount an isolated lysin and/or a lysin-antimicrobial peptide (AMP) polypeptide construct,

[0036] wherein the isolated lysin comprises at least one of: (i) GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN121 (SEQ ID NO: 175), GN123 (SEQ ID NO: 173), GN217 (SEQ ID NO: 8), GN316 variant (SEQ ID NO: 24), GN316 (SEQ ID NO: 22), GN329 (SEQ ID NO: 26), GN333 (SEQ ID NO: 28), GN394 (SEQ ID NO: 48), GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52), GN418 (SEQ ID NO: 54), GN424 (SEQ ID NO: 56), GN425 (SEQ ID NO:58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN485 (SEQ ID NO: 68), Lysin PaP2_gp17 (SEQ ID NO: 96), or (ii) an active fragment thereof, or (iii) a polypeptide having lysin activity and at least 80% sequence identity with the polypeptide sequence of at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

[0037] wherein the lysin-AMP polypeptide construct comprises: (a) a first component comprising the polypeptide sequence of: (i) a lysin selected from the group consisting of GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN76 (SEQ ID NO: 203), GN4 (SEQ ID NO: 74), GN146 (SEQ ID NO: 78), GN14 (SEQ ID NO: 124), GN37 (SEQ ID NO: 84) optionally with a single pI-increasing mutation, GN316 (SEQ ID NO: 22) optionally with a single point mutation, lysin Pap2_gp17 (SEQ ID NO: 96), GN329 (SEQ ID NO: 26), GN424 (SEQ ID NO: 56), GN202 (SEQ ID NO: 118), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN333 (SEQ ID NO: 28), GN485 (SEQ ID NO: 68), GN123 (SEQ ID NO: 173) and GN121 (SEQ ID NO: 175); or (ii) a polypeptide having lysin activity and having at least 80% sequence identity with the polypeptide sequence of at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 203, 74, 78, 124, 84, 22, 96, 26, 56, 118, 58, 60, 64, 66, 28, 68, 173 or 175; or (iii) an active fragment of the lysin; and (b) a second component comprising the polypeptide sequence of: (i) at least one antimicrobial peptide (AMP) selected from the group consisting of Chp1 (SEQ ID NO: 133), Chp2 (SEQ ID NO: 70), CPAR39 (SEQ ID NO: 135), Chp3 (SEQ ID NO: 137), Chp4 (SEQ ID NO: 102), Chp6 (SEQ ID NO: 106), Chp7 (SEQ ID NO: 139), Chp8 (SEQ ID NO: 141), Chp9 (SEQ ID NO: 143), Chp10 (SEQ ID NO: 145), Chp11 (SEQ ID NO: 147), Chp12 (SEQ ID NO: 149), Gkh1 (SEQ ID NO: 151), Gkh2 (SEQ ID NO: 90), Unp1 (SEQ ID NO: 153), Ecp1 (SEQ ID NO: 155), Ecp2 (SEQ ID NO: 104), Tma1 (SEQ ID NO: 157), Osp1 (SEQ ID NO: 108), Unp2 (SEQ ID NO: 159), Unp3 (SEQ ID NO: 161), Gkh3 (SEQ ID NO: 163), Unp5 (SEQ ID NO: 165), Unp6 (SEQ ID NO: 167), Spi1 (SEQ ID NO: 169), Spi2 (SEQ ID NO: 171), Ecp3 (SEQ ID NO: 177), Ecp4 (SEQ ID NO: 179), ALCES1 (SEQ ID NO: 181), AVQ206 (SEQ ID NO: 183), AVQ244 (SEQ ID NO: 185), CDL907 (SEQ ID NO: 187), AGT915 (SEQ ID NO: 189), HH3930 (SEQ ID NO: 191), Fen7875 (SEQ ID NO: 193), SBR77 (SEQ ID NO: 195), Bdp1 (SEQ ID NO: 197), LVP1 (SEQ ID NO: 199), Lvp2 (SEQ ID NO: 201), an esculentin fragment (SEQ ID NO: 80), RI12 (SEQ ID NO: 88), 1115 (SEQ ID NO: 94), RI18 (SEQ ID NO: 92), FIRL (SEQ ID NO: 114), a fragment of LPS binding protein (SEQ ID NO: 76), RR12whydro (SEQ ID NO: 110), RI18 peptide derivative (SEQ ID NO: 131) and cationic peptide (SEQ ID NO: 120) or (ii) a polypeptide having AMP activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 133, 70, 135, 137, 102, 106, 139, 141, 143, 145, 147, 149, 151, 90, 153, 155, 104, 157, 108, 159, 161, 163, 165, 167, 169, 171, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 80, 88, 94, 92, 114, 76, 110, 131 and 120, and wherein the composition comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

[0038] In another aspect, the present disclosure is directed to a method of inhibiting the growth, or reducing the population, or killing of at least one species of Gram-negative bacteria, wherein the at least one species of Gram-negative bacteria is *P. aeruginosa* and optionally one or more additional species of Gram-negative bacteria, which method comprises: contacting the bacteria with a composition containing an effective amount (i) a lysin-AMP polypeptide construct comprising GN75 (SEQ ID NO: 212), GN83 (SEQ ID NO: 216) or a dispersin-like molecule, such as GN80 (SEQ ID NO: 214) or (ii) a polypeptide having lysin activity and having at least 80% identity to SEQ ID NOS: 212, 216 or 214 or (iii) an active fragment of SEQ ID NOS: 212, 216 or 214, wherein the lysin-AMP polypeptide construct comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum or in the presence of pulmonary surfactant.

BRIEF DESCRIPTION OF THE DRAWINGS

[0039] FIG. **1** depicts three-dimensional models predicted by I-Tasser for structures of *Chlamydia* phage peptide (Chp) family members Chp1, Chp 2, Chp4, Chp5, Chp6, Chp7, Ecp1, Ecp2, and Osp1. The human innate immune effector peptide LL-37 is included for comparison. Alpha helical structures are evident, and the top terminal is generally the N-terminal.

[0040] FIG. **2**A is a graph showing the percent relative fluorescence unit (RFU) over time for *P. aeruginosa* in the presence of N-phenyl-1-napthylamine (NPN) and buffer, GN121, or GN351, as described in Example 6.

[0041] FIG. **2**B is a graph showing the percent RFU over time for *P. aeruginosa* in the presence of NPN and buffer, GN428, or GN370, as described in Example 6.

[0042] FIG. **3** is a series of photomicrographs showing microscopic analysis (×2000 magnification) of *Pseudomonas aeruginosa* strain 1292 treated for 15 minutes with GN121 (10 μg/mL) or a buffer control ("untreated") in 100% human serum. Samples were stained using the Live/Dead

Cell Viability Kit (ThermoFisher) and examined by both differential interference contrast (DIC) and fluorescence microscopy. The photomicrographs show an absence of dead bacteria in the untreated row and a reduction of live bacteria in the treated row, as described in Example 7.

[0043] FIGS. **4**A-**4**E show the fold change in GN lysin and Ciprofloxacin needed to achieve a Minimal Inhibitory Concentration (MIC) for *P. aeruginosa* (strain WC-452) over 21 day serial passage as described in Example 9: GN121 (FIG. **4**A), GN351 (FIG. **4**B), GN370 (FIG. **4**C), GN428 (FIG. **4**D) and Ciprofloxacin (FIG. **4**E).

[0044] FIG. **5** depicts the MIC values for GN370 against *P. aeruginosa* isolates as described in Example 17.

DETAILED DESCRIPTION

Definitions

[0045] As used herein, the following terms and cognates thereof shall have the following meanings unless the context clearly indicates otherwise:

[0046] "Carrier" refers to a solvent, additive, excipient, dispersion medium, solubilizing agent, coating, preservative, isotonic and absorption delaying agent, surfactant, propellant, diluent, vehicle and the like with which an active compound is administered. Such carriers can be sterile liquids, such as water, saline solutions, aqueous dextrose solutions, aqueous glycerol solutions, and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil, and the like.

[0047] "Pharmaceutically acceptable carrier" refers to any and all solvents, additives, excipients, dispersion media, solubilizing agents, coatings, preservatives, isotonic and absorption delaying agents, surfactants, propellants, diluents, vehicles and the like that are physiologically compatible. The carrier(s) must be "acceptable" in the sense of not being deleterious to the subject to be treated in amounts typically used in medicaments. Pharmaceutically acceptable carriers are compatible with the other ingredients of the composition without rendering the composition unsuitable for its intended purpose. Furthermore, pharmaceutically acceptable carriers are suitable for use with subjects as provided herein without undue adverse side effects (such as toxicity, irritation, and allergic response). Side effects are "undue" when their risk outweighs the benefit provided by the composition. Non-limiting examples of pharmaceutically acceptable carriers or excipients include any of the standard pharmaceutical carriers such as phosphate buffered saline solutions, water, and emulsions such as oil/water emulsions and microemulsions. Suitable pharmaceutical carriers are described, for example, in Remington's Pharmaceutical Sciences by E. W. Martin, 18th Edition. The pharmaceutically acceptable carrier may be a carrier that does not exist in nature.

[0048] "Bactericidal" or "bactericidal activity" refers to the property of causing the death of bacteria or capable of killing bacteria to an extent of at least a 3-log10 (99.9%) or better reduction among an initial population of bacteria over an 18-24 hour period.

[0049] "Bacteriostatic" or "bacteriostatic activity" refers to the property of inhibiting bacterial growth, including inhibiting growing bacterial cells, thus causing a 2-log 10 (99%) or better and up to just under a 3-log reduction among an initial population of bacteria over an 18-24 hour period.

[0050] "Antibacterial" refers to both bacteriostatic and bactericidal agents.

[0051] "Antibiotic" refers to a compound having properties that have a negative effect on bacteria, such as lethality or reduction of growth. An antibiotic can have a negative effect on Gram-positive bacteria, Gram-negative bacteria, or both. By way of example, an antibiotic can affect cell wall peptidoglycan biosynthesis, cell membrane integrity, or DNA or protein synthesis in bacteria. Nonlimiting examples of antibiotics active against Gram-negative bacteria include cephalosporins, such as ceftriaxone-cefotaxime, ceftazidime, cefepime, cefoperazone, and ceftobiprole; fluoroquinolones such as ciprofloxacin and levofloxacin; aminoglycosides such as gentamicin, tobramycin, and amikacin; piperacillin, ticarcillin, imipenem, meropenem, doripenem, broad spectrum penicillins with or without beta-lactamase inhibitors, rifampicin, polymyxin B, and colistin.

[0052] "Drug resistant" generally refers to a bacterium that is resistant to the antibacterial activity of a drug. When used in certain ways, drug resistance may specifically refer to antibiotic resistance. In some cases, a bacterium that is generally susceptible to a particular antibiotic can develop resistance to the antibiotic, thereby becoming a drug resistant microbe or strain. A "multi-drug resistant" ("MDR") pathogen is one that has developed resistance to at least two classes of antimicrobial drugs, each used as monotherapy. For example, certain strains of *S. aureus* have been found to be resistant to several antibiotics including methicillin and/or vancomycin (Antibiotic Resistant Threats in the United States, 2013, U.S. Department of Health and Services, Centers for Disease Control and Prevention). One skilled in the art can readily determine if a bacterium is drug resistant using routine laboratory techniques that determine the susceptibility or resistance of a bacterium to a drug or antibiotic.

[0053] "Effective amount" refers to an amount which, when applied or administered in an appropriate frequency or dosing regimen, is sufficient to prevent, reduce, inhibit, or eliminate bacterial growth or bacterial burden or to prevent, reduce, or ameliorate the onset, severity, duration, or progression of the disorder being treated (for example, Gram-negative bacterial pathogen growth or infection), prevent the advancement of the disorder being treated, cause the regression of the disorder being treated, or enhance or improve the prophylactic or therapeutic effect(s) of another therapy, such as antibiotic or bacteriostatic therapy.

[0054] "Co-administer" refers to the administration of two agents, such as a lysin or lysin-AMP polypeptide and an antibiotic or any other antibacterial agent, in a sequential manner, as well as administration of these agents in a substantially simultaneous manner, such as in a single mixture/composition or in doses given separately, but nonetheless administered substantially simultaneously to the subject, for example at different times in the same day or 24-hour period. Such co-administration of two agents, such as a lysin or lysin-AMP polypeptide with one or more additional antibacterial agents can be provided as a continuous treatment lasting up to days, weeks, or months. Additionally, depending on the use, the co-administration need not be continuous or coextensive. For example, if the use were as a topical antibacterial agent to treat, e.g., a bacterial ulcer or an infected diabetic ulcer, a lysin or lysin-AMP polypeptide could be administered only initially within 24 hours of an additional antibiotic, and then the additional

antibiotic use may continue without further administration of the lysin or lysin-AMP polypeptide.

[0055] "Subject" refers to a mammal, a plant, a lower animal, a single cell organism, or a cell culture. For example, the term "subject" is intended to include organisms, e.g., prokaryotes and eukaryotes, which are susceptible to or afflicted with bacterial infections, for example Gram-positive or Gram-negative bacterial infections. Examples of subjects include mammals, e.g., humans, dogs, cows, horses, pigs, sheep, goats, cats, mice, rabbits, rats, and transgenic non-human animals. In certain embodiments, the subject is a human, e.g., a human suffering from, at risk of suffering from, or susceptible to infection by Gram-negative bacteria, whether such infection be systemic, topical or otherwise concentrated or confined to a particular organ or tissue.

[0056] "Polypeptide" is used herein interchangeably with the term "peptide" or "protein" and refers to a polymer made from amino acid residues and generally having at least about 30 amino acid residues. The term includes not only polypeptides in isolated form, but also active fragments and derivatives thereof. The term "polypeptide" also encompasses fusion proteins or fusion polypeptides comprising a lysin or AMP as described herein and maintaining, for example a lytic function. Depending on context, a polypeptide can be a naturally occurring polypeptide or a recombinant, engineered, or synthetically produced polypeptide. A particular lysin polypeptide, for example, can be, for example, derived or removed from a native protein by enzymatic or chemical cleavage, or can be prepared using conventional peptide synthesis techniques (e.g., solid phase synthesis) or molecular biology techniques (such as those disclosed in Sambrook, J. et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (1989)) or can be strategically truncated or segmented yielding active fragments, maintaining, e.g., lytic activity against the same or at least one common target bacterium.

[0057] "Fusion polypeptide" refers to an expression product resulting from the fusion of two or more nucleic acid segments, resulting in a fused expression product typically having two or more domains or segments, which typically have different properties or functionality. In a more particular sense, the term "fusion polypeptide" may also refer to a polypeptide or peptide comprising two or more heterologous polypeptides or peptides covalently linked, either directly or via an amino acid or peptide linker. The polypeptides forming the fusion polypeptide are typically linked C-terminus to N-terminus, although they can also be linked C-terminus to C-terminus, N-terminus to N-terminus, or N-terminus to C-terminus. The term "fusion polypeptide" can be used interchangeably with the term "fusion protein." The open-ended expression "a polypeptide comprising" a certain structure includes larger molecules than the recited structure, such as fusion polypeptides.

[0058] "Heterologous" refers to nucleotide, peptide, or polypeptide sequences that are not naturally contiguous. For example, in the context of the present disclosure, the term "heterologous" can be used to describe a combination or fusion of two or more peptides and/or polypeptides wherein the fusion peptide or polypeptide is not normally found in nature, such as for example a lysin or active fragment thereof and an antimicrobial peptide, including a cationic and/or a polycationic peptide, an amphipathic peptide, a sushi peptide (Ding et al. Cell Mol Life Sci., 65(7-8):1202-19 (2008)), a defensin peptide (Ganz, T. Nature Reviews Immunology 3, 710-720 (2003)), a hydrophobic peptide, which may have enhanced lytic activity.

[0059] "Active fragment" refers to a portion of a polypeptide that retains one or more functions or biological activities of the isolated polypeptide from which the fragment was taken, for example bactericidal activity against one or more Gram-negative bacteria.

[0060] "Amphipathic peptide" refers to a peptide having both hydrophilic and hydrophobic functional groups. In certain embodiments, secondary structure may place hydrophobic and hydrophilic amino acid residues at opposite sides (e.g., inner side vs outer side when the peptide is in a solvent, such as water) of an amphipathic peptide. These peptides may in certain embodiments adopt a helical secondary structure, such as an alpha-helical secondary structure.

[0061] "Cationic peptide" refers to a peptide having a high percentage of positively charged amino acid residues. In certain embodiments, a cationic peptide has a pKa-value of 8.0 or greater. The term "cationic peptide" in the context of the present disclosure also encompasses polycationic peptides that are synthetically produced peptides composed of mostly positively charged amino acid residues, such as lysine (Lys) and/or arginine (Arg) residues. The amino acid residues that are not positively charged can be neutrally charged amino acid residues, negatively charged amino acid residues, and/or hydrophobic amino acid residues.

[0062] "Hydrophobic group" refers to a chemical group such as an amino acid side chain that has low or no affinity for water molecules but higher affinity for oil molecules. Hydrophobic substances tend to have low or no solubility in water or aqueous phases and are typically apolar but tend to have higher solubility in oil phases. Examples of hydrophobic amino acids include glycine (Gly), alanine (Ala), valine (Val), Leucine (Leu), isoleucine (Ile), proline (Pro), phenylalanine (Phe), methionine (Met), and tryptophan (Trp).

[0063] "Augmenting" refers to a degree of activity of an agent, such as antimicrobial activity, that is higher than it would be otherwise. "Augmenting" encompasses additive as well as synergistic (superadditive) effects.

[0064] "Synergistic" or "superadditive" refers to a beneficial effect brought about by two substances in combination that exceeds the sum of the effects of the two agents working independently. In certain embodiments the synergistic or superadditive effect significantly, i.e., statistically significantly, exceeds the sum of the effects of the two agents working independently. One or both active ingredients may be employed at a sub-threshold level, i.e., a level at which if the active substance is employed individually produces no or a very limited effect. The effect can be measured by assays such as the checkerboard assay, described here.

[0065] "Treatment" refers to any process, action, application, therapy, or the like, wherein a subject, such as a human being, is subjected to medical aid with the object of curing a disorder, eradicating a pathogen, or improving the subject's condition, directly or indirectly. Treatment also refers to reducing incidence, alleviating symptoms, eliminating recurrence, preventing recurrence, preventing incidence, reducing the risk of incidence, improving symptoms, improving prognosis, or combinations thereof. "Treatment" may further encompass reducing the population, growth rate, or virulence of a bacteria in the subject and thereby controlling or reducing a bacterial infection in a subject or

bacterial contamination of an organ, tissue, or environment. Thus "treatment" that reduces incidence may, for example, be effective to inhibit growth of at least one Gram-negative bacterium in a particular milieu, whether it be a subject or an environment. On the other hand, "treatment" of an already established infection refers to inhibiting the growth, reducing the population, killing, including eradicating, a Gram-negative bacteria responsible for an infection or contamination.

[0066] "Preventing" refers to the prevention of the incidence, recurrence, spread, onset or establishment of a disorder such as a bacterial infection. It is not intended that the present disclosure be limited to complete prevention or to prevention of establishment of an infection. In some embodiments, the onset is delayed, or the severity of a subsequently contracted disease or the chance of contracting the disease is reduced, and such constitute examples of prevention.

[0067] "Contracted diseases" refers to diseases manifesting with clinical or subclinical symptoms, such as the detection of fever, sepsis, or bacteremia, as well as diseases that may be detected by growth of a bacterial pathogen (e.g., in culture) when symptoms associated with such pathology are not yet manifest.

[0068] The term "derivative" in the context of a peptide or polypeptide or active fragments thereof is intended to encompass, for example, a polypeptide modified to contain one or more chemical moieties other than an amino acid that do not substantially adversely impact or destroy the polypeptide's activity (e.g., lytic activity). The chemical moiety can be linked covalently to the peptide, e.g., via an amino terminal amino acid residue, a carboxy terminal amino acid residue, or at an internal amino acid residue. Such modifications may be natural or non-natural. In certain embodiments, a non-natural modification may include the addition of a protective or capping group on a reactive moiety, addition of a detectable label, such as antibody and/or fluorescent label, addition or modification of glycosylation, or addition of a bulking group such as PEG (pegylation) and other changes known to those skilled in the art. In certain embodiments, the non-natural modification may be a capping modification, such as N-terminal acetylations and C-terminal amidations. Exemplary protective groups that may be added to lysin polypeptides or AMPs include, but are not limited to, t-Boc and Fmoc. Commonly used fluorescent label proteins such as, but not limited to, green fluorescent protein (GFA), red fluorescent protein (RFP), cyan fluorescent protein (CFP), yellow fluorescent protein (YFP), and mCherry, are compact proteins that can be bound covalently or noncovalently to a polypeptide or fused to a polypeptide without interfering with normal functions of cellular proteins. In certain embodiments, a polynucleotide encoding a fluorescent protein may be inserted upstream or downstream of the lysin or AMP polynucleotide sequence. This will produce a fusion protein (e.g., Lysin Polypeptide::GFP) that does not interfere with cellular function or function of a polypeptide to which it is attached. Polyethylene glycol (PEG) conjugation to proteins has been used as a method for extending the circulating half-life of many pharmaceutical proteins. Thus, in the context of polypeptide derivatives, such as lysin polypeptide derivatives, the term "derivative" encompasses polypeptides, such as lysin polypeptides, chemically modified by covalent attachment of one or more PEG molecules. It is anticipated that lysin polypeptides, such as pegylated lysins, will exhibit prolonged circulation half-life compared to the unpegylated polypeptides, while retaining biological and therapeutic activity.

[0069] "Percent amino acid sequence identity" refers to the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the reference polypeptide sequence, such as a lysin polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for example, using publicly available software such as BLAST or software available commercially, for example from DNASTAR. Two or more polypeptide sequences can be anywhere from 0-100% identical, or any integer value there between. In the context of the present disclosure, two polypeptides are "substantially identical" when at least 80% of the amino acid residues (such as at least about 85%, at least about 90%, at least about 92.5%, at least about 95%, at least about 98%, or at least about 99%) are identical. The term "percent (%) amino acid sequence identity" as described herein applies to peptides as well. Thus, the term "substantially identical" will encompass mutated, truncated, fused, or otherwise sequence-modified variants of isolated lysin polypeptides and peptides and AMPs described herein, and active fragments thereof, as well as polypeptides with substantial sequence identity (e.g., at least 80%, at least 85%, at least 90%, at least 92.5%, at least 95%, at least 98%, or at least 99% identity as measured for example by one or more methods referenced above) as compared to the reference (wild type or other intact) polypeptide.

[0070] As used herein, two amino acid sequences are "substantially homologous" when at least about 80% of the amino acid residues (such as at least about 85%, at least about 90%, at least about 92.5%, at least about 95%, at least about 98%, or at least about 99%) are identical, or represent conservative substitutions. The sequences of the polypeptides of the present disclosure are substantially homologous when one or more, such as up to 10%, up to 15%, or up to 20% of the amino acids of the polypeptide, such as the lysin, AMP, and/or fusion polypeptides described herein, are substituted with a similar or conservative amino acid substitution, and wherein the resulting peptides have at least one activity (e.g., antibacterial effect) and/or bacterial specificities of the reference polypeptide, such as the lysin, AMP, and/or fusion polypeptides described herein.

[0071] As used herein, a "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a side chain with a similar charge. Families of amino acid residues having side chains with similar charges have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

[0072] "Inhalable composition" refers to pharmaceutical compositions of the present disclosure that are formulated for direct delivery to the respiratory tract during or in conjunction with routine or assisted respiration (e.g., by intratracheobronchial, pulmonary, and/or nasal administration), including, but not limited to, atomized, nebulized, dry powder, and/or aerosolized formulations.

[0073] "Biofilm" refers to bacteria that attach to surfaces and aggregate in a hydrated polymeric matrix that may be comprised of bacterial- and/or host-derived components. A biofilm is an aggregate of microorganisms in which cells adhere to each other on a biotic or abiotic surface. These adherent cells are frequently embedded within a matrix comprised of, but not limited to, extracellular polymeric substance (EPS). Biofilm EPS, which is also referred to as slime (although not everything described as slime is a biofilm) or plaque, is a polymeric conglomeration generally composed of extracellular DNA, proteins, and polysaccharides.

[0074] "Preventing biofilm formation" refers to the prevention of the incidence, recurrence, spread, onset or establishment of a biofilm. It is not intended that the present disclosure be limited to complete prevention or to prevention of establishment of biofilm. In some embodiments, the onset of a biofilm is delayed, or the establishment of a biofilm is reduced or the chance of formation of a new biofilm is reduced, and such constitute examples of prevention of a biofilm. Further, prevention of a biofilm may be due to any mechanism including 1) effectively killing planktonic bacteria; 2) killing "persister" bacterial cells in suspensions, i.e., bacteria that are metabolically inactive, tolerant of antibiotics, and highly associated with biofilm formation; and/or 3) preventing "aggregation", i.e., the ability of bacteria to attach to one another via proteins or polysaccharides.

[0075] "Eradication" in reference to a biofilm includes 1) effectively killing bacteria in a biofilm including persister bacterial cells in the biofilm and, optionally 2) effectively destroying and/or damaging the biofilm matrix.

[0076] "Disruption" in reference to a biofilm refers to a mechanism that falls between prevention and eradication. A biofilm, which is disrupted, may be "opened", or otherwise damaged, thus permitting, e.g., an antibiotic, to more readily penetrate the biofilm and kill the bacteria.

[0077] "Suitable" in the context of an antibiotic being suitable for use against certain bacteria refers to an antibiotic that was found to be effective against those bacteria even if resistance subsequently developed.

[0078] "Outer Membrane" or "OM" refers to a feature of Gram-negative bacteria. The outer membrane is comprised of a lipid bilayer with an internal leaflet of phospholipids and an external amphiphilic leaflet largely consisting of lipopolysaccharide (LPS). The LPS has three main sections: a hexa-acylated glucosamine-based phospholipid called lipid A, a polysaccharide core and an extended, external polysaccharide chain called 0-antigen. The OM presents a non-fluid continuum stabilized by three major interactions, including: i) the avid binding of LPS molecules to each other, especially if cations are present to neutralize phosphate groups; ii) the tight packing of largely saturated acyl chains; and iii) hydrophobic stacking of the lipid A moiety. The resulting structure is a barrier for both hydrophobic and hydrophilic molecules. Below the OM, the peptidoglycan forms a thin layer that is very sensitive to hydrolytic cleavage—unlike the peptidoglycan of Gram-negative bacteria which is 30-100 nanometers (nm) thick and consists of up to 40 layers, the peptidoglycan of Gram-negative bacteria is only 2-3 nm thick and consists of only 1-3 layers.

Polypeptides

[0079] Lysins, Variant Lysins, Active Fragments Thereof or Derivatives

[0080] The present disclosure is directed to isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives. In some embodiments, the isolated polypeptides comprising the lysins, variant lysins, active fragments thereof or derivatives are combined with antimicrobial peptides ("AMPs") to form a lysin-AMP polypeptide construct, such as the lysin-AMP polypeptide construct of SEQ ID NO: 44 (GN370), wherein the lysin-AMP polypeptide construct has lysin activity. As used herein "lysin activity" encompasses the ability of a lysin to kill bacteria (e.g., *P. aeruginosa*), reduce the population of bacteria or inhibit bacterial growth (e.g.; by penetrating the outer membrane of a Gram-negative bacteria), optionally in the presence of human serum or pulmonary surfactant. Lysin activity also encompasses the ability to remove or reduce a biofilm and/or the ability to reduce the minimum inhibitory concentration (MIC) of an antibiotic, optionally in the presence of human serum or pulmonary surfactant.

[0081] In some embodiments, the present isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives thereof are capable of penetrating the outer membrane of Gram-negative bacteria. Without being limited by theory, after penetration of the outer membrane, the present isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives thereof can degrade peptidoglycan, a major structural component of the bacterial cell wall, resulting in e.g., cell lysis or non-lethal damage that inhibits bacterial growth. In some embodiments, the present isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives disclosed herein contain positively charged (and amphipathic) N- and/or C-terminal α-helical domains that facilitate binding to the anionic outer membrane of a Gram-negative bacteria to effect translocation into the sub-adjacent peptidoglycan.

[0082] The ability of a lysin to penetrate an outer membrane of a Gram-negative bacteria may be assessed by any method known in the art, such as described in WO 2017/049233, which is herein incorporated by reference in its entirety. For example, the lysin may be incubated with Gram-negative bacteria and a hydrophobic compound. Most Gram-negative bacteria are strongly resistant to hydrophobic compounds, due to the presence of the outer membrane and, thus, do not allow the uptake of hydrophobic agents such as 1-N-phenylnaphthylamine (NPN), crystal violet, or 8-anilino-1-naphthalenesulfonic acid (ANS). NPN, for example, fluoresces strongly under hydrophobic conditions and weakly under aqueous conditions. Accordingly, NPN fluorescence can be used as a measurement of the outer membrane permeability.

[0083] More particularly, the ability of a lysin to penetrate an outer wall may be assessed by incubating, e.g., NPN with a Gram-negative bacteria, e.g., *P. aeruginosa* strain PA01, in the presence of the lysin to be tested for activity. A higher induction of fluorescence in comparison to the fluorescence emitted in the absence of a lysin (negative control) indicates outer membrane penetration. In addition, fluorescence

induction can be compared to that of established permeabilizing agents, such as EDTA (ethylene diamine tetraacetate) or an antibiotic such as an antibiotic of last resort used in the treatment of *P. aeruginosa*, i.e., Polymyxin B (PMB) to assess the level of outer membrane permeability.

[0084] In some embodiments, the present isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives exhibit lysin activity in the presence and/or absence of human serum. Suitable methods for assessing the activity of a lysin in human serum are known in the art and described in the examples. Briefly, a MIC value (i.e., the minimum concentration of peptide sufficient to suppress at least 80% of the bacterial growth compared to control) may be determined for a lysin and compared to, e.g., a parent lysin or compound inactive in human serum, e.g., T4 phage lysozyme or artilysin GN126 (SEQ ID NO: 224, pI 9.8). T4 phage lysozyme is commercially available, e.g. from Sigma-Aldrich, Inc. GN126 (SEQ ID NO: 224) corresponds to Art-175, which is described in the literature and is obtained by fusing AMP SMAP-29 to GN lysin KZ144. See Briers et al. 2014, *Antimicrob. Agents Chemother.* 58:3774-3784, which is herein incorporated by reference in its entirety. Lysin GN65 (SEQ ID NO: 22, pI9.9) and dispersin B, which is an enzyme that degrades biofilm (GN81, SEQ ID NO: 226, pI 6.0), may also be used as controls.

[0085] More particularly, MIC values for a lysin may be determined against e.g., the laboratory *P. aeruginosa* strain PA01, in e.g., Mueller-Hinton broth, Mueller-Hinton broth supplemented with human serum, CAA as described herein, which includes physiological salt concentrations, and CAA supplemented with human serum. The use of PA01 enables testing in the presence of elevated serum concentrations since unlike most clinical isolates, PA01 is insensitive to the antibacterial activity of human blood matrices.

[0086] In some embodiments, the present isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives are capable of reducing a biofilm. Methods for assessing the Minimal Biofilm Eradicating Concentration (MBEC) of a lysin or AMP may be determined using a variation of the broth microdilution MIC method with modifications (See Ceri et al. 1999. *J. Clin. Microbial.* 37:1771-1776, which is herein incorporated by reference in its entirety and Schuch et al., 2017, *Antimicrob. Agents Chemother.* 61, pages 1-18, which is herein incorporated by reference in its entirety.) In this method, fresh colonies of e.g., a *P. aeruginosa* strain, such as ATCC 17647, are suspended in medium, e.g., phosphate buffer solution (PBS) diluted e.g., 1:100 in TSBg (tryptic soy broth supplemented with 0.2% glucose), added as e.g., 0.15 ml aliquots, to a Calgary Biofilm Device (96-well plate with a lid bearing 96 polycarbonate pegs; Innovotech Inc.) and incubated e.g., 24 hours at 37° C. Biofilms are then washed and treated with e.g., a 2-fold dilution series of the lysin in TSBg at e.g., 37° C. for 24 hours. After treatment, wells are washed, air-dried at e.g., 37° C. and stained with e.g., 0.05% crystal violet for 10 minutes. After staining, the biofilms are destained in e.g., 33% acetic acid and the OD600 of e.g., extracted crystal violet is determined. The MBEC of each sample is the minimum lysin concentration required to remove >95% of the biofilm biomass assessed by crystal violet quantitation.

[0087] In some embodiments, the present isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives reduce the minimum inhibitory concentration (MIC) of an antibiotic needed to inhibit bacteria in the presence and/or absence of human serum or in the presence of pulmonary surfactant. Any known method to assess MIC may be used. In some embodiments, a checkerboard assay is used to determine the effect of a lysin on antibiotic concentration. The checkerboard assay is based on a modification of the CLSI method for MIC determination by broth microdilution (See Clinical and Laboratory Standards Institute (CLSI), CLSI. 2015. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-10th Edition. Clinical and Laboratory Standards Institute, Wayne, Pa., which is herein incorporated by reference in its entirety and Ceri et al. 1999. *J. Clin. Microbial.* 37: 1771-1776, which is also herein incorporated by reference in its entirety).

[0088] Checkerboards are constructed by first preparing columns of e.g., a 96-well polypropylene microtiter plate, wherein each well has the same amount of antibiotic diluted 2-fold along the horizontal axis. In a separate plate, comparable rows are prepared in which each well has the same amount of lysin diluted e.g., 2-fold along the vertical axis. The lysin and antibiotic dilutions are then combined, so that each column has a constant amount of antibiotic and doubling dilutions of lysin, while each row has a constant amount of lysin and doubling dilutions of antibiotic. Each well thus has a unique combination of lysin and antibiotic. Bacteria are added to the drug combinations at concentrations of 1×10^5 CFU/ml in CAA, for example, with or without human serum or pulmonary surfactant (such as SURVANTA®). The MIC of each drug, alone and in combination, is then recorded after e.g., 16 hours at 37° C. in ambient air. Summation fractional inhibitory concentrations (ΣFICs) are calculated for each drug and the minimum ΣFIC value (ΣFICmin) is used to determine the effect of the lysin/antibiotic combination.

[0089] In some embodiments, the present lysins and lysin-AMP polypeptide constructs are able to synergize with antibiotics, such as imipenem and meropenem, and drive the resensitization of Gram-negative bacteria including MDR organisms, such as carbapenem-resistant *P. aeruginosa*. Such resensitization may be determined by combining the present lysins or lysin-AMP polypeptide constructs with an antibiotic in a checkerboard assay as described herein. Antibiotic-resistant bacteria, such as carbapenem-resistant *P. aeruginosa*, are added to the lysin or lysin-AMP polypeptide construct combination. Generally resensitization occurs in synergistic combinations in which the antibiotic MIC values fall below established breakpoints, e.g., a MIC value of <2 for antibiotic sensitive bacteria, a MIC value of 4 for intermediately sensitive bacteria and a MIC value of >8 for antibiotic resistant bacteria, e.g. carbapenem-resistant isolates. See Clinical and Laboratory Standards Institute (CLSI), CLSI. 2019. M100 Performance Standards for Antimicrobial Susceptibility Testing; 29th Edition. Clinical and Laboratory Standards Institute, Wayne, Pa., which is herein incorporated by reference in its entirety.

[0090] In some embodiments, the present isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives show low toxicity against erythrocytes. Any methodology known in the art may be used to assess the potential for hemolytic activity of the present isolated polypeptides comprising lysins, variant lysins, active fragments thereof or derivatives including the method described in the Examples.

[0091] Examples of suitable lysins of the present disclosure, particularly for use with the lysin-AMP polypeptide constructs described herein, include the GN316 lysin obtained from *Klebsiella* phage 0507-KN2-1 (NCBI Reference Sequence: YP_008531963.1, SEQ ID NO: 22), Lysin PaP2_gp17 obtained from *Pseudomonas* phage (NCBI Reference Sequence: YP_024745.1, SEQ ID NO: 96), GN333 obtained from *Delftia* sp. (NCBI Reference Sequence: WP_016064791.1, SEQ ID NO: 28), GN424 obtained from *Burkholderia pseudomultivorans* (NCBI Reference Sequence: WP_060250996.1, SEQ ID NO: 56), GN425 lysin obtained from *Pseudomonas flexibilis* (NCBI Reference Sequence: WP_039605935.1, SEQ ID NO: 58), GN428 obtained from *Escherichia* virus CBA120 (NCBI Reference Sequence: YP_004957781.1, SEQ ID NO: 60), GN431 obtained from *Dickeya* phage phiD3 (NCBI Reference Sequence: AIM51349.1, SEQ ID NO: 64), GN485 obtained from *Erwinia* sp. Leaf5 (NCBI Reference Sequence: WP_056233282.1, SEQ ID NO: 68) and GN123 obtained from *Pseudomonas* phage PhiPA3 (NCBI Reference Sequence: YP_009217242.1, SEQ ID NO: 173).

[0092] The above described lysins were identified by bioinformatics techniques. Although some of the identified sequences had been annotated as putative peptidoglycan binding proteins, no function had been previously definitively attributed to polypeptides having these sequences. The inventors have surprisingly recognized that the above-identified sequences are suitable for use as antibacterial agents, in particular, against Gram-negative bacteria as described in the examples.

[0093] Additional examples of suitable lysins of the present disclosure, particularly those for use with the present lysin-AMP polypeptide constructs, include the GN7 (SEQ ID NO: 206, pI 5.6), obtained from a marine metagenome, NCBI Accession Number ECF75988.1; GN11 (SEQ ID NO: 208, pI 7.3), obtained from *Pseudomonas putida* KT2440, NCBI Accession Number NP 744418.1; GN40 (SEQ ID NO: 210, pI 5.1), obtained from *Pseudomonas putida* strain PA14H7, NCBI Accession Number NZ_KN639176.1; GN122 (SEQ ID NO: 218, pI 5.4), obtained from *Pseudomonas putida* strain PA14H7, NCBI Accession Number NZ_KN639176.1; GN328 (SEQ ID NO: 220, pI 7.9), obtained from *Pseudomonas protegens*, NCBI Accession Number NC_021237.1; GN76 (SEQ ID NO: 203), obtained from *Acinetobacter* phage vB_AbaP_CEB1, NCBI Reference Sequence ALC76575.1, GenBank: ALC76575.1; GN4 (SEQ ID NO: 74), obtained from *Pseudomonas* phage PAJU2, NCBI Reference Sequence YP 002284361.1; GN14 (SEQ ID NO: 124), obtained from *Pseudomonas* phage Lull, NCBI Reference Sequence YP 006382555.1; and GN37 (SEQ ID NO: 84), obtained from *Micavibrio aeruginosavorus*, NCBI Reference Sequence WP_014102102.1. GN4, GN14 and GN37 are also disclosed in WO 2017/049233, which is herein incorporated by reference in its entirety.

[0094] Suitable lysin-AMP constructs of the present disclosure include GN75 (SEQ ID NO: 212, pI 10.1) and GN83 (SEQ ID NO: 216, pI 9.4). GN75 comprises the AMP OBPgpLYS (SEQ ID NO: 88 of U.S. Pat. No. 8,846,865) fused to the N-terminus of lysin GN13 described in WO 2019/118632. GN83 comprises the AMP OBPgpLYS (SEQ ID NO: 88 of U.S. Pat. No. 8,846,865) fused to the N-terminus of lysin GN4 described in WO 2019/118632. U.S. Pat. No. 8,846,865 and WO 2019/118632 are each incorporated herein by reference in its entirety.

[0095] In some embodiments, a suitable polypeptide of the disclosure is a dispersin B-like molecule, such as an enzyme, which is capable of disrupting biofilm formation. Suitable dispersin B-like molecules include GN80 (SEQ ID NO: 214, pI 4.6).

[0096] In some embodiments, the present isolated polypeptides comprise a lysin variant, e.g., a lysin containing one or more insertions, deletions and/or amino acid substitutions in comparison to a reference lysin polypeptide, e.g., a naturally occurring lysin or a parent lysin, which itself is a variant lysin. In some embodiments, an isolated polypeptide sequence comprising a variant lysin, active fragment thereof or derivative has at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98% or such as at least 99% sequence identity with the reference lysin (e.g., GN202 (SEQ ID NO: 118) and/or active fragment thereof described herein.

[0097] The lysin variants of the present disclosure typically retain one or more functional or biological activities of a reference lysin. In some embodiments, the modification improves the antibacterial activity of the lysin. Typically, the lysin variant has improved in vitro antibacterial activity (e.g., in buffer and/or media) in comparison to the reference lysin. In other embodiments, the lysin variant has improved in vivo antibacterial activity (e.g., in an animal infection model). In some embodiments, the modification improves the antibacterial activity of the lysin in the absence and/or presence of human serum. In some embodiments, the modification improves the antibacterial activity of the lysin in the presence of pulmonary surfactant.

[0098] Suitable variant lysins, particularly those for use in the present lysin-AMP polypeptide constructs, include the GN146 lysin (SEQ ID NO: 78), GN156 lysin (SEQ ID NO: 126), the GN202 lysin (SEQ ID NO: 118) and GN121 lysin (SEQ ID NO: 175). Each of the foregoing lysins is also disclosed in U.S. Provisional Application No. 62,597,577, which was filed on Dec. 12, 2017 and U.S. Provisional Application No. 62/721,969, which was filed on 23 Aug. 2018, and is herein incorporated by reference in its entirety. The lysins described in U.S. Provisional Application No. 62/721,969, typically, are modified in reference to their naturally occurring counterpart to enhance the activity of the lysin in serum, e.g., by introducing amino acid substitutions and/or introducing amino acid fragments from larger antimicrobial peptides. For example, the amino acid sequence GPRRPRRPGRRAPV (residues 1-14 of SEQ ID NO: 126) described by Daniels and Scepartz, 2007, *J. Am. Chem. Soc.* 129:14578-14579, which is herein incorporated by reference in its entirety, is introduced, for example, at the N terminus of GN4 (SEQ ID NO: 74), to generate GN156 (SEQ ID NO: 126), a non-naturally occurring lysin-AMP polypeptide construct.

[0099] In some embodiments, the variant lysins are obtained by modifying a reference lysin to include a modification resulting in a change in the overall isoelectric point (pI) of the lysin, i.e., the pH at which a molecule has a net neutral charge by, for example, incorporating a single pI-increasing mutation, such as a single point mutation, into a reference lysin. Suitable reference lysin polypeptides include a lysin selected from the group consisting of GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN76 (SEQ ID NO: 203), GN4 (SEQ ID NO: 74), GN146 (SEQ ID NO: 78), GN14 (SEQ ID NO: 124),

GN37 (SEQ ID NO: 84) GN316 (SEQ ID NO: 22) lysin Pap2 gp17 (SEQ ID NO: 96), GN329 (SEQ ID NO: 26), GN424 (SEQ ID NO: 56), GN202 (SEQ ID NO: 118), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN333 (SEQ ID NO: 28) GN485 (SEQ ID NO: 68) GN123 (SEQ ID NO: 173) and GN121 (SEQ ID NO: 175). In certain embodiments, the lysin variant has at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% sequence identity to a reference lysin polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO: 206, 208, 210, 218, 220, 203, 74, 78, 124, 84, 22, 96, 26, 56, 118, 58, 60, 64, 66, 28, 68, 173 and 175. In some embodiments, the lysin variant has at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, such as at least 99% sequence identity to a reference lysin polypeptide having the amino acid sequence of GN202 (SEQ ID NO: 118).

[0100] For example, the GN37 lysin (SEQ ID NO: 84) can be modified to increase the pI by introducing the amino acid substitution, R79H, to generate the GN217 lysin (SEQ ID NO: 8). In this embodiment, the potency of the GN217 lysin (SEQ ID NO: 8) is increased in both the presence and absence of human serum in comparison to that of the reference lysin, GN37 (SEQ ID NO: 84), as described in the examples.

[0101] Other examples of suitable pI modifying mutations include introducing an amino acid substitution such as K218D, K228D, R85H and/or K22D into a reference lysin, such as GN316 (SEQ ID NO: 22), to generate e.g., the GN394 lysin (SEQ ID NO: 48), the GN396 lysin (SEQ ID NO: 50), the GN408 lysin (SEQ ID NO: 52) and the GN418 lysin (SEQ ID NO: 54), respectively. In some embodiments, the foregoing pI modifying mutations improve the antibacterial activity of the lysin in the absence and/or presence of human serum as exemplified herein.

[0102] In some embodiments, the lysin variants of the present disclosure are typically designed to retain an α-helix domain, the presence or absence of which can be readily determined using various software programs, such as Jpred4 (compio.dundee.ac.ukljpred), Helical Wheel (hael.net/helical.htm), HeliQuest (zhanglab.ccmb.med.umich.edu/I-TASSER/) and PEP-FOLD 3 (bioserv.rpbs.univ-pans-diderot.fr/services/PEP-FOLD3).

[0103] In some embodiments, the α-helix domain is located at the C terminus of a lysin. In other embodiments, the α-helix domain is located at the N-terminus of a lysin. More typically, the α-helix domain is located at the C terminus. The α-helix domain of the lysins of the present disclosure varies in size between about 20 and 40 amino acids, more typically between about 15 and 33 amino acid residues. For example, the GN14 α-helix domain, which is located at the N terminus, contains 15 amino acids (residues 66 to 80 of SEQ ID NO: 124). The GN37 α-helix domain, which is located at the C terminus, contains 14 amino acids (residues 113 to 126 of SEQ ID NO: 84). The GN4 α-helix domain, which is also located at the C terminus, contains 25 amino acids (residues 116 to 140 of SEQ ID NO: 74).

[0104] In some embodiments, the variant lysins, active fragments thereof or derivatives thereof disclosed herein are modified to include a purification tag, e.g. GSHHHHHHG (SEQ ID NO: 100), The purification tag may be inserted anywhere within the lysin, such as the GN202 (SEQ ID NO: 118) lysin, typically between the first and second amino acids. For example, the purification tag may be inserted between the first methionine and first alanine at the N terminus of the GN316 lysin (SEQ ID NO: 22) to obtain a variant GN316 lysin (SEQ ID NO: 24) without adversely affecting the activity. In other embodiments, the purification tag may be inserted between the first methionine and the first glycine at the N terminus of the GN156 lysin (SEQ ID NO: 126) to obtain the variant GN486 (SEQ ID NO: 66).

[0105] Lysin variants may be formed by any method known in the art and as described in WO 2017/049233, which is herein incorporated by reference in its entirety, e.g., by modifying any of the lysins, active fragments thereof and derivatives described herein through site-directed mutagenesis or via mutations in hosts that produce the present lysins which retain one or more of the biological functions as described herein. The present lysin variants may be truncated, chimeric, shuffled or "natural," and may be in combination as described, for example, in U.S. Pat. No. 5,604,109, which is incorporated herein in its entirety by reference.

[0106] For example, one of skill in the art can reasonably make and test substitutions or replacements to, e.g., the α-helix domain or regions outside of the α-helix domain. Sequence comparisons to the Genbank database can be made with e.g., a full amino acid sequence as described herein, for instance, to identify amino acids for substitution.

[0107] Mutations can be made in the amino acid sequences, or in the nucleic acid sequences encoding the polypeptides and lysins, active fragments or derivatives, such that a particular codon is changed to a codon which codes for a different amino acid, an amino acid is substituted for another amino acid, or one or more amino acids are deleted.

[0108] Such a mutation is generally made by making the fewest nucleotide changes possible. A substitution mutation of this sort can be made to change an amino acid in the resulting protein in a non-conservative manner (for example, by changing the codon from an amino acid belonging to a grouping of amino acids having a particular size or characteristic to an amino acid belonging to another grouping) or in a conservative manner (for example, by changing the codon from an amino acid belonging to a grouping of amino acids having a particular size or characteristic to an amino acid belonging to the same grouping). Such a conservative change generally leads to less change in the structure and function of the resulting protein. A non-conservative change is more likely to alter the structure, activity or function of the resulting protein. The present disclosure should be considered to include sequences containing conservative changes which do not significantly alter the activity or binding characteristics of the resulting protein. Thus, one of skill in the art, based on a review of the sequence of lysins provided herein and on their knowledge and the public information available for other lysin polypeptides, can make amino acid changes or substitutions in the lysin polypeptide sequence. Amino acid changes can be made to replace or substitute one or more, one or a few, one or several, one to five, one to ten, or such other number of amino acids in the sequence of the lysin(s) provided herein to generate mutants or variants thereof. Such mutants or variants thereof may be predicted for function or tested for function or capability for antibacterial activity as described herein against, e.g., *P. aeruginosa*, and/or for having comparable activity to the lysin(s) as described and particularly provided herein. Thus, changes made to the sequence of lysin, and mutants or variants

described herein can be tested using the assays and methods known in the art and described herein. One of skill in the art, on the basis of the domain structure of the lysin(s) hereof can predict one or more, one or several amino acids suitable for substitution or replacement and/or one or more amino acids which are not suitable for substitution or replacement, including reasonable conservative or non-conservative substitutions.

[0109] In some embodiments, the present isolated polypeptides comprise active fragments of lysins or derivatives. The term "active fragment" refers to a portion of a full-length lysin, which retains one or more biological activities of the reference lysin. Thus, as used herein, an active fragment of a lysin or variant lysin inhibits the growth, or reduces the population, or kills e.g., *P. aeruginosa* and and/or other Gram-negative bacteria as described herein in the absence or presence of, or in both the absence and presence of, human serum or in the presence of pulmonary surfactant. Suitable active fragments of lysins include, but are not limited, to those described in WO2017/049233, which is herein incorporated by reference in its entirety. The active lysin fragments typically retain an α-helix domain. Examples of active lysin fragments include those of the GN4 lysin (SEQ ID NO: 74) set forth in SEQ ID NOS: 127-129.

[0110] In some embodiments, the lysin, variant lysin, active fragment thereof or derivative included in the present isolated polypeptides is selected from the group consisting of GN217 (SEQ ID NO: 8), GN316 variant (SEQ ID NO: 24) GN316 (SEQ ID NO: 22), GN329 (SEQ ID NO: 26), GN333 (SEQ ID NO: 28), GN394 (SEQ ID NO: 48), GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52), (SEQ ID NO: 54), GN424 (SEQ ID NO: 56), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN485 (SEQ ID NO: 68), Lysin PaP2 gp17 (SEQ ID NO: 96), GN123 (SEQ ID NO: 173), GN121 (SEQ ID NO: 175), and GN202 (SEQ ID NO: 118) or an active fragment thereof, wherein the lysin or active fragment thereof inhibits the growth, or reduces the population, or kills *P. aeruginosa* and/or at least one other species of Gram-negative bacteria as described herein in the absence or presence of, or in both the absence and presence of, human serum or in the presence of pulmonary surfactant. In some embodiments, the lysin or active fragment thereof contains at least one amino acid substitution, deletion, or insertion relative to at least one of SEQ ID NOS: 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, 96, 118, 173 or 175. In certain embodiments, the at least one amino acid substitution is a conservative amino acid substitution.

[0111] In some embodiments, the lysin of the disclosure is selected from the group consisting of GN329 (SEQ ID NO: 26), GN333 (SEQ ID NO: 28), GN424 (SEQ ID NO: 56), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN485 (SEQ ID NO: 68) and Lysin PaP2_gp17 (SEQ ID NO: 96) or an active fragment thereof, wherein the lysin or active fragment thereof inhibits the growth, or reduces the population, or kills *P. aeruginosa* and/or at least one other species of Gram-negative bacteria species of Gram-negative bacteria as described herein in the absence or presence of, or in both the absence and presence of, human serum or in the presence of pulmonary surfactant. In some embodiments, the lysin, derivative or active fragment thereof contains at least one substitution, deletion, or insertion modification relative to SEQ ID NOS: 26, 28, 56, 58, 60, 64, 68 or 96. In certain embodiments, the at least one amino acid substitution is a conservative amino acid substitution.

[0112] In some embodiments, the isolated polypeptide sequence comprises a lysin selected from the group consisting of GN217 lysin (SEQ ID NO: 8), GN394 lysin (SEQ ID NO: 48), GN396 lysin (SEQ ID NO: 50), GN408 lysin (SEQ ID NO: 52), GN418 lysin (SEQ ID NO: 54) and GN486 (SEQ ID NO: 66) or an active fragment thereof, wherein the lysin or active fragment thereof inhibits the growth, or reduces the population, or kills *P. aeruginosa* and/or at least one other species of Gram-negative bacteria as described herein in the absence or presence of, or in both the absence and presence of, human serum or in the presence of pulmonary surfactant. In some embodiments, the lysin or active fragment thereof contains at least one substitution, deletion, or insertion modification relative to SEQ ID NOS: 8, 48, 50, 52, 54, or 66. In certain embodiments, the at least one amino acid substitution is a conservative amino acid substitution.

[0113] Anti-Microbial Peptides

[0114] In some embodiments, the polypeptides of the present disclosure comprise lysin-Anti-Microbial Peptide (AMP) polypeptide constructs. The lysin-AMP polypeptide constructs comprise an isolated polypeptide comprising a lysin, variant lysin, active fragment thereof or derivative as described herein and an antimicrobial peptide or fragment thereof. The term "antimicrobial peptide" (AMP) as used herein refers to a member of a wide range of short (generally 3 to 50 amino acid residues in length) gene-encoded peptides, typically antibiotics, that can be found in virtually every organism. The term encompasses helical peptides, β-sheet peptides and those that display largely disordered random coil structures. AMPs include defensins, cathelicidins, sushi peptides, cationic peptides, polycationic peptides, amphipathic peptides, hydrophobic peptides and/or AMP-like peptides, e g., amurin peptides as described herein. Fragments of AMPs, AMP variants and derivatives of AMPs are also encompassed by this term.

[0115] The term "AMP activity" as used herein encompasses the ability of an AMP or fragment thereof to kill bacteria, reduce the population of bacteria or inhibit bacterial growth e.g., by penetrating the outer membrane of a Gram-negative bacteria, e.g., in the presence and/or absence of human serum or pulmonary surfactant. Typically, translocation of the AMPs is driven by a primary electrostatic interaction with the lipopolysaccharide portion of the outer membrane followed by cation displacement, membrane disorganization and transient openings, and in some cases, internalization of the AMP.

[0116] AMP activity also encompasses the ability of an AMP or fragment thereof to reduce the minimum inhibitory concentration (MIC) of an antibiotic in the presence and/or absence of human serum or pulmonary surfactant. Suitable methods for assessing the ability of the present AMPs and fragments thereof to penetrate the outer membrane of Gram-negative bacteria and determining a reduction in the MIC of an antibiotic in the presence and absence of serum or pulmonary surfactant are known in the art and include those methods described above for the present lysins, derivatives and active fragments thereof.

[0117] In some embodiments, the present AMPs are variant AMPs having at least 50%, at least 60%, at least 75%, at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98% or such as at least 99%

sequence identity with any of the AMPs described herein (e.g., SEQ ID NO: 114), wherein the variant AMP thereof retains an AMP activity. 11091 In some embodiments, the present AMPs comprise a helical domain, such as an α-helical domain. In some embodiments, the α-helical domain spans most of the molecule. See, for example, Chp1 and Chp4 of FIG. **1**. In other embodiments, the α-helix domain is either interrupted (e.g., Chp2) or truncated (e.g., Chp6 and Osp1). The α-helix domain of the present AMPs, such as the Chps, described herein vary in size from between about 3 to 32 amino acids, more typically between about 10 and 25 amino acid residues. Generally, the helical domains are required for activity and typically must be retained when fused to a C- or N-terminus of a lysin.

[0118] Typically, helical peptides display amphipathic characteristics and contain a substantial proportion (e.g. 50%) of hydrophobic residues, frequently appearing in repeated patterns. Upon formation of an α-helical structure, the hydrophilic residues typically end up on the same side of the helix, thereby resulting in a conformation-dependent amphiphilicity. Frequently, these peptides are unstructured in an aqueous environment, but adopt a helical conformation upon encountering lipid membranes. Peptides belonging to this group typically display an overall positive charge ranging from +2 to +11 and usually kill microbes, such as Gram-negative bacteria, by creating membrane defects, leading to a loss of gradients in electrolytes, signal substances and other factors.

[0119] In some embodiments, the present AMPs are "AMP-like" peptides including phage lytic agents referred to herein as *Chlamydia* phage (Chp) peptides or amurin peptides. The amurin peptides of the present disclosure are distinguishable from amurins. As is known in the art, amurins, which are obtained from ssDNA or ssRNA phages (Microviridae and Leviviridae, respectively), are integral membrane proteins with a putative domain structure including an internal LS dipeptide immediately preceded by a stretch of 10-17 hydrophobic residues. Examples of amurins include the protein E amurin from phage <pX174 (Family Microviridae, genus Microvints), which is a 91 amino acid membrane protein that causes lysis by inhibiting the bacterial translocase Mra Y, an essential membrane-embedded enzyme that catalyzes the formation of the murein precursor, Lipid I; the A2 capsid protein of phage Q~ (Family Leviviridae, genus *Allolevivirus*), which is a 420-amino acid structural protein that causes lysis by interfering with MurA activity and dysregulating the process of peptidoglycan biosynthesis; the protein L amurin of phage MS2 (Family Levivirdae, genus *Levivirus*), which is a 75 amino acid integral membrane protein that causes lysis using a mechanism that requires the activity of host chaperone DnaJ. Typically, amurins cannot be purified and are not suitable for use as antibacterial therapeutics.

[0120] In contrast to amurins, the amurin peptides of the present disclosure are small cationic peptides with predicted α-helical structures similar to those of AMPs obtained from the innate immune systems of a variety of vertebrates (but with amino acid sequences dissimilar to AMPs). Amurin peptides are primarily found in Chlamydiamicroviruses and, to a lesser extent, in other related members of the subfamily Gokushovirinae. The amurin peptides from a variety of Microviridae phages exhibit 30-100% identity to each other and have no homology with other peptides. Unlike the amurins of Microviridae, which have cytoplasmic targets in the cell wall biosynthetic apparatus, and, accordingly, may not be easily accessed by externally applied proteins, the present amurin peptides can be used in purified form to exert bactericidal activity "from without."

[0121] Suitable amurin peptides for use in the present lysin-AMP polypeptide constructs include those described in U.S. Provisional Application No. 62/650,235, which was filed on 29 Mar. 2018, and which is herein incorporated by reference in its entirety. In some embodiments, amurin peptides such as the *chlamydia* phage (Chp)-derived lytic agents may be used. Such Chp-derived lytic agents include Chp1 (NCBI Reference Sequence: NP_044319.1, SEQ ID NO: 133), Chp2 (NCBI Reference Sequence: NP_0546521.1, SEQ ID NO: 70), CPAR39 (NCBI Reference Sequence: NP_063898.1, SEQ ID NO: 135), Chp3 (NCBI Reference Sequence: YP_022484.1, SEQ ID NO: 137), Chp4 (NCBI Reference Sequence: YP_338243.1, SEQ ID NO: 102), Chp6 (NCBI Reference Sequence: NP_510878.1, SEQ ID NO: 106), Chp7 (NCBI Reference Sequence: CRH73061.1, SEQ ID NO: 139), Chp8 (NCBI Reference Sequence: CRH64983.1, SEQ ID NO: 141), Chp9 (NCBI Reference Sequence: CRH84960.1, SEQ ID NO: 143), Chp10 (NCBI Reference Sequence: CRH73061.1, SEQ ID NO: 145), Chp11 (NCBI Reference Sequence: CRH59954.1 SEQ ID NO: 147) and Chp12 (NCBI Reference Sequence: CRH59965.1 SEQ ID NO: 149).

[0122] Additional, suitable Chp family members include Gkh1 (NCBI Reference Sequence: YP_008798245.1, SEQ ID NO: 151), Gkh2 (NCBI Reference Sequence: YP_009160382.1, SEQ ID NO: 90), Unp1 (NCBI Reference Sequence: CDL66944.1, SEQ ID NO: 153), Ecp1 (NCBI Reference Sequence: WP_100756432.1, SEQ ID NO: 155), Ecp2 (NCBI Reference Sequence: OAC1404.1, SEQ ID NO: 104), Tma1 (NCBI Reference Sequence: SHG47122.1, SEQ ID NO: 157), Osp1 (NCBI Reference Sequence: SFP13761.1, SEQ ID NO: 108), Unp2 (NCBI Reference Sequence: CDL65918.1, SEQ ID NO: 159), Unp3 (NCBI Reference Sequence: CDL65808.1, SEQ ID NO: 161), Gkh3 (NCBI Reference Sequence: AGT39941.1, SEQ ID NO: 163), Unp5 (NCBI Reference Sequence: AGT39924.1, SEQ ID NO: 165), Unp6 (NCBI Reference Sequence: AGT39915.1, SEQ ID NO: 167), Spi1 (NCBI Reference Sequence: NP_598337.1, SEQ ID NO: 169) and Spit (NCBI Reference Sequence: NP_598336.1, SEQ ID NO: 171), Ecp3 (NCBI Reference Sequence: WP_105269219.1, SEQ ID NO: 177), Ecp4 (NCBI Reference Sequence: WP_105466506.1, SEQ ID NO: 179), ALCES1 (NCBI Reference Sequence: AXB22573.1, SEQ ID NO: 181), AVQ206 (NCBI Reference Sequence: AVQ10236.1, SEQ ID NO: 183), AVQ244 (NCBI Reference Sequence: AVQ10244.1, SEQ ID NO: 185), CDL907 (NCBI Reference Sequence: CDL65907.1, SEQ ID NO: 187), AGT915 (NCBI Reference Sequence: AGT39915.1, SEQ ID NO: 189), HH3930 (NCBI Reference Sequence: CCH66548.1, SEQ ID NO: 191), Fen7875 (NCBI Reference Sequence: YP_009160399.1, SEQ ID NO: 193), SBR77 (NCBI Reference Sequence: AOT25441, SEQ ID NO: 195), Bdp1 NCBI Reference Sequence: NP 073546.1, SEQ ID NO: 197), LVP1 (NCBI Reference Sequence: NP 042306.1, SEQ ID NO: 199) and Lvp2 (NCBI Reference Sequence: NP_085469.1, SEQ ID NO: 201).

[0123] More typically, the AMPs are selected from one or more of the following amurin peptides, Chp2 (SEQ ID NO:

70), Gkh2 (SEQ ID NO: 90), Chp4 (SEQ ID NO: 102), Ecp2 (SEQ ID NO: 104), Chp6 (SEQ ID NO: 106) and Osp1 (SEQ ID NO: 108).

[0124] In some embodiments, the amurin peptides are modified to produce variant amurin peptides. As described herein, amurin peptides typically comprise a helical domain such as an α-helical domain. Typically, the variant amurin peptides retain the α-helical domain. The retention of the α-helical domain in any variant amurin peptide is typically accurately identified using various software programs, such as Jpred4 (compio.dundee.ac.uk/jpred), Helical Wheel (hael.net/helical.htm), HeliQuest (zhanglab.ccmb.med.umich.edu/I-TASSER/) and PEP-FOLD 3 (bioserv.rpbs.univ-paris-diderot.fr/services/PEP-FOLD3). In some embodiments, the amurin peptide variants are modified by converting (=) charged residues, such as arginine and lysine, within the amurin peptide to a "D" amino acid form. The utility of conversions to the D form is described in the literature, e.g., Manabe et al., *Sci. Rep.,* 2017, pages 1-10, which is herein incorporated by reference in its entirety. Variant AMPs may be prepared according to any method known in the art including as described herein above for the lysins, variants, active fragments thereof and derivatives.

[0125] In some embodiments, the AMPs for use in the lysin-AMP polypeptide constructs of the present disclosure include a fragment of a larger AMP that retains antibacterial activity. For example, in certain embodiments, the AMP portion of the lysin-AMP polypeptide construct may include a fragment of porcine myeloid antimicrobial peptide-36 ("PMAP-36", SEQ ID NO: 204) that retains antibacterial activity. PMAP-36 is a cathelicidin-related AMP deduced from porcine myeloid cDNA with an amphipathic α-helical conformation at the N-terminus. Accordingly, suitable PMAP-36 fragments are typically selected from the N-terminus to obtain fragments retaining antibacterial activity. In some embodiments, the PMAP-36 fragment of the present disclosure includes the hydrophobic amino acid (Trp) at position 23. In other embodiments, the random coil C-terminal is omitted from the PMAP-36 fragment to reduce or eliminate hemolysis that may be caused by PMAP-36. Further features of PMAP-36 fragments are described, for example, in Lyu et al., *Scientific Reports,* 2016, 6, pages 1-12, which is herein incorporated by reference in its entirety.

[0126] Particularly desirable PMAP-36 fragments include RI12 (SEQ ID NO: 88), RI18 (SEQ ID NO: 92) and TI15 (SEQ ID NO: 94). Other suitable AMP fragments include those from Esculentin (NCBI Reference Sequence: P40843.1), such as the fragment set forth in SEQ ID NO: 80 and anti-lipopolysaccharide factor isoform 2 (NCBI Reference Sequence: AFU61125.1), such as the fragment set forth in SEQ ID NO: 76.

[0127] In some embodiments, the AMPs of the present disclosure include synthetic peptides. In some embodiments, the synthetic peptide reduces the minimum inhibitory concentration (MIC) of an antibiotic, which prevents visible growth of bacterium, but does not itself exhibit antibacterial activity. A particularly desirable synthetic peptide for use with the lysin-AMP polypeptide constructs of the present disclosure includes the FIRL peptidomimetic (SEQ ID NO: 114). Without being limited by theory, FIRL (SEQ ID NO: 114), which is related to a sequence of a protein involved in outer membrane protein biogenesis, BamD, appears to increase the permeability of the outer membrane to antibiotics. Further information regarding the proposed mechanism is found, for example, in Mori et al., *Journal of Antimicrobial Chemotherapy,* 2012, 67: 2173-2181, which is herein incorporated by reference in its entirety.

[0128] Other synthetic peptides useful for sensitizing gram-negative bacteria to antibiotics, which may be incorporated into the lysin-AMP polypeptide construct of the present disclosure includes the cationic peptide KFFKFFKFFK (SEQ ID NO: 120) described in Vaara and Porro, *Antimicrobial agents and Chemotherapy,* 1996, 1801-1805, which is herein incorporated by reference in its entirety.

[0129] In some embodiments, the synthetic peptides are resistant to salts and serum inactivation as described, for example, in Monhanram et al., *Biopolymers,* 2016, 106: 345-346, which is herein incorporated by reference in its entirety. Particularly desirable salt and serum-resistant synthetic peptides include RR12Whydro (SEQ ID NO: 110) and RI18 peptide derivative (SEQ ID NO: 131).

[0130] Structure Stabilizing Components

[0131] In some embodiments, the lysin-AMP polypeptide constructs of the present disclosure further include at least one structure stabilizing component to maintain at least a portion of the structure of the first and/or second component in the construct, e.g., the lysin and/or AMP, substantially the same as in the unconjugated lysin and/or AMP. In some embodiments, the stabilizing structure is a linker. Typically, the at least one structure stabilizing component, such as a linker enables the lysin and AMP to substantially preserve the three-dimensional structure of the first and/or second protein moieties, such that at least one biological activity of the lysin and/or AMP is retained.

[0132] Suitable linkers for connecting two polypeptides are known in the art. In certain embodiments, the linker is a peptide, such as a peptide comprising glycine and serine residues. Specific suitable linkers include, but are not limited to, a TAGGTAGG linker (SEQ ID NO: 72), an IGEM linker GGSGSGSGSGSP (BBa_K1485002) (SEQ ID NO: 82). GGGSGGGGSGGGS (BBA_K1486037, (SEQ ID NO: 86), or a linker as described in Briers et al., *mBio,* 2014, 5:e01379-14, which is herein incorporated by reference in its entirety, i.e., AGAGAGAGAGAGAGAGAS (SEQ ID NO: 122).

[0133] In some embodiments, the structure stabilizing component is a peptide moiety, e.g., an RPP or PP moiety. Such peptide moieties may be included in the present lysin-AMP polypeptide constructs to assist in maintaining the structure of the lysin and/or AMP protein moieties. For example, the RPP or PP amino acid may be inserted at the C terminus or N terminus of a linker, e.g. at the N terminus of the BBA_K1486037 linker (RPPGGGSGGGGSGGGS residues 126 to 141 of SEQ ID NO: 12), at the N terminus of the BBA_K1486037 linker (PPGGGSGGGGSGGGS, residues 144-158 of SEQ ID NO: 16), at the N terminus of the TAGGTAGG linker (SEQ ID NO: 72), such as depicted in residues 137-144 of SEQ ID NO: 18) or at the C terminus of the BBA_K1486037 linker (GGGSGGGGSGGGSPP, residues 135-149 of SEQ ID NO: 20).

[0134] In other embodiments, the peptides MIDR (SEQ ID NO: 112) and/or NPTH (SEQ ID NO: 116) are included in the construct to assist in maintaining the structure of the lysin and/or AMP protein moieties. For example, in some embodiments an AMP structure, such as FIRL (SEQ ID NO: 114), is maintained by the addition of MIDR (SEQ ID NO:

112) and/or NPTH (SEQ ID NO: 116) such as depicted at residues 1-12 of SEQ ID NO: 46 (MIDRFIRLNPTH) and residues 1-12 of SEQ ID NO: 44.

Examples of Lysin-AMP Polypeptide Constructs

[0135] In some embodiments, the lysin-AMP construct comprises: (a) a first component comprising (i) at least one lysin selected from the group consisting of GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN76 (SEQ ID NO: 203), GN4 (SEQ ID NO: 74), GN146 (SEQ ID NO: 78), GN14 (SEQ ID NO: 124), GN37 (SEQ ID NO: 84) optionally with a single pI-increasing mutation, GN316 (SEQ ID NO: 22) optionally with a single point mutation, lysin Pap2_gp17 (SEQ ID NO: 96), GN329 (SEQ ID NO: 26), GN424 (SEQ ID NO: 56), GN202 (SEQ ID NO: 118), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN333 (SEQ ID NO: 28), GN485 (SEQ ID NO: 68), GN123 (SEQ ID NO: 173) and GN121 (SEQ ID NO: 175), typically GN202 (SEQ ID NO: 118) or (ii) a polypeptide having lysin activity and having at least 80%, such as at least such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity with the polypeptide sequence of any of SEQ ID NOs: 206, 208, 210, 218, 220, 203, 74, 78, 124, 84, 22, 96, 26, 56, 118, 58, 60, 64, 66, 28, 68, 173 or 175, typically SEQ ID NO: 118; or (iii) an active fragment of the lysin, said fragment including single point mutations and/or single pI increasing mutations if any; (b) a second component comprising (i) at least one antimicrobial peptide (AMP) selected from the group consisting of Chp1 (SEQ ID NO: 133), Chp2 (SEQ ID NO: 70), CPAR39 (SEQ ID NO: 135), Chp3 (SEQ ID NO: 137), Chp4 (SEQ ID NO: 102), Chp6 (SEQ ID NO: 106), Chp7 (SEQ ID NO: 139), Chp8 (SEQ ID NO: 141), Chp9 (SEQ ID NO: 143), Chp10 (SEQ ID NO: 145), Chp11 (SEQ ID NO: 147), Chp12 (SEQ ID NO: 149), Gkh1 (SEQ ID NO: 151), Gkh2 (SEQ ID NO: 90), Unp1 (SEQ ID NO: 153), Ecp1 (SEQ ID NO: 155), Ecp2 (SEQ ID NO: 104), Tma1 (SEQ ID NO: 157), Osp1 (SEQ ID NO: 108), Unp2 (SEQ ID NO: 159), Unp3 (SEQ ID NO: 161), Gkh3 (SEQ ID NO: 163), Unp5 (SEQ ID NO: 165), Unp6 (SEQ ID NO: 167), Spi1 (SEQ ID NO: 169), Spi2 (SEQ ID NO: 171), Ecp3 (SEQ ID NO: 177), Ecp4 (SEQ ID NO: 179), ALCES1 (SEQ ID NO: 181), AVQ206 (SEQ ID NO: 183), AVQ244 (SEQ ID NO: 185), CDL907 (SEQ ID NO: 187), AGT915 (SEQ ID NO: 189), HH3930 (SEQ ID NO: 191), Fen7875 (SEQ ID NO: 193), SBR77 (SEQ ID NO: 195), Bdp1 (SEQ ID NO: 197), LVP1 (SEQ ID NO: 199), Lvp2 (SEQ ID NO: 201), an esculentin fragment (SEQ ID NO: 80), RI12 (SEQ ID NO: 88), TI15 (SEQ ID NO: 94), RI18 (SEQ ID NO: 92), FIRL (SEQ ID NO: 114), a fragment of LPS binding protein (SEQ ID NO: 76), RR12whydro (SEQ ID NO: 110), RI18 peptide derivative (SEQ ID NO: 131) and cationic peptide (SEQ ID NO: 120), typically FIRL (SEQ ID NO: 114) or (ii) a polypeptide having AMP activity, wherein the polypeptide is at least 75%, such as at least 80% identical to at least one of SEQ ID NOS: 133, 70, 135, 137, 102, 106, 139, 141, 143, 145, 147, 149, 151, 90, 153, 155, 104, 157, 108, 159, 161, 163, 165, 167, 169, 171, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 80, 88, 94, 92, 114, 76, 110, 131 and 120, typically 114.

[0136] Typically, any of the AMP variants sharing at least 75%, such as at least 80% identity or more with the disclosed AMPS (e.g., SEQ ID NO: 114) or fragments thereof retain its alpha-helical structure and any residues associated with activity. For example, as noted above, fragments of PMAP-36 (SEQ ID NO: 204) typically retain the hydrophobic amino acid (Trp) at position 23.

[0137] In some embodiments, GN37 (SEQ ID NO: 84) comprises a single pI-increasing mutation, wherein the GN37 (SEQ ID NO: 84) with the single pI-increasing mutation is GN217 (SEQ ID NO: 8). In some embodiments, GN316 (SEQ ID NO: 22) comprises a single point mutation, wherein the GN37 (SEQ ID NO: 84) with the single point mutation is GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52), GN418 (SEQ ID NO: 54) and/or GN394 (SEQ ID NO: 48).

[0138] In some embodiments, the construct further comprises at least one structure stabilizing component. In some embodiments, the at least one structure stabilizing component is a peptide linker, such as a peptide comprising glycine and serine residues. In certain embodiments, the peptide linker is selected from the group consisting of TAGGTAGG (SEQ ID NO: 72), IGEM (BBa_K1485002) (SEQ ID NO: 82), PPTAGGTAGG (SEQ ID NO: 98), IGEM+PP (residues 44-58 of SEQ ID NO: 16) and AGAGAGAGAGAGAGA-GAS (SEQ ID NO: 122).

[0139] In some embodiments, the lysin-AMP polypeptide construct is selected from at least one of GN168 lysin (SEQ ID NO: 2), GN176 lysin (SEQ ID NO: 4), GN178 lysin (SEQ ID NO: 6), GN218 lysin (SEQ ID NO: 10), GN223 lysin (SEQ ID NO: 12), GN239 lysin (SEQ ID NO: 14), GN243 lysin (SEQ ID NO: 16), GN280 lysin (SEQ ID NO: 18), GN281 lysin (SEQ ID NO: 20), GN349 lysin (SEQ ID NO: 30), GN351 lysin (SEQ ID NO: 32), GN352 lysin (SEQ ID NO: 34), GN353 lysin (SEQ ID NO: 36), GN357 lysin (SEQ ID NO: 38), GN359 lysin (SEQ ID NO: 40), GN369 lysin (SEQ ID NO: 42), GN370 lysin (SEQ ID NO: 44), GN371 lysin (SEQ ID NO: 46) or GN 93 lysin (SEQ ID NO: 62), typically GN370 lysin (SEQ ID NO: 44) or a polypeptide having lysin activity and having at least 80%, such as at least such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity with the polypeptide sequence of at least one of SEQ ID NOs: 2, 4, 6, 10, 12, 14, 16, 18, 20, 30, 32, 34, 36, 38, 40, 42, 44, 46, or 62, typically SEQ ID NO: 44.

[0140] More particularly, in some embodiments, the lysin-AMP polypeptide construct comprises a Chp2 amurin polypeptide (SEQ ID NO: 70) and a TAGGTAGG linker (SEQ ID NO: 72) introduced N-terminally to the GN4 lysin (SEQ ID NO: 74) to generate the GN168 lysin (SEQ ID NO: 2) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 2.

[0141] In some embodiments, the encoded lysin-AMP polypeptide construct comprises a fragment of LPS binding protein (SEQ ID NO: 76) and a TAGGTAGG linker (SEQ ID NO: 72) introduced N-terminally to the GN146 lysin (SEQ ID NO: 78) to generate the GN176 lysin (SEQ ID NO: 4) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 4.

[0142] In some embodiments, the lysin-AMP polypeptide construct comprises an Esculentin fragment (SEQ ID NO: 80) and an IGEM linker (SEQ ID NO: 82) introduced

N-terminally to the GN146 lysin (SEQ ID NO: 78) to generate the GN178 lysin (SEQ ID NO: 6) or a polypeptide having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 6.

[0143] In some embodiments, the encoded lysin-AMP polypeptide construct comprises an IGEM linker (SEQ ID NO: 86) and an RI12 antimicrobial peptide (SEQ ID NO: 88) introduced C-terminally to the GN37 lysin (SEQ ID NO: 84) to generate the GN218 lysin (SEQ ID NO: 10) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 10.

[0144] In some embodiments, the lysin-AMP polypeptide construct comprises an RPP moiety, an IGEM linker (SEQ ID NO: 86), and the antimicrobial amurin peptide Gkh2 (SEQ ID NO: 90) introduced C-terminally to the GN37 lysin (SEQ ID NO: 84) to generate the GN223 lysin (SEQ ID NO: 12) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98% or such as at least 99% sequence identity to SEQ ID NO: 12.

[0145] In some embodiments, the lysin-AMP polypeptide construct comprises an IGEM linker (SEQ ID NO: 86) and an RI18 peptide (SEQ ID NO: 92) introduced C-terminally to the GN37 lysin (SEQ ID NO: 84) to generate the GN239 lysin (SEQ ID NO: 14) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 14.

[0146] In some embodiments, the lysin-AMP polypeptide construct comprises a PP amino acid moiety, an IGEM linker (SEQ ID NO: 86) and a TI15 peptide (SEQ ID NO: 94), introduced C-terminally to the GN37 lysin (SEQ ID NO: 84) to generate the GN243 lysin (SEQ ID NO: 16) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 16.

[0147] In some embodiments, the lysin-AMP polypeptide construct comprises an RI18 antimicrobial peptide (SEQ ID NO: 92), a linker having the amino acid sequence PPTAGGTAGG (SEQ ID NO: 98), and a TI15 antimicrobial peptide (SEQ ID NO: 94) introduced C terminally to a Lysin PaP2_gp17 (SEQ ID NO: 96) to generate GN280 lysin (SEQ ID NO: 18) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 18.

[0148] In some embodiments, the lysin-AMP polypeptide construct comprises an RI18 peptide (SEQ ID NO: 92), an IGEM linker (SEQ ID NO: 86), a PP amino acid moiety (added to maintain structure of the lysin and/or the AMP), and a T115 peptide (SEQ ID NO: 94) introduced C terminally to a Lysin PaP2_gp17 (SEQ ID NO: 96) to generate GN281 lysin (SEQ ID NO: 20) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 20.

[0149] In some embodiments, the lysin-AMP polypeptide construct comprises a linker having the amino acid sequence TAGGTAGG (SEQ ID NO: 72), and an amurin peptide Chp4 (SEQ ID NO: 102) introduced C-terminally to the GN316 lysin (SEQ ID NO: 22) to generate the GN349 lysin (SEQ ID NO: 30) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 30.

[0150] In some embodiments, the lysin-AMP polypeptide construct comprises a linker having the amino acid sequence TAGGTAGG (SEQ ID NO: 72), and an amurin peptide Ecp2 (SEQ ID NO: 104), introduced C-terminally to the GN316 lysin (SEQ ID NO: 22) to generate the GN351 lysin (SEQ ID NO: 32) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 32.

[0151] In some embodiments, the lysin-AMP polypeptide construct comprises a linker having the amino acid sequence TAGGTAGG (SEQ ID NO: 72), and an amurin peptide Chp7 (SEQ ID NO: 139) introduced C-terminally to the GN316 lysin (SEQ ID NO: 22) to generate the GN352 lysin (SEQ ID NO: 34) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 34.

[0152] In some embodiments, the lysin-AMP polypeptide construct comprises a linker having the amino acid sequence TAGGTAGG (SEQ ID NO: 72) and an amurin peptide Osp1 (SEQ ID NO: 108), introduced C-terminally to the GN316 lysin (SEQ ID NO: 22) to generate the GN353 lysin (SEQ ID NO: 36) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 36.

[0153] In some embodiments, the lysin-AMP polypeptide construct comprises a linker having the amino acid sequence TAGGTAGG (SEQ ID NO: 72), and a RR12Whydro (SEQ ID NO: 110) introduced C-terminally to the GN316 lysin (SEQ ID NO: 22) to generate the GN357 lysin (SEQ ID NO: 38) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 38.

[0154] In some embodiments, the lysin-AMP polypeptide construct comprises a linker having the amino acid sequence TAGGTAGG (SEQ ID NO: 72) and a TI15 peptide derivative of PMAP-36 (SEQ ID NO: 94), introduced C-terminally to the GN316 lysin (SEQ ID NO: 22) to generate the GN359 lysin (SEQ ID NO: 40) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 40.

[0155] In some embodiments, the lysin-AMP polypeptide construct comprises RR18 (SEQ ID NO: 92), introduced C-terminally to the GN316 lysin (SEQ ID NO: 22) to generate the GN369 lysin (SEQ ID NO: 42) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 42.

[0156] In some embodiments, the lysin-AMP polypeptide construct comprises a MIDR moiety (SEQ ID NO: 112), a FIRL moiety (SEQ ID NO:114) and an NPTH moiety (SEQ ID NO: 116) introduced N-terminally to the GN202 lysin (SEQ ID NO: 118) to generate the GN370 lysin (SEQ ID NO: 44) or a polypeptide having lysin activity and having at

least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 44.

[0157] In some embodiments, the lysin-AMP polypeptide construct comprises a MIDR moiety (SEQ ID NO: 112), FIRL (SEQ ID NO: 114) and an NPTH moiety (SEQ ID NO: 116) introduced N-terminally to the GN146 lysin (SEQ ID NO: 78) to generate the GN371 lysin (SEQ ID NO: 46) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 46.

[0158] In some embodiments, the lysin-AMP polypeptide construct comprises a cationic peptide (SEQ ID NO: 120) and a linker domain (SEQ ID NO: 122) introduced N-terminally to the GN14 lysin (SEQ ID NO: 124) to generate a GN93 lysin (SEQ ID NO: 62) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 62.

[0159] Table 1, below, depicts specific examples of the lysins and lysin-AMP constructs described herein. The AMP portion of the construct is double-underlined for GN168 (SEQ ID NO: 2), GN176 (SEQ ID NO: 4), GN178 (SEQ ID NO: 6), GN370 (SEQ ID NO: 44), GN371 (SEQ ID NO: 46) and GN93 (SEQ ID NO: 62). For all other constructs, double underlines correspond to a lysin. Structure stabilizing components, such as linkers, are italicized with dashed underlining. The purification tag for GN486 (SEQ ID NO: 66) is italicized and bolded. Single point mutations are bolded.

TABLE 1

GN #	Polypeptide Sequence
GN168	MRLKMARRRYRLPRRRSRRLFSRTALRMHPRNRLRRIMRGGIRF*TAGGTA* *GG*RTSQRGIDLIKSFEGLRLSAYQDSVGVWTIGYGTTRGVTRYMTITVEQ AERMLSNDIQRFEPELDRLAKVPLNQNQWDALMSFVYNLGAANLASSTL LDLLNKGDYQGAADQFPHWVNAGGKRLDGLVKRRAAERALFLEPLS (SEQ ID NO: 2)
GN176	MSFNVTPKFKRWQLYFRGRMW*TAGGTAGG*RTSQRGIDLIKSFEGLRLSAY QDSVGVWTIGYGTTRGVTRYMTITVEQAERMLSNDIQRFEPELDRLAKVP LNQNQWDALMSFVYNLGAANLASSTLLDLLNKGDYQGAADQFPHWVN AGGKRLDGLVKRRAAERALFLEPLS (SEQ ID NO: 4)
GN178	MPPIFSKLAGKKIKNLLISGLK*GGSGSGSGSGSP*RTSQRGIDLIKSFEGL RLSAYQDSVGVWTIGYGTTRGVTRYMTITVEQAERMLSNDIQRFEPELDR LAKVPLNQNQWDALMSFVYNLGAANLASSTLLDLLNKGDYQGAADQFPH WVNAGGKRLDGLVKRRAAERALFLEPLS (SEQ ID NO: 6)
GN217	MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL VAAGASKTMNSRHLTGHAVDLAAYVNGI**H**WDWPLYDAIAVAVKAAAK ELGVAIVWGGDWTTFKDGPHFELDRSKYR (SEQ ID NO: 8)
GN218	MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL VAAGASKTMNSRHLTGHAVDLAAYVNGIRWDWPLYDAIAVAVKAAAK ELGVAIVWGGDWTTFKDGPHFELDRSKY*GGGSGGGGSGGGS*RLKKIGKV LKWI (SEQ ID NO: 10)
GN223	MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL VAAGASKTMNSRHLTGHAVDLAAYVNGIRWDWPLYDAIAVAVKAAAK ELGVAIVWGGDWTTFKDGPHFELDRSKY**RPP***GGGSGGGGSGGGS*SKKAS RKSFTKGAVKVHKKNVPTRVPMRGGIRL (SEQ ID NO: 12)
GN239	MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL VAAGASKTMNSRHLTGHAVDLAAYVNGIRWDWPLYDAIAVAVKAAAK

TABLE 1-continued

GN #	Polypeptide Sequence
	ELGVAIVWGGDWTTFKDGPHFELDRSKY*GGGSGGGGSGGGS*RKKTRKRL KKIGKVLKWI (SEQ ID NO: 14)
GN243	MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL VAAGASKTMNSRHLTGHAVDLAAYVNGIRWDWPLYDAIAVAVKAAAK ELGVAIVWGGDWTTFKDGPHFELDRSKYRKKTRKRLKKIGKVLKWI**PP***G* *GGGGSGGGS*TRKRLKKIGKVLKWI (SEQ ID NO: 16)
GN280	MKLSEKRALFTQLLAQLILWAGTQDRVSVALDQVKRTQAEADANAKSG AGIRNSLHLLGLAGDLILYKDGKYMDKSEDYKFLGDYWKSLHPLCRWG GDFKSRPDGNHFSLEHEGV*QRKKTRKRLKKIGKVLKWI***PPTAGGTAGG***TR KRLKKIGKVLKWI (SEQ ID NO: 18)
GN281	MKLSEKRALFTQLLAQLILWAGTQDRVSVALDQVKRTQAEADANAKSG AGIRNSLHLLGLAGDLILYKDGKYMDKSEDYKFLGDYWKSLHPLCRWG GDFKSRPDGNHFSLEHEGV*QRKKTRKRLKKIGKVLKWI***GGGSGGGGSGG* ***G***SPPTRKRLKKIGKVLKWI (SEQ ID NO: 20)
GN316	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY AQNQYDTKLAAAYKSFS (SEQ ID NO: 22)
GN329	MITDREYQQAAEMLGVDVPAIKAVTKVEAPVGGFQPTGEPTILYERHQM YRQLQAKGLPTEGHPPDLVNKVAGGYGKYSEQHAKLARAVKIDRDSALE SCSWGMFQIMGYHWKLMGYPTLQAFVNAMYASEGAQMDAFCRFIKAQP TTHAALKAHDWAKFARLYNGPGYAKNKYDVKLEKAYAEASG (SEQ ID NO: 26)
GN333	MALTEQDFQSAADDLGVDVASVKAVTKVESRGSGFLLSGVPKILFERHW MFKLLKRKLGRDPEINDVCNPKAGGYLGGQAEHERLDKAVKMDRDCAL QSASWGLFQIMGFHWEALGYASVQAFVNAQYASEGSQLNTFVRFIKTNP AIHKALKSKDWAEFARRYNGPDYKKNNYDVKLAEAYQSFK (SEQ ID NO: 28)
GN349	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY AQNQYDTKLAAAYKSFS*TAGGTAGG*ARRYRLSRRRSRRLFSRTALRMHR RNRLRRIMRGGIRF (SEQ ID NO: 30)

TABLE 1-continued

GN #	Polypeptide Sequence
GN351	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY AQNQYDTKLAAAYKSFS*TAGGTAGG*ARSRRRMSKRSSRRSFRKYAKSHK KNFKARSMRGGIRL (SEQ ID NO: 32)
GN352	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY AQNQYDTKLAAAYKSFS*TAGGTAGG*KRRKMTRKGSKRLFTATADKTKSI NTAPPPMRGGIRL (SEQ ID NO: 34)
GN353	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY AQNQYDTKLAAAYKSFS*TAGGTAGG*RKRMSKRVDKKVFRRTAASAKKIN IDPKIYRGGIRL (SEQ ID NO: 36)
GN357	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGI VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY AQNQYDTKLAAAYKSFS*TAGGTAGG*RRLIRLWLRLLR (SEQ ID NO: 38)
GN359	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY AQNQYDTKLAAAYKSFS*TAGGTAGG*TRKRLKKIGKVLKWI (SEQ ID NO: 40)
GN369	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV

TABLE 1-continued

GN #	Polypeptide Sequence
	ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK
	AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE
	EMFNDFLTGERAQLMAFVKFIKADANLWKATKDKNWAEFARRYNGPAY
	AQNQYDTKLAAAYKSFSRKKTRKRLKKIGKVLKWI (SEQ ID NO: 42)
GN370	*MIDR*FIRL*NPTH*GPRRPRRPGRRAPVRTSQRGIDLIKSFEGLRLSAYQDS
	VGVWTIGYGTTRGVTRYMTITVEQAERMLSNDIQRFEPELDRLAKVPLNQ
	NQWDALMSFVYNLGAANLASSTLLDLLNKGDYQGAADQFPHWVNAGGKR
	LDGLVKRRAAERALFLEPLS (SEQ ID NO: 44)
GN371	*MIDR*FIRL*NPTH*RTSQRGIDLIKSFEGLRLSAYQDSVGVWTIGYGTTRGV
	TRYMTITVEQAERMLSNDIQRFEPELDRLAKVPLNQNQWDALMSFVYNLG
	AANLASSTLLDLLNKGDYQGAADQFPHWVNAGGKRLDGLVKRRAAERAL
	FLEPLS (SEQ ID NO: 46)
GN394	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL
	VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV
	ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK
	AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE
	EMFNDFLTGERAQLMAFV**D**FIKADANLWKALKDKNWAEFARRYNGPAY
	AQNQYDTKLAAAYKSFS (SEQ ID NO: 48)
GN396	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL
	VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV
	ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK
	AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE
	EMFNDFLTGERAQLMAFVKFIKADANLW**D**ALKDKNWAEFARRYNGPAY
	AQNQYDTKLAAAYK*SFS* (SEQ ID NO: 50)
GN408	MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL
	VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAA**H**ELSVDLASIKAVNQV
	ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK
	AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE
	EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY
	AQNQYDTKLAAAYKSFS(SEQ ID NO: 52)
GN418	MAILKIGSKGLEVKNLQTSLN**D**IGFNLVADGIFGKATDNAVRAVQAGAGL
	VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV
	ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK
	AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE
	EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY
	AQNQYDTKLAAAYK*SFS* (SEQ ID NO: 54)
GN424	MNTLRFNSRGAEVGVLQQRLVRAGYPIDVTHLYDEATEQAVKALQAAA
	GIVVDGIAGPNTYAVLSAGQRDRKHLTEADIARAADKLGVSPACVRAVN

TABLE 1-continued

GN #	Polypeptide Sequence
	EVESRGSGFLADGRPVILFERHVMYNRLVAAKRAVDAASAAQRFPNVVS
	AKPGGYQGGAAEYVRLDTAARIDAAIAYESASWGAFQVMGYHWERLGY
	SSIDEFVARMETSEGEQLDAFVRFVAADSSLRTALKNRKWAAFAKGYNG
	PDYARNLYDAKLAQAYERYAGTKAAA (SEQ ID NO: 56)
GN425	MTLRLDDVGLDVLHLQKRLNELGANPRLLPDGQFGEVTERAVRAFQQRA
	GLVVDGVAGPKTMAALSGHSTSRLLGQRDLQRAADRLGVPLASVMALN
	AVESRGEGFAANGRPVILFERHVMHERLQVNGLSEAEADALAARHPGLV
	SRRPGGYVGDTAEHQRLANARLLHDTAALESASWGLFQVMGYHWQAL
	GYDTTQDFTERMARHEAEHLEAFVRFIEADPALHKALKGRKWAEFARRY
	NGPAYARNLYDVKLARAFEQFSDALQAAA (SEQ ID NO: 58)
GN428	MAILKLGNRGSEVKALQQSLNKIGFSLTADGIFGKATENAVKSVQAGAGL
	VIDGIAGPKTFYAIRNAGDAHQEHLTEADLVDAARELGVELASMKAVNQ
	VESRGTGFTKTGKIKTLFERHIMYKKVTAKFGQARANALYQLYPTLVNPN
	SGGYIGGDAELERLQGAIALDEDCAYESASYGLFQIMGFNCQICGYSNAK
	EMFTDFLTGERAHLLAFVKFIKADANMWKALKNKNWAEFARRYNGPAY
	AKNQYDTKLAAAYKSFC (SEQ ID NO: 60)
GN93	MKFFKFFKFFKAGAGAGAGAGAGAGASNNELPWVAEARKYIGLREDTS
	KTSHNPKLLAMLDRMGEFSNESRAWWHDDETPWCGLFVGYCLGVAGR
	YVVREWYRARAWEAPQLTKLDRPAYGALVTFTRSGGGHVGFIVGKDAR
	GNLMVLGGNQSNAVSIAPFAVSRVTGYFWPSFWRNKTAVKSVPFEERYS
	LPLLKSNGELSTNEA (SEQ ID NO: 62)
GN431	MAILKLGNRGTEVKALQDSLNKIGFTLVADGIFGKATENAVKTVQAGAG
	LVIDGIVGPKTSYAIRNAGEAHQDHLTEADLIEAANQLGVDLASVKAVNQ
	VESRGTGFTKSGKIKTLFERHIMYKKLMAKFGQARANAMGQMYPTLVSP
	VAGGYTGGDAELDRLHAAINIDEDCAYESASYGLFQIMGFNCQVCGYAN
	AKEMFNDFLTGERAHLMAFVKFIKADAKLWQALKDKNWAEFARRYNGP
	AYTKNQYDTKLAAAYNSFN (SEQ ID NO: 64)
GN486	M***GSHHHHHHG***GPRRPRRPGRRAPVRTSQRGIDLIKSFEGLRLSAYQDSV
	GVWTIGYGTTRGVTRYMTITVEQAERMLSNDIQRFEPELDRLAKVPLNQN
	QWDALMSFVYNLGAANLASSTLLKLLNKGDYQGAADQFPRWVNAGGK
	RLDGLVKRRAAERALFLEPLS (SEQ ID NO: 66)
GN485	MPGLSGFIRNADTPVTSLGSAGHVHVPEGPLIRINPDCLLGTPFKFFKFF
	KFFKFFKFFKFFKFFKNECVLL (SEQ ID NO: 68)

[0160] In some embodiment, the lysins and/or lysin-AMP polypeptide constructs of the present disclosure are chemically modified. A chemical modification includes but is not limited to, adding chemical moieties, creating new bonds, and removing chemical moieties. Chemical modifications can occur anywhere in a lysin and/or lysin-AMP polypeptide construct, including the amino acid side chains, as well as the amino or carboxyl termini. For example, in certain embodiments, the lysin or lysin-AMP polypeptide construct comprises an N-terminal acetylation modification. In certain

embodiments, the lysin or lysin-AMP polypeptide construct comprises a C-terminal amidation modification. Such modification can be present at more than one site in a lysin and/or lysin-AMP polypeptide construct.

[0161] Furthermore, one or more side groups, or terminal groups of a lysin and/or lysin-AMP polypeptide construct may be protected by protective groups known to the person ordinarily-skilled in the art.

[0162] In some embodiments, the lysins and/or lysin-AMP polypeptide constructs are conjugated to a duration enhancing moiety. In some embodiment, the duration enhancing moiety is polyethylene glycol. Polyethylene glycol ("PEG") has been used to obtain therapeutic polypeptides of enhanced duration (Zalipsky, S., *Bioconjugate Chemistry,* 6:150-165 (1995); Mehvar, R., *J. Pharm. Pharmaceut Sci.,* 3:125-136 (2000), which is herein incorporated by reference in its entirety). The PEG backbone, (CH2CH2-0-)n, wherein n is a number of repeating monomers, is flexible and amphiphilic. When attached to another chemical entity, such as a lysin and/or lysin-AMP polypeptide construct, PEG polymer chains can protect such polypeptides from immune response and other clearance mechanisms. As a result, pegylation can lead to improved efficacy and safety by optimizing pharmacokinetics, increasing bioavailability, and decreasing immunogenicity and dosing amount and/or frequency.

Polynucleotides

[0163] In one aspect, the present disclosure is directed an isolated polynucleotide comprising a nucleic acid molecule encoding a lysin, a variant lysin, an active fragment thereof or derivative as described herein. In some embodiments, the isolated polynucleotide sequence is a DNA sequence. In other embodiments, the isolated polynucleotide is a cDNA sequence.

[0164] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a polypeptide having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity with a lysin, a variant lysin, an active fragment thereof or derivative as described herein, wherein the encoded polypeptide inhibits the growth, or reduces the population, or kills *P. aeruginosa* and optionally at least one other species of Gram-negative bacteria as described herein in the absence or presence of, or in both the absence and presence of, human serum, or in the presence of pulmonary surfactant.

[0165] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin selected from GN217 (SEQ ID NO: 8), GN316 variant (SEQ ID NO: 24) GN316 (SEQ ID NO: 22), GN329 (SEQ ID NO: 26), GN333 (SEQ ID NO: 28), GN394 (SEQ ID NO: 48), GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52), GN418 (SEQ ID NO: 54), GN424 (SEQ ID NO: 56), GN425 (SEQ ID NO:58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN485 (SEQ ID NO: 68), Lysin PaP2 gp17 (SEQ ID NO: 96), GN123 (SEQ ID NO: 173) or GN121 (SEQ ID NO: 175) or a variant or an active fragment thereof or derivative, wherein the lysin variant or an active fragment thereof or derivative encoded by the isolated polynucleotide inhibits the growth, or reduces the population, or kills *P. aeruginosa* and/or at least one other species of Gram-negative bacteria in the absence or presence of, or in both the absence and presence of, human serum, or in the presence of pulmonary surfactant. In certain embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin, variant or active fragment thereof or derivative that contains at least one modification relative to at least one of SEQ ID NOS: 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, 96, 173 and 175 such as at least one amino acid substitution, insertion or deletion. In certain embodiments, the isolated polynucleotide comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 7, 23, 21, 25, 27, 47, 49, 51, 53, 55, 57, 59, 63, 65, 67 95, 172 and 174 respectively, complements thereof or a nucleic acid sequence having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to one of SEQ ID NOS: 7, 23, 21, 25, 27, 47, 49, 51, 53, 55, 57, 59, 63, 65, 67 95, 172 and 174, or complements thereof, wherein the encoded polypeptide inhibits the growth, or reduces the population, or kills *P. aeruginosa* and/or at least one other species of Gram-negative bacteria in the absence or presence of, or in both the absence and presence of, human serum, or in the presence of pulmonary surfactant.

[0166] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin selected from at least one of GN217 lysin (SEQ ID NO: 8), GN394 lysin (SEQ ID NO: 48), GN396 lysin (SEQ ID NO: 50), GN408 lysin (SEQ ID NO: 52), GN418 lysin (SEQ ID NO: 54) and GN486 (SEQ ID NO: 66) or a variant or an active fragment thereof or derivative. In certain embodiments, the polynucleotide comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 7, 47, 49, 51, 53, and 65 complements thereof or a nucleic acid sequence having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to one of SEQ ID NOS: 77, 47, 49, 51, 53, or 65, or complements thereof, wherein the encoded polypeptide inhibits the growth, or reduces the population, or kills *P. aeruginosa* and optionally at least one other species of Gram-negative bacteria in the absence or presence of, or in both the absence and presence of, human serum, or in the presence of pulmonary surfactant.

[0167] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin selected from at least one of GN316 (SEQ ID NO: 22), GN329 (SEQ ID NO: 26), GN333 (SEQ ID NO: 28), GN424 (SEQ ID NO: 56), GN425 (SEQ ID NO:58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN485 (SEQ ID NO: 68) or a variant or an active fragment thereof or derivative, wherein the encoded polypeptide inhibits the growth, or reduces the population, or kills *P. aeruginosa* and optionally at least one other species of Gram-negative bacteria in the absence or presence of, or in both the absence and presence of, human serum, or in the presence of pulmonary surfactant. In certain embodiments, the variant, active fragment thereof or derivative contains at least one modification relative to at least one of SEQ ID NOS: 22, 26, 28, 56, 58, 60, 64 or 68, such as at least one amino acid substitution, insertion or deletion. In certain embodiments, the polynucleotide comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 21, 25, 27, 55, 57, 59, 63 and 67, complements thereof or a nucleic acid sequence having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to one of SEQ ID NOS: 21, 25, 27, 55, 57,

59, 63 or 67, or complements thereof, wherein the encoded polypeptide inhibits the growth, or reduces the population, or kills *P. aeruginosa* and optionally at least one other species of Gram-negative bacteria in the absence or presence of, or in both the absence and presence of, human serum, or in the presence of pulmonary surfactant.

[0168] In another aspect, the present disclosure is directed to an isolated polynucleotide comprising a nucleic acid molecule encoding a lysin-AMP polypeptide construct comprising:

[0169] (a) a first nucleic acid molecule encoding a first component comprising: (i) a lysin selected from the group consisting of GN7 (SEQ ID NO: 206), GN11 (SEQ ID NO: 208), GN40 (SEQ ID NO: 210), GN122 (SEQ ID NO: 218), GN328 (SEQ ID NO: 220), GN76 (SEQ ID NO: 203), GN4 (SEQ ID NO: 74), GN146 (SEQ ID NO: 78), GN14 (SEQ ID NO: 124), GN37 (SEQ ID NO: 84) optionally with a single pI-increasing mutation, GN316 (SEQ ID NO: 22) optionally with a single point mutation, lysin Pap2_gp17 (SEQ ID NO: 96), GN329 (SEQ ID NO: 26), GN424 (SEQ ID NO: 56), GN202 (SEQ ID NO: 118), GN425 (SEQ ID NO: 58), GN428 (SEQ ID NO: 60), GN431 (SEQ ID NO: 64), GN486 (SEQ ID NO: 66), GN333 (SEQ ID NO: 28), and GN485 (SEQ ID NO: 68), GN123 (SEQ ID NO: 173) and GN121 (SEQ ID NO: 175); or (ii) a polypeptide having lysin activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 206, 208, 210, 218, 220, 203, 74, 78, 124, 84, 22, 96, 26, 56, 118, 58, 60, 64, 66, 28, 68, 173 or 175; or (iii) an active fragment of the lysin;

[0170] (b) a second nucleic acid molecule encoding a second component comprising: (i) at least one antimicrobial peptide (AMP) selected from the group consisting of Chp1 (SEQ ID NO: 133), Chp2 (SEQ ID NO: 70), CPAR39 (SEQ ID NO: 135), Chp3 (SEQ ID NO: 137), Chp4 (SEQ ID NO: 102), Chp6 (SEQ ID NO: 106), Chp7 (SEQ ID NO: 139), Chp8 (SEQ ID NO: 141), Chp9 (SEQ ID NO: 143), Chp10 (SEQ ID NO: 145), Chp11 (SEQ ID NO: 147), Chp12 (SEQ ID NO: 149), Gkh1 (SEQ ID NO: 151), Gkh2 (SEQ ID NO: 90), Unp1 (SEQ ID NO: 153), Ecp1 (SEQ ID NO: 155), Ecp2 (SEQ ID NO: 104), Tma1 (SEQ ID NO: 157), Osp1 (SEQ ID NO: 108), Unp2 (SEQ ID NO: 159), Unp3 (SEQ ID NO: 161), Gkh3 (SEQ ID NO: 163), Unp5 (SEQ ID NO: 165), Unp6 (SEQ ID NO: 167), Spi1 (SEQ ID NO: 169), Spi2 (SEQ ID NO: 171), Ecp3 (SEQ ID NO: 177), Ecp4 (SEQ ID NO: 179), ALCES1 (SEQ ID NO: 181), AVQ206 (SEQ ID NO: 183), AVQ244 (SEQ ID NO: 185), CDL907 (SEQ ID NO: 187), AGT915 (SEQ ID NO: 189), HH3930 (SEQ ID NO: 191), Fen7875 (SEQ ID NO: 193), SBR77 (SEQ ID NO: 195), Bdp1 (SEQ ID NO: 197), LVP1 (SEQ ID NO: 199), Lvp2 (SEQ ID NO: 201), an esculentin fragment (SEQ ID NO: 80), RI12 (SEQ ID NO: 88), TI15 (SEQ ID NO: 94), RI18 (SEQ ID NO: 92), FIRL (SEQ ID NO: 114), a fragment of LPS binding protein (SEQ ID NO: 76), RR12whydro (SEQ ID NO: 110), RI18 peptide derivative (SEQ ID NO: 131) and cationic peptide (SEQ ID NO: 120) or (ii) a polypeptide having AMP activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 133, 70, 135, 137, 102, 106, 139, 141, 143, 145, 147, 149, 151, 90, 153, 155, 104, 157, 108, 159, 161, 163, 165, 167, 169, 171, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 80, 88, 94, 92, 114, 76, 110, 131 and 120.

[0171] In some embodiments, the isolated polynucleotides of the present disclosure comprise a nucleic acid molecule encoding a first component of a lysin-AMP construct, wherein the first component is selected from the group consisting of GN394 (SEQ ID NO: 48), GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52) and GN418 (SEQ ID NO: 54).

[0172] In some embodiments, the isolated polynucleotides of the present disclosure comprise a nucleic acid molecule encoding a first component of a lysin-AMP construct, wherein the first component is GN202 (SEQ ID NO: 118).

[0173] In some embodiments, the isolated polynucleotides of the present disclosure comprise a nucleic acid molecule encoding a first component of a lysin-AMP construct, wherein the first component is GN202 (SEQ ID NO: 118) or has lysin activity and is at least 80% identical to SEQ ID NO: 118.

[0174] In some embodiments, the isolated polynucleotides of the present disclosure comprise a nucleic acid molecule encoding a second component of a lysin-AMP construct wherein the second component is selected from a from the group consisting of Chp1 (SEQ ID NO: 133), Chp2 (SEQ ID NO: 70), CPAR39 (SEQ ID NO: 135), Chp3 (SEQ ID NO: 137), Chp4 (SEQ ID NO: 102), Chp6 (SEQ ID NO: 106), Chp7 (SEQ ID NO: 139), Chp8 (SEQ ID NO: 141), Chp9 (SEQ ID NO: 143), Chp10 (SEQ ID NO: 145), Chp11 (SEQ ID NO: 147), Chp12 (SEQ ID NO: 149), Gkh1 (SEQ ID NO: 151), Gkh2 (SEQ ID NO: 90), Unp1 (SEQ ID NO: 153), Ecp1 (SEQ ID NO: 155), Ecp2 (SEQ ID NO: 104), Tma1 (SEQ ID NO: 157), Osp1 (SEQ ID NO: 108), Unp2 (SEQ ID NO: 159), Unp3 (SEQ ID NO: 161), Gkh3 (SEQ ID NO: 163), Unp5 (SEQ ID NO: 165), Unp6 (SEQ ID NO: 167), Spi1 (SEQ ID NO: 169), Spi2 (SEQ ID NO: 171), Ecp3 (SEQ ID NO: 177), Ecp4 (SEQ ID NO: 179), ALCES1 (SEQ ID NO: 181), AVQ206 (SEQ ID NO: 183), AVQ244 (SEQ ID NO: 185), CDL907 (SEQ ID NO: 187), AGT915 (SEQ ID NO: 189), HH3930 (SEQ ID NO: 191), Fen7875 (SEQ ID NO: 193), SBR77 (SEQ ID NO: 195), Bdp1 (SEQ ID NO: 197), LVP1 (SEQ ID NO: 199), Lvp2 (SEQ ID NO: 201), an esculentin fragment (SEQ ID NO: 80), RI12 (SEQ ID NO: 88), TI15 (SEQ ID NO: 94), RI18 (SEQ ID NO: 92), FIRL (SEQ ID NO: 114), a fragment of LPS binding protein (SEQ ID NO: 76), RR12whydro (SEQ ID NO: 110), RI18 peptide derivative (SEQ ID NO: 131) and cationic peptide (SEQ ID NO: 120) or (ii) a polypeptide having AMP activity, wherein the polypeptide is at least 80% identical to at least one of SEQ ID NOS: 133, 70, 135, 137, 102, 106, 139, 141, 143, 145, 147, 149, 151, 90, 153, 155, 104, 157, 108, 159, 161, 163, 165, 167, 169, 171, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 80, 88, 94, 92, 114, 76, 110, 131 and 120.

[0175] In some embodiments, the isolated polynucleotides of the present disclosure comprise a nucleic acid molecule encoding a second component of a lysin-AMP construct, wherein the second component is FIRL (SEQ ID NO: 114) or has AMP activity and is at least 75% identical to SEQ ID NO: 114.

[0176] In some embodiments, isolated polynucleotides of the present disclosure further comprise a nucleic acid molecule encoding at least one structure stabilizing component of a lysin-AMP polypeptide construct to maintain at least a portion of the structure of the first and/or second component in the construct substantially the same as in the unconjugated lysin and/or AMP. In some embodiments, the present isolated polynucleotides comprise a nucleic acid molecule encoding at least one structure stabilizing component,

wherein the at least one structure stabilizing component is a peptide, such as a peptide comprising glycine and/or serine residues. In one embodiment, the peptide is selected from the group consisting of TAGGTAGG (SEQ ID NO: 72), IGEM (BBa_K1485002) (SEQ ID NO: 82), PPTAGGTAGG (SEQ ID NO: 98), IGEM +PP (residues 44-58 of SEQ ID NO: 16) and AGAGAGAGAGAGAGA-GAS (SEQ ID NO: 122).

[0177] More particularly, in some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN168 lysin (SEQ ID NO: 2) or a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 2.

[0178] In some embodiments, the nucleic acid molecule encoding the GN168 lysin comprises the nucleic acid sequence of SEQ ID NO: 1, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 1, or a complement thereof.

[0179] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN176 lysin (SEQ ID NO: 4) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 4.

[0180] In some embodiments, the nucleic acid molecule encoding the GN176 lysin comprises the nucleic acid sequence of SEQ ID NO: 3, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 3, or a complement thereof.

[0181] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN178 lysin (SEQ ID NO: 6) or a nucleic acid sequence encoding a polypeptide having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 6.

[0182] In some embodiments, the nucleic acid molecule encoding the GN178 lysin comprises the nucleic acid sequence of SEQ ID NO: 5, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 5, or a complement thereof.

[0183] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN218 lysin (SEQ ID NO: 10) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 10.

[0184] In some embodiments, the nucleic acid molecule encoding the GN218 lysin comprises the nucleic acid sequence of SEQ ID NO: 9, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 9, or a complement thereof.

[0185] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN223 lysin (SEQ ID NO: 12) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98% or such as at least 99% sequence identity to SEQ ID NO: 12.

[0186] In some embodiments, the nucleic acid molecule encoding the GN223 lysin comprises the nucleic acid sequence of SEQ ID NO: 11, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98% or such as at least 99% sequence identity to SEQ ID NO: 11, or a complement thereof.

[0187] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN239 lysin (SEQ ID NO: 14) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 14.

[0188] In some embodiments, the nucleic acid molecule encoding the GN239 lysin comprises the nucleic acid sequence of SEQ ID NO: 13, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 13, or a complement thereof.

[0189] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN243 lysin (SEQ ID NO: 16) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 16.

[0190] In some embodiments, the nucleic acid molecule encoding the GN243 lysin comprises the nucleic acid sequence of SEQ ID NO: 15, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 15, or a complement thereof.

[0191] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN280 lysin (SEQ ID NO: 18) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 18.

[0192] In some embodiments, the nucleic acid molecule encoding the GN280 lysin comprises the nucleic acid sequence of SEQ ID NO: 17, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 17, or a complement thereof.

[0193] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN281 lysin (SEQ ID NO: 20) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 20.

[0194] In some embodiments, the nucleic acid molecule encoding the GN281 lysin comprises the nucleic acid sequence of SEQ ID NO: 19, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 19, or a complement thereof.

[0195] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN349 lysin (SEQ ID NO: 30) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 30.

[0196] In some embodiments, the nucleic acid molecule encoding the GN349 lysin comprises the nucleic acid sequence of SEQ ID NO: 29, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 29, or a complement thereof.

[0197] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN351 lysin (SEQ ID NO: 32) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 32.

[0198] In some embodiments, the nucleic acid molecule encoding the GN351 lysin comprises the nucleic acid sequence of SEQ ID NO: 31, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 31, or a complement thereof.

[0199] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN352 lysin (SEQ ID NO: 34) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 34.

[0200] In some embodiments, the nucleic acid molecule encoding the GN352 lysin comprises the nucleic acid sequence of SEQ ID NO: 33, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 33, or a complement thereof.

[0201] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN353 lysin (SEQ ID NO: 36) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 36.

[0202] In some embodiments, the nucleic acid molecule encoding the GN353 lysin comprises the nucleic acid sequence of SEQ ID NO: 35, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 35, or a complement thereof.

[0203] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN357 lysin (SEQ ID NO: 38) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 38.

[0204] In some embodiments, the nucleic acid molecule encoding the GN357 lysin comprises the nucleic acid sequence of SEQ ID NO: 37, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 37, or a complement thereof.

[0205] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN359 lysin (SEQ ID NO: 40) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 40.

[0206] In some embodiments, the nucleic acid molecule encoding the GN359 lysin comprises the nucleic acid sequence of SEQ ID NO: 39, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 39, or a complement thereof.

[0207] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN369 lysin (SEQ ID NO: 42) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 42.

[0208] In some embodiments, the nucleic acid molecule encoding the GN369 lysin comprises the nucleic acid sequence of SEQ ID NO: 41, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 41, or a complement thereof.

[0209] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN370 lysin (SEQ ID NO: 44) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 44.

[0210] In some embodiments, the nucleic acid molecule encoding the GN370 lysin comprises the nucleic acid sequence of SEQ ID NO: 43, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 43, or a complement thereof.

[0211] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN371 lysin (SEQ ID NO: 46) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 46.

[0212] In some embodiments, the nucleic acid molecule encoding the GN371 lysin comprises the nucleic acid sequence of SEQ ID NO: 45, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 45, or a complement thereof.

[0213] In some embodiments, the isolated polynucleotide comprises a nucleic acid molecule encoding a lysin-AMP polypeptide construct, wherein the lysin-AMP polypeptide construct is the GN93 lysin (SEQ ID NO: 62) or a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 62.

[0214] In some embodiments, the nucleic acid molecule encoding the GN93 comprises the nucleic acid sequence of SEQ ID NO: 61, a complement thereof or a nucleic acid sequence encoding a polypeptide having lysin activity and having at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 98%, or such as at least 99% sequence identity to SEQ ID NO: 61, or a complement thereof.

Vectors and Host Cells

[0215] In another aspect, the present disclosure is directed to a vector comprising an isolated polynucleotide comprising a nucleic acid molecule encoding any of the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives disclosed herein, such as GN370 (SEQ ID NO: 44) or a complementary sequence of the present isolated polynucleotides. In some embodiments, the vector is a plasmid or cosmid. In other embodiments, the vector is a viral vector, wherein additional DNA segments can be ligated into the viral vector. In some embodiments, the vector can autonomously replicate in a host cell into which it is introduced. In some embodiments, the vector can be integrated into the genome of a host cell upon introduction into the host cell and thereby be replicated along with the host genome.

[0216] In some embodiments, particular vectors, referred to herein as "recombinant expression vectors" or "expression vectors", can direct the expression of genes to which they are operatively linked. A polynucleotide sequence is "operatively linked" when it is placed into a functional relationship with another nucleotide sequence. For example, a promoter or regulatory DNA sequence is said to be "operatively linked" to a DNA sequence that codes for an RNA and/or a protein if the two sequences are operatively linked, or situated such that the promoter or regulatory DNA sequence affects the expression level of the coding or structural DNA sequence. Operatively linked DNA sequences are typically, but not necessarily, contiguous.

[0217] Generally, any system or vector suitable to maintain, propagate or express a polypeptide in a host may be used for expression of the present lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives. The appropriate DNA/polynucleotide sequence may be inserted into the expression system by any of a variety of well-known and routine techniques, such as, for example, those set forth in Sambrook et al., eds., *Molecular Cloning: A Laboratory Manual* (3rd Ed.), Vols. 1-3, Cold Spring Harbor Laboratory (2001). Additionally, tags can also be added to the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure to provide convenient methods of isolation, e.g., c-myc, biotin, poly-His, etc. Kits for such expression systems are commercially available.

[0218] A wide variety of host/expression vector combinations may be employed in expressing the polynucleotide sequences encoding the present lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives. Large numbers of suitable vectors are known to those of skill in the art, and are commercially available. Examples of suitable vectors are provided, e.g., in Sambrook et al, eds., *Molecular Cloning. A Laboratory Manual* (3rd Ed.), Vols. 1-3, Cold Spring Harbor Laboratory (2001). Such vectors include, among others, chromosomal, episomal and virus derived vectors, e.g., vectors derived from bacterial plasmids, from bacteriophage, from transposons, from yeast episomes, from insertion elements, from yeast chromosomal elements, from viruses such as baculoviruses, papova viruses, such as SV40, vaccinia viruses, adenoviruses, fowl pox viruses, pseudorabies viruses and retroviruses, and vectors derived from combinations thereof, such as those derived from plasmid and bacteriophage genetic elements, such as cosmids and phagemids.

[0219] Furthermore, the vectors may provide for the constitutive or inducible expression of the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure. Suitable vectors include but are not limited to derivatives of SV40 and known bacterial plasmids, e.g., *E. coli* plasmids colE1, pCR1, pBR322, pMB9 and their derivatives, plasmids such as RP4, pBAD24 and pBAD-TOPO; phage DNAS, e.g., the numer-

ous derivatives of phage A, e.g., NM989, and other phage DNA, e.g., M13 and filamentous single stranded phage DNA; yeast plasmids such as the 2 D plasmid or derivatives thereof; vectors useful in eukaryotic cells, such as vectors useful in insect or mammalian cells; vectors derived from combinations of plasmids and phage DNAs, such as plasmids that have been modified to employ phage DNA or other expression control sequences; and the like. Many of the vectors mentioned above are commercially available from vendors such as New England Biolabs Inc., Addgene, Takara Bio Inc., ThermoFisher Scientific Inc., etc.

[0220] Additionally, vectors may comprise various regulatory elements (including promoter, ribosome binding site, terminator, enhancer, various cis-elements for controlling the expression level) wherein the vector is constructed in accordance with the host cell. Any of a wide variety of expression control sequences (sequences that control the expression of a polynucleotide sequence operatively linked to it) may be used in these vectors to express the polynucleotide sequences encoding the lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44) lysin polypeptides, variants, active fragments thereof or derivatives thereof of the present disclosure. Useful control sequences include, but are not limited to: the early or late promoters of SV40, CMV, vaccinia, polyoma or adenovirus, the lac system, the trp system, the TAC system, the TRC system, the LTR system, the major operator and promoter regions of phage A, the control regions of fd coat protein, the promoter for 3-phosphoglycerate kinase or other glycolytic enzymes, the promoters of acid phosphatase (e.g., Pho5), the promoters of the yeast-mating factors, *E. coli* promoter for expression in bacteria, and other promoter sequences known to control the expression of genes of prokaryotic or eukaryotic cells or their viruses, and various combinations thereof. Typically, the polynucleotide sequences encoding the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives is operatively linked to a heterologous promoter or regulatory element.

[0221] In another aspect, the present disclosure is directed to a host cell comprising any of the vectors disclosed herein including the expression vectors comprising the polynucleotide sequences encoding the lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure. A wide variety of host cells are useful in expressing the present polypeptides. Non-limiting examples of host cells suitable for expression of the present polypeptides include well known eukaryotic and prokaryotic hosts, such as strains of *E. coli, Pseudomonas, Bacillins, Streptomyces*, fungi such as yeasts, and animal cells, such as CHO, R1.1, B-W and L-M cells, African Green Monkey kidney cells (e.g., COS 1, COS 7, BSC1, BSC40, and BMT10), insect cells (e.g., Sf9), and human cells and plant cells in tissue culture. While the expression host may be any known expression host cell, in a typical embodiment the expression host is one of the strains of *E. coli*. These include, but are not limited to commercially available *E. coli* strains such as Top10 (ThermoFisher Scientific, Inc.), DH5a (Thermo Fisher Scientific, Inc.), XLI-Blue (Agilent Technologies, Inc.), SCS110 (Agilent Technologies, Inc.), JM109 (Promega, Inc.), LMG194 (ATCC), and BL21 (Thermo Fisher Scientific, Inc.).

[0222] There are several advantages of using *E. coli* as a host system including: fast growth kinetics, where under the optimal environmental conditions, its doubling time is about 20 min (Sezonov et al., *J. Bacterial.* 189 8746-8749 (2007)), easily achieved high density cultures, easy and fast transformation with exogenous DNA, etc. Details regarding protein expression in *E. coli*, including plasmid selection as well as strain selection are discussed in details by Rosano, G. and Ceccarelli, E., *Front Microbial.,* 5: 172 (2014).

[0223] Efficient expression of the present lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives depends on a variety of factors such as optimal expression signals (both at the level of transcription and translation), correct protein folding, and cell growth characteristics. Regarding methods for constructing the vector and methods for transducing the constructed recombinant vector into the host cell, conventional methods known in the art can be utilized. While it is understood that not all vectors, expression control sequences, and hosts will function equally well to express the polynucleotide sequences encoding lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure, one skilled in the art will be able to select the proper vectors, expression control sequences, and hosts without undue experimentation to accomplish the desired expression without departing from the scope of this disclosure.

[0224] In some embodiments, the present inventors have found a correlation between level of expression and activity of the expressed polypeptide; in *E. coli* expression systems in particular, moderate levels of expression (for example between about 1 and 10 mg/liter) have produced lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives with higher levels of activity than those that were expressed at higher levels in *E. coli* (for example between about 20 and about 100 mg/liter), the latter having sometimes produced wholly inactive polypeptides.

[0225] Lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography, and lectin chromatography. High performance liquid chromatography can also employed for lysin polypeptide purification.

[0226] Alternatively, the vector system used for the production of lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure may be a cell-free expression system. Various cell-free expression systems are commercially available, including, but are not limited to those available from Promega, LifeTechnologies, Clonetech, etc.

[0227] As indicated above, there is an array of choices when it comes to protein production and purification. Examples of suitable methods and strategies to be considered in protein production and purification are provided in WO 2017/049233, which is herein incorporated by reference in its entirety and further provided in Structural Genomics Consortium et al., *Nat. Methods.,* 5(2): 135-146 (2008).

Pharmaceutical Compositions

[0228] In another aspect, the present disclosure is directed to a pharmaceutical composition comprising an effective

amount of lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives as described herein and a pharmaceutically acceptable carrier. In some embodiments, the present pharmaceutical composition comprises at least one activity selected from inhibiting *P. aeruginosa* bacterial growth, reducing a *P. aeruginosa* bacterial population and/or killing *P. aeruginosa* in the absence and/or presence of human serum, or in the presence of pulmonary surfactant.

[0229] In some embodiments, the present pharmaceutical compositions further comprise one or more antibiotics suitable for the treatment of Gram-negative bacteria. Typical antibiotics include one or more of ceftazidime, cefepime, cefoperazone, ceftobiprole, ciprofloxacin, levofloxacin, aminoglycosides, imipenem, meropenem, doripenem, gentamicin, tobramycin, amikacin, piperacillin, ticarcillin, penicillin, rifampicin, polymyxin B, and colistin. Additional suitable antibiotics are described in Table 3.

[0230] In some embodiments, the pharmaceutical composition is a solution, a suspension, an emulsion, an inhalable powder, an aerosol, or a spray. The pharmaceutical compositions of the present disclosure can take the form of solutions, suspensions, emulsion, tablets, pills, pellets, capsules, capsules containing liquids, powders, sustained-release formulations, suppositories, tampon applications emulsions, aerosols, sprays, suspensions, lozenges, troches, candies, injectants, chewing gums, ointments, smears, time-release patches, liquid absorbed wipes, and combinations thereof.

[0231] Administration of the pharmaceutical compositions of the present disclosure may be topical, i.e., the pharmaceutical composition is applied directly where its action is desired (for example directly to a wound). The topical compositions of the present disclosure may further comprise a pharmaceutically or physiologically acceptable carrier, such as a dermatologically or an otically acceptable carrier. Such carriers, in the case of dermatologically acceptable carriers, are preferably compatible with skin, nails, mucous membranes, tissues and/or hair, and can include any conventionally used dermatological carrier meeting these requirements. In the case of otically acceptable carriers, the carrier is preferably compatible with all parts of the ear. Such carriers can be readily selected by one of ordinary skill in the art.

[0232] Carriers for topical administration of the lysin, active fragment thereof and/or lysin-AMP polypeptide construct of the present disclosure include, but are not limited to, mineral oil, liquid petroleum, white petroleum, propylene glycol, polyoxyethylene and/or polyoxypropylene compounds, emulsifying wax, sorbitan monostearate, polysorbate 60, cetyl esters wax, cetearyl alcohol, 2-octyldodecanol, benzyl alcohol, and water. In formulating skin ointments, the active components of the present disclosure may be formulated in an oleaginous hydrocarbon base, an anhydrous absorption base, a water-in-oil absorption base, an oil-in-water water-removable base and/or a water-soluble base. In formulating otic compositions, the active components of the present disclosure may be formulation in an aqueous polymeric suspension including such carriers as dextrans, polyethylene glycols, polyvinylpyrrolidone, polysaccharide gels, Gelrite®, cellulosic polymers like hydroxypropyl methylcellulose, and carboxy-containing polymers such as polymers or copolymers of acrylic acid, as well as other polymeric demulcents.

[0233] The topical compositions according to the present disclosure may be in any form suitable for topical application, including aqueous, aqueous-alcoholic or oily solutions, lotion or serum dispersions, aqueous, anhydrous or oily gels, emulsions obtained by dispersion of a fatty phase in an aqueous phase (OAV or oil in water) or, conversely, (W/O or water in oil), microemulsions or alternatively microcapsules, microparticles or lipid vesicle dispersions of ionic and/or nonionic type, creams, lotions, gels, foams (which will generally require a pressurized canister, a suitable applicator an emulsifier and an inert propellant), essences, milks, suspensions, or patches. Topical compositions of the present disclosure may also contain adjuvants such as hydrophilic or lipophilic gelling agents, hydrophilic or lipophilic active agents, preserving agents, antioxidants, solvents, fragrances, fillers, sunscreens, odor-absorbers and dyestuffs. In a further aspect, the topical compositions may be administered in conjunction with devices such as transdermal patches, dressings, pads, wraps, matrices and bandages capable of being adhered to or otherwise associated with the skin or other tissue of a subject, being capable of delivering a therapeutically effective amount of one or more antibacterial peptides in accordance with the present disclosure.

[0234] In one embodiment, the topical compositions of the present disclosure additionally comprise one or more components used to treat topical burns. Such components typically include, but are not limited to, a propylene glycol hydrogel; a combination of a glycol, a cellulose derivative and a water soluble aluminum salt; an antiseptic; an antibiotic; and a corticosteroid. Humectants (such as solid or liquid wax esters), absorption promoters (such as hydrophilic clays, or starches), viscosity building agents, and skin-protecting agents may also be added. Topical formulations may be in the form of rinses such as mouthwash. See, e.g., WO2004/004650.

[0235] In some embodiments, administration of the pharmaceutical compositions of the present disclosure may be systemic. Systemic administration can be enteral or oral, i.e., a substance is given via the digestive tract, parenteral, i.e., a substance is given by other routes than the digestive tract such as by injection or inhalation. Thus, the polypeptides including lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure can be administered to a subject orally, parenterally, by inhalation, topically, rectally, nasally, buccally or via an implanted reservoir or by any other known method. The lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure can also be administered by means of sustained release dosage forms.

[0236] For oral administration, the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure can be formulated into solid or liquid preparations, for example tablets, capsules, powders, solutions, suspensions and dispersions. The lysin, active fragment thereof and/or lysin-AMP polypeptide constructs can be formulated with excipients such as, e.g., lactose, sucrose, corn starch, gelatin, potato starch, alginic acid and/or magnesium stearate.

[0237] For preparing solid compositions such as tablets and pills, lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure is mixed with a pharmaceutical excipient to form a solid pre-formulation composition. If desired, tablets may

be sugar coated or enteric coated by standard techniques. The tablets or pills may be coated or otherwise compounded to provide a dosage form affording the advantage of prolonged action. For example, the tablet or pill can include an inner dosage and an outer dosage component, the latter being in the form of an envelope over the former. The two dosage components can be separated by an enteric layer, which serves to resist disintegration in the stomach and permit the inner component to pass intact into the duodenum or to be delayed in release. A variety of materials can be used for such enteric layers or coatings, such materials including a number of polymeric acids and mixtures of polymeric acids with such materials as shellac, cetyl alcohol, and cellulose acetate.

[0238] The pharmaceutical compositions of the present disclosure may also be administered by injection. For example, the pharmaceutical compositions can be administered intramuscularly, intrathecally, subdermally, subcutaneously, or intravenously to treat infections by Gram-negative bacteria, more specifically those caused by *P. aeruginosa*. The pharmaceutically acceptable carrier may be comprised of distilled water, a saline solution, albumin, a serum, or any combinations thereof. Additionally, pharmaceutical compositions of parenteral injections can comprise pH buffered solutions, adjuvants (e.g., preservatives, wetting agents, emulsifying agents, and dispersing agents), liposomal formulations, nanoparticles, dispersions, suspensions or emulsions as well as sterile powders for reconstitution into sterile injectable solutions or dispersions just prior to use

[0239] In cases where parenteral injection is the chosen mode of administration, an isotonic formulation is preferably used. Generally, additives for isotonicity can include sodium chloride, dextrose, mannitol, sorbitol, and lactose. In some cases, isotonic solutions such as phosphate buffered saline are preferred. Stabilizers can include gelatin and albumin. A vasoconstriction agent can be added to the formulation. The pharmaceutical preparations according to this type of application are provided sterile and pyrogen free.

[0240] In another embodiment, the pharmaceutical compositions of the present disclosure are inhalable compositions. In some embodiments, the present pharmaceutical compositions are advantageously formulated as a dry, inhalable powder. In specific embodiments, the present pharmaceutical compositions may further be formulated with a propellant for aerosol delivery. Examples of suitable propellants include, but are not limited to: dichlorodifluoromethane, trichlorofluoromethane, dichloro-tetrafluoroethane and carbon dioxide. In certain embodiments, the formulations may be nebulized.

[0241] A surfactant can be added to an inhalable pharmaceutical composition of the present disclosure in order to lower the surface and interfacial tension between the medicaments and the propellant. The surfactant may be any suitable, non-toxic compound which is non-reactive with the present polypeptides.

[0242] Examples of suitable surfactants include, but are not limited to: oleic acid; sorbitan trioleate; cetyl pyridinium chloride; soya lecithin; polyoxyethylene(20) sorbitan monolaurate; polyoxyethylene (10) stearyl ether; polyoxyethylene (2) oleyl ether; polyoxypropylene-polyoxyethylene ethylene diamine block copolymers; polyoxyethylene(20) sorbitan monostearate; polyoxyethylene(20) sorbitan monooleate; polyoxypropylene-polyoxyethylene block copolymers; castor oil ethoxylate; and combinations thereof.

[0243] In some embodiments, the inhalable pharmaceutical compositions include excipients. Examples of suitable excipients include, but are not limited to: lactose, starch, propylene glycol diesters of medium chain fatty acids; triglyceride esters of medium chain fatty acids, short chains, or long chains, or any combination thereof; perfluorodimethylcyclobutane; perfluorocyclobutane; polyethylene glycol; menthol; lauroglycol; diethylene glycol monoethylether; polyglycolized glycerides of medium chain fatty acids; alcohols; *eucalyptus* oil; short chain fatty acids; and combinations thereof.

[0244] In some embodiments, the pharmaceutical compositions of the present disclosure comprise nasal formulations. Nasal formulations include, for instance, nasal sprays, nasal drops, nasal ointments, nasal washes, nasal injections, nasal packings, bronchial sprays and inhalers, or indirectly through use of throat lozenges, mouthwashes or gargles, or through the use of ointments applied to the nasal nares, or the face or any combination of these and similar methods of application.

[0245] In another embodiment, the pharmaceutical compositions of the present disclosure comprise a complementary agent, including one or more antimicrobial agents and/or one or more conventional antibiotics. In order to accelerate the treatment of the infection, or augment the antibacterial effect, the therapeutic agent containing the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure may further include at least one complementary agent that can also potentiate the bactericidal activity of the peptide. The complementary agent may be one or more antibiotics used to treat Gram-negative bacteria. In one embodiment, the complementary agent is an antibiotic or antimicrobial agent used for the treatment of infections caused by *P. aeruginosa.*

[0246] The pharmaceutical compositions of the present disclosure may be presented in unit dosage form and may be prepared by any methods well known in the art. The amount of active ingredients which can be combined with a carrier material to produce a single dosage form will vary depending upon the host being treated, the duration of exposure of the recipient to the infectious bacteria, the size and weight of the subject, and the particular mode of administration. The amount of active ingredients that can be combined with a carrier material to produce a single dosage form will generally be that amount of each compound which produces a therapeutic effect. Generally, out of one hundred percent, the total amount will range from about 1 percent to about ninety-nine percent of active ingredients, preferably from about 5 percent to about 70 percent, most preferably from about 10 percent to about 30 percent.

Dosage and Administration

[0247] Dosages administered depend on a number of factors including the activity of infection being treated, the age, health and general physical condition of the subject to be treated, the activity of a particular lysin-AMP polypeptide, lysin polypeptide, variant, active fragment thereof or derivative, the nature and activity of the antibiotic if any with which a lysin-AMP polypeptide, lysin polypeptide, variant, active fragment thereof or derivative according to the present disclosure is being paired and the combined effect of such pairing. Generally, effective amounts of the present lysin-AMP polypeptide, lysin polypeptide, variant,

active fragment thereof or derivative to be administered are anticipated to fall within the range of 1-50 mg/kg (or 1 to 50 mcg/ml) administered 1-4 times daily for a period up to 14 days, e.g. about 3 mg/kg to about 30 mg/kg, in split dosages or a single dosage such as described in the examples. In some embodiments, GN370 is administered at dosages ranging from about 3 mg/ml to about 30 mg/ml. The antibiotic if one is also used will be administered at standard dosing regimens or in lower amounts in view of the synergy. All such dosages and regimens however (whether of the lysin-AMP polypeptide, lysin polypeptide, variant, active fragment thereof or derivative or any antibiotic administered in conjunction therewith) are subject to optimization. Optimal dosages can be determined by performing in vitro and in vivo pilot efficacy experiments as is within the skill of the art but taking the present disclosure into account.

[0248] It is contemplated that the present lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives provide a bactericidal and, when used in smaller amounts, bacteriostatic effect, and are active against a range of antibiotic-resistant bacteria and are not associated with evolving resistance. Based on the present disclosure, in a clinical setting, the present lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives are a potent alternative (or additive or component) of compositions for treating infections arising from drug- and multidrug-resistant bacteria alone or together with antibiotics (even antibiotics to which resistance has developed). Existing resistance mechanisms for Gram-negative bacteria should not affect sensitivity to the lytic activity of the present polypeptides.

[0249] In some embodiments, time exposure to the present lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives may influence the desired concentration of active polypeptide units per ml. Carriers that are classified as "long" or "slow" release carriers (such as, for example, certain nasal sprays or lozenges) could possess or provide a lower concentration of polypeptide units per ml, but over a longer period of time, whereas a "short" or "fast" release carrier (such as, for example, a gargle) could possess or provide a high concentration polypeptide units (mcg) per ml, but over a shorter period of time. There are circumstances where it may be necessary to have a much higher unit/ml dosage or a lower unit/ml dosage.

[0250] For any polypeptide of the present disclosure, the therapeutically effective dose can be estimated initially either in cell culture assays or in animal models, usually mice, rabbits, dogs, or pigs. The animal model can also be used to achieve a desirable concentration range and route of administration. Obtained information can then be used to determine the effective doses, as well as routes of administration in humans. Dosage and administration can be further adjusted to provide sufficient levels of the active ingredient or to maintain the desired effect. Additional factors which may be taken into account include the severity of the disease state, age, weight and gender of the patient; diet, desired duration of treatment, method of administration, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy and the judgment of the treating physician.

[0251] A treatment regimen can entail daily administration (e.g., once, twice, thrice, etc daily), every other day (e.g., once, twice, thrice, etc. every other day), semi-weekly, weekly, once every two weeks, once a month, etc. In one embodiment, treatment can be given as a continuous infusion. Unit doses can be administered on multiple occasions. Intervals can also be irregular as indicated by monitoring clinical symptoms. Alternatively, the unit dose can be administered as a sustained release formulation, in which case less frequent administration is required. Dosage and frequency may vary depending on the patient. It will be understood by one of skill in the art that such guidelines will be adjusted for localized administration, e.g. intranasal, inhalation, rectal, etc., or for systemic administration, e.g. oral, rectal (e.g., via enema), i.m. (intramuscular), i.p. (intraperitoneal), i.v. (intravenous), s.c. (subcutaneous), transurethral, and the like.

Methods

[0252] In another aspect, the present disclosure is directed to a method of treating a bacterial infection caused by Gram-negative bacteria such as *P. aeruginosa* as described herein, comprising administering to a subject diagnosed with, at risk for, or exhibiting symptoms of a bacterial infection, a pharmaceutical composition as herein described. In one aspect, the bacterial infection is an infection of an organ or tissue in which pulmonary surfactant is present.

[0253] The terms "infection" and "bacterial infection" are meant to include respiratory tract infections (RTIs), such as respiratory tract infections in patients having cystic fibrosis (CF), lower respiratory tract infections, such as acute exacerbation of chronic bronchitis (ACEB), acute sinusitis, community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP) and nosocomial respiratory tract infections; sexually transmitted diseases, such as gonococcal cervicitis and gonococcal urethritis; urinary tract infections; acute otitis media; sepsis including neonatal septisemia and catheter-related sepsis; and osteomyelitis. Infections caused by drug-resistant bacteria and multidrug-resistant bacteria are also contemplated.

[0254] Non-limiting examples of infections caused by *P. aeruginosa* include: A) Nosocomial infections: 1. Respiratory tract infections especially in cystic fibrosis patients and mechanically-ventilated patients; 2. Bacteraemia and sepsis; 3. Wound infections, particularly those of burn victims; 4. Urinary tract infections; 5. Post-surgery infections on invasive devises; 6. Endocarditis by intravenous administration of contaminated drug solutions; 7. Infections in patients with acquired immunodeficiency syndrome, cancer chemotherapy, steroid therapy, hematological malignancies, organ transplantation, renal replacement therapy, and other conditions with severe neutropenia. B) Community-acquired infections: 1. Community-acquired respiratory tract infections; 2. Meningitis; 3. Folliculitis and infections of the ear canal caused by contaminated water; 4. Malignant otitis externa in the elderly and diabetics; 5. Osteomyelitis of the caleaneus in children; 6. Eye infections commonly associated with contaminated contact lens; 7. Skin infections such as nail infections in people whose hands are frequently exposed to water; 8. Gastrointestinal tract infections; and 9. Muscoskeletal system infections.

[0255] In some embodiments, the Gram-negative bacteria of the present methods include *Achromobacter* spp., such as *Achromobacter xylosoxidans, Acinetobacter baumannii, Acinetobacter haemolyticus, Actinobacillus actinomycetemcomitans, Aeromonas hydrophila, Bacteroides* spp., such as, *Bacteroides fragilis, Bacteroides theataioatamicron, Bacteroides distasonis, Bacteroides ovatus, Bacteroides vulgatus,*

Bartonella Quintana, Bartonella hensenae, Bordetella pertussis, Brucella spp., such as, *Brucella melitensis, Brucella abortus, Burkholderia* spp, such as, *Burkholderia cepacia, Burkholderia pseudomallei*, and *Burkholderia mallei, Campylobacter jejuni, Campylobacter fetus, Campylobacter coli, Chlamydia* spp., such as *Chlamydia psittaci, Chlamydia pneumoniae* and *Chlamydia trachomatis, Citrobacter freundii, Citrobacter koseri, Coxiella burnetii, Edwarsiella* spp., such as, *Edwarsiella tarda, Ehrlichia chafeensis, Eikenella corrodens, Enterobacter* spp., such as, *Enterobacter cloacae, Enterobacter aerogenes*, and *Enterobacter agglomerans, Escherichia coli, Francisella tularensis, Fusobacterium, Haemophilus influenzae, Haemophilus ducreyi, Helicobacter pylori, Kingella kingae, Klebsiella* spp., such as, *Klebsiella pneumoniae, Klebsiella oxytoca, Klebsiella rhinoscleromatis*, and *Klebsiella ozaenae, Legionella penumophila, Moraxella* spp., such as, *Moraxella catarrhalis, Morganella* spp., such as, *Morganella morganii, Neisseria gonorrhoeae, Neisseria meningitidis, Pandorea apista, Pseudomonas aeruginosa, Pasteurella multocida, Plesiomonas shigelloides, Prevotella corporis, Prevotella intermedia, Prevotella endodontalis, Porphyromonas asaccharolytica, Proteus mirabilis, Proteus vulgaris, Proteus penneri, Proteus myxofaciens, Providencia* spp., such as, *Providencia stuartii, Providencia rettgeri, Providencia alcalifaciens, Pseudomonas fluorescens, Ralstonia* spp., such as *Ralstonia mannitolilytica, Ricketsia prowazekii, Salmonella typhi, Salmonella typhimurium, Salmonella paratyphi, Serratia* spp., such as, *Serratia marcescens, Shigella* spp., such as, *Shigella flexneri, Shigella boydii, Shigella sonnei*, and *Shigella dysenteriae, Stenotrophomonas maltophilia, Streptobacillus moniliformis, Vibrio cholerae, Vibrio parahaemolyticus, Vibrio vulnificus, Vibrio alginolyticus, Yersinia enterocolitica, Yersinia pestis*, and/or *Yersinia pseudotuberculosis.*

[0256] More typically, the Gram-negative bacteria of the present disclosure is selected from one or more of *Acinetobacter baumannii, Bordetella pertussis, Burkholderia cepacia, Burkholderia pseudomallei, Burkholderia mallei, Campylobacter jejuni, Campylobacter coli, Enterobacter cloacae, Enterobacter aerogenes, Escherichia coli, Francisella tularensis, Haemophilia influenzae, Haemophilus ducreyi, Helicobacter pylori, Klebsiella pneumoniae, Legionella pneumophila, Moraxella catarrhalis, Morganella morganii, Neisseria gonorrhoeae, Neisseria meningitidis, Pasteurella multocida, Proteus mirabilis, Proteus vulgaris, Salmonella typhi, Serratia marcescens, Shigella flexneri, Shigella boydii, Shigella sonnei, Shigella dysenteriae, Stentrophomonas maltophilia, Vibrio cholerae*, and/or *Chlamydia pneumoniae.*

[0257] Even more typically, the at least one other species of Gram-negative bacteria is selected from one or more of *Salmonella typhimurium, Salmonella typhi, Shigella* spp., *Escherichia coli, Acinetobacter baumanii, Klebsiella pneumonia, Neisseria gonorrhoeae, Neisseria meningitides, Serratia* spp. *Proteus mirabilis, Morganella morganii, Providencia* spp., Edwardsiella spp., *Yersinia* spp., *Haemophilus* influenza, *Bartonella quintana, Brucella* spp., *Bordetella pertussis, Burkholderia* spp., *Moraxella* spp., *Francisella tularensis, Legionella pneumophila, Coxiella burnetii, Bacteroides* spp., *Enterobacter* spp., and/or *Chlamydia* spp.

[0258] Yet even more typically, the one or more additional species of Gram-negative bacteria are *Klebsiella* spp., *Enterobacter* spp., *Escherichia coli, Citrobacter freundii, Salmonella typhimurium, Yersinia pestis*, and/or *Francisella tulerensis.*

[0259] In yet other embodiments, the Gram-negative bacteria include *Brucella* spp., such as, *Brucella melitensis, Brucella abortus, Burkholderia* spp, such as, *Burkholderia cepacia, Burkholderia pseudomallei*, and *Burkholderia mallei, Coxiella burnetii, Francisella tularensis* and *Yersinia* pest's.

[0260] In some embodiments, infection with Gram-negative bacteria results in a localized infection, such as a topical bacterial infection, e.g., a skin wound. In other embodiments, the bacterial infection is a systemic pathogenic bacterial infection. Common Gram-negative pathogens and associated infections are listed in Table 2 of the present disclosure. These are meant to serve as examples of the bacterial infections that may be treated, mitigated or prevented with the present lysins, active fragments thereof and lysin-AMP polypeptide constructs and are not intended to be limiting.

TABLE 2

Medically relevant Gram-negative bacteria and associated diseases.

Salmonella typhimurium	Gastrointestinal (GI) infections-salmonellosis
Shigella spp.	shigellosis
Escherichia coli	Urinary tract infections (UTIs)
Acinetobacter baumanii	Wound infections
Pseudomonas aeruginosa	bloodstream infections and pneumonia
Klebsiella pneumoniae	UTIs, and bloodstream infections
Neisseria gonorrhoeae	Sexually transmitted disease (STD)-gonorrhea
Neisseria meningitides	Meningitis
Serratia spp.	Catheter contaminations, UTIs, and pneumonia
Proteus mirabilis	UTIs
Morganella spp.	UTIs
Providencia spp.	UTIs
Edwardsiella spp	UTIs
Salmonella typhi	GI infections-typhoid fever
Yersinia pestis	Bubonic and pneumonic plague
Yersinia enterocohtica	GI infections
Yersinia pseudotuberculosis	GI infections
Haemophilus influenza	Meningitis

TABLE 2-continued

Medically relevant Gram-negative bacteria and associated diseases.

Bartonella Quintana	Trench fever
Brucella spp.	Brucellosis
Bordetella pertussis	Respiratory-Whooping cough
Burkholderia spp.	Respiratory
Moraxella spp.	Respiratory
Francisella tularensis	Tularemia
Legionella pneumophila	Respiratory-Legionnaires' disease
Coxiella burnetiid	Q fever
Bacteroides spp.	Abdominal infections
Enterobacter spp.	UTIs and respiratory
Chlamydia spp.	STDs, respiratory, and ocular
Escherichia coli, *Klebsiella pneumoniae*, Acinetobacter spp., *Proteus mirabilis* and/or *Pseudomonas aeruginosa*	Infections of implants, catheters, prosthetic joints and other medical devices

[0261] In some embodiments, the lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure are used to treat a subject at risk for acquiring an infection due to *P. aeruginosa* and/or another Gram-negative bacterium. Subjects at risk for acquiring a *P. aeruginosa* or other Gram-negative bacterial infection include, for example, cystic fibrosis patients, neutropenic patients, patients with necrotising enterocolitis, burn victims, patients with wound infections, and, more generally, patients in a hospital setting, in particular surgical patients and patients being treated using an implantable medical device such as a catheter, for example a central venous catheter, a Hickman device, or electrophysiologic cardiac devices, for example pacemakers and implantable defibrillators. Other patient groups at risk for infection with Gram-negative bacteria including *P. aeruginosa* include without limitation patients with implanted prostheses such a total joint replacement (for example total knee or hip replacement).

[0262] In another aspect, the present disclosure is directed to a method of preventing or treating a bacterial infection comprising co-administering to a subject diagnosed with, at risk for, or exhibiting symptoms of a bacterial infection, a combination of a first effective amount of the composition containing an effective amount of a lysin-AMP polypeptide, such as GN370 (SEQ ID NO: 44), lysin polypeptide, variant, active fragment thereof or derivative as described herein, and a second effective amount of an antibiotic suitable for the treatment of Gram-negative bacterial infection.

[0263] The lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure can be co-administered with standard of care antibiotics or with antibiotics of last resort, individually or in various combinations as within the skill of the art. Traditional antibiotics used against *P. aeruginosa* are described in Table 3. Antibiotics for other Gram-negative bacteria, such as *Klebsiella* spp., *Enterobacter* spp., *Escherichia coli, Citrobacter freundii, Salmonella typhimurium, Yersinia pestis*, and *Franciscella tularensis*, are similar to that provided in Table 3 for *P. aeruginosa*.

TABLE 3

Antibiotics used for the treatment of *Pseudomonas aeruginosa*

Class	Agent
Penicillins	Ticarcillin-clavulanate
	Piperacillin-tazobactam
Cephalosporins	Ceftazidime
	Cefepime
	Cefoperazone
Monobactams	Aztreonam
Fluoroquinolones	Ciprofloxacin
	Levofloxacin
Carbapenems	Imipenem
	Meropenem
	Doripenem
Aminoglycosides	Gentamicin
	Tobramycin
	Amikacin
Polymixins	Colistin
	Polymixin B
Macrolides	Azithromycin
Rifamycin	Rifampicin
Fosfomycin	Fosfomycin

[0264] In more specific embodiments, the antibiotic is selected from one or more of ceftazidime, cefepime, cefoperazone, ceftobiprole, ciprofloxacin, levofloxacin, aminoglycosides, imipenem, meropenem, doripenem, gentamicin, tobramycin, amikacin, piperacillin, ticarcillin, penicillin, rifampicin, polymyxin B and colistin. In certain embodiments, the antibiotic is meropenem.

[0265] Combining lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure with antibiotics provides an efficacious antibacterial regimen. In some embodiments, the lysin-AMP polypeptides of the disclosure, such as GN370, exhibit synergy when combined with standard of care antibiotics.

[0266] In some embodiments, co-administration of lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure with one or more antibiotics may be carried out at reduced doses and amounts of either the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives or the antibiotic or both, and/or reduced frequency and/or duration of treatment with augmented bactericidal and bacteriostatic activity, reduced risk of antibiotic resistance and with reduced risk of deleterious neurological or renal side effects (such as those associated with colistin or

polymyxin B use). Prior studies have shown that total cumulative colistin dose is associated with kidney damage, suggesting that decrease in dosage or shortening of treatment duration using the combination therapy with lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives could decrease the incidence of nephrotoxicity (Spapen et al. *Ann Intensive Care.* 1: 14 (2011), which is herein incorporated by reference in its entirety). As used herein the term "reduced dose" refers to the dose of one active ingredient in the combination compared to monotherapy with the same active ingredient. In some embodiments, the dose of the lysins, active fragments thereof and lysin-AMP polypeptide constructs or the antibiotic in a combination may be suboptimal or even subthreshold compared to the respective monotherapy.

[0267] In some embodiments, the present disclosure provides a method of augmenting antibiotic activity of one or more antibiotics against Gram-negative bacteria compared to the activity of said antibiotics used alone by administering to a subject one or more lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives disclosed herein together with an antibiotic of interest. The combination is effective against the bacteria and permits resistance against the antibiotic to be overcome and/or the antibiotic to be employed at lower doses, decreasing undesirable side effects, such as the nephrotoxic and neurotoxic effects of polymyxin B.

[0268] The lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives optionally in combination with antibiotics of the present disclosure can be further combined with additional permeabilizing agents of the outer membrane of the Gram-negative bacteria, including, but not limited to metal chelators, such as e.g. EDTA, TRIS, lactic acid, lactoferrin, polymyxins, citric acid (Vaara M. *Microbial Rev.* 56(3):395-441 (1992), which is herein incorporated by reference in its entirety).

[0269] In yet another aspect, the present disclosure is directed to a method of inhibiting the growth, or reducing the population, or killing of at least one species of Gram-negative bacteria, the method comprising contacting the bacteria with a composition containing an effective amount of lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives as described herein, wherein the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives inhibits the growth, or reduces the population, or kills *P. aeruginosa* and optionally at least one other species of Gram-negative bacteria.

[0270] In some embodiments, inhibiting the growth, or reducing the population, or killing at least one species of Gram-negative bacteria comprises contacting bacteria with the lysins, active fragments thereof and/or lysin-AMP polypeptide constructs such as GN370 (SEQ ID NO: 44), as described herein, wherein the bacteria are present on a surface of e.g., medical devices, floors, stairs, walls and countertops in hospitals and other health related or public use buildings and surfaces of equipment in operating rooms, emergency rooms, hospital rooms, clinics, and bathrooms and the like.

[0271] Examples of medical devices that can be protected using the lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives described herein include but are not limited to tubing and other surface medical devices, such as urinary catheters, mucous extraction catheters, suction catheters, umbilical cannulae, contact lenses, intrauterine devices, intravaginal and intraintestinal devices, endotracheal tubes, bronchoscopes, dental prostheses and orthodontic devices, surgical instruments, dental instruments, tubings, dental water lines, fabrics, paper, indicator strips (e.g., paper indicator strips or plastic indicator strips), adhesives (e.g., hydrogel adhesives, hot-melt adhesives, or solvent-based adhesives), bandages, tissue dressings or healing devices and occlusive patches, and any other surface devices used in the medical field. The devices may include electrodes, external prostheses, fixation tapes, compression bandages, and monitors of various types. Medical devices can also include any device which can be placed at the insertion or implantation site such as the skin near the insertion or implantation site, and which can include at least one surface which is susceptible to colonization by Gram-negative bacteria.

[0272] The lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure, which can be used in vivo or in vitro as described herein may also be used to treat bacterial infections due to Gram-negative bacteria, such as *P. aeruginosa*, that are associated with biofilm formation.

[0273] For example, in some embodiments, the present lysin-AMP polypeptides, such as GN370 (SEQ ID NO: 44), lysin polypeptides, variants, active fragments thereof or derivatives may be used for the prevention, control, disruption, and/or eradication of bacterial biofilm formed by Gram-negative bacteria, such as *P. aeruginosa*. Biofilm formation occurs when microbial cells adhere to each other and are embedded in a matrix of extracellular polymeric substance (EPS) on a surface. The growth of microbes in such a protected environment that is enriched with biomacromolecules (e.g. polysaccharides, nucleic acids and proteins) and nutrients allows for enhanced microbial cross-talk and increased virulence. Biofilm may develop in any supporting environment including living and nonliving surfaces such as the mucus plugs of the CF lung, contaminated catheters, contact lenses, etc (Sharma et al. *Biologicals,* 42(1):1-7 (2014), which is herein incorporated by reference in its entirety). Thus, in one embodiment, the lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure can be used for the prevention, control, disruption, eradication and treatment of bacterial infections due to Gram-negative bacteria, such as *P. aeruginosa*, when the bacteria are protected by a bacterial biofilm.

[0274] More particularly, in some aspects, the present disclosure is directed to a method for prevention, disruption or eradication of a Gram-negative bacterial biofilm comprising contacting a surface, including a biotic or abiotic surface, with a composition comprising a lysin-AMP polypeptide, such as GN370 (SEQ ID NO: 44), lysin polypeptide, variant, active fragment thereof or derivative of the present disclosure effective to kill Gram negative bacteria, wherein a biofilm is effectively prevented, disrupted or eradicated.

[0275] In some aspects, the present disclosure is directed to a method for prevention, disruption or eradication of a Gram-negative bacterial biofilm comprising administering a

composition to a subject in need thereof, wherein the composition comprises a lysin-AMP polypeptide, such as GN370 (SEQ ID NO: 44), lysin polypeptide, variant, active fragment thereof or derivative of the present disclosure effective to kill Gram negative bacteria on a surface, wherein a biofilm is effectively prevented, disrupted or eradicated.

[0276] In some embodiments, the surface is a biotic surface, such as a solid biological surface, e.g., skin. In other embodiments, the surface is a non-biotic surface. In some embodiments, the surface is a surface of a medical device such as contact lenses; drug pumps, implants, including dental implants, cardiac implants such as pacemakers, prosthetic heart valves, ventricular assist devices, synthetic vascular grafts and stents; catheters including peritoneal dialysis catheters, indwelling catheters for hemodialysis and for chronic administration of chemotherapeutic agents (Hickman catheters), urinary catheters and prosthetic devices including urinary tract prostheses, prosthetic joints; orthopedic material; and tracheal and ventilator tubing.

[0277] In some embodiments, the subject is suffering from a Gram-negative bacterial infection associated with a biofilm. Such bacterial infections include tonsillitis, osteomyelitis, bacterial endocarditis, sinusitis, infections of the cornea, urinary tract infection, infection of the biliary tract, infectious kidney stones, urethritis, prostatitis, middle-ear infections, formation of dental plaque, gingivitis, periodontitis, cystic fibrosis, wound infections, in particular wounds associated with diabetes mellitus, and infections of medical devices as described herein including catheter infections and infections of joint prostheses and heart valves.

[0278] In some embodiments, the composition for treating biofilm infections comprises one or more antibiotics as described herein. In other embodiments, the present lysins or active fragments thereof or variants or derivatives thereof as described herein are administered to a subject and/or contacted to a surface simultaneously with one or more antibiotics as herein described. In other embodiments, a lysin-AMP polypeptide, lysin polypeptide, variant, active fragment thereof or derivative of the present disclosure and the one or more antibiotics as described herein are administered to a subject and/or contacted to a surface sequentially in any order. In some embodiments, the present lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure and the one or more antibiotics as described herein may be administered to a subject and/or contacted to a surface in a single dose or multiple doses, singly or in combination.

[0279] In some embodiments, the present composition is used to prevent biofilm formation. In these embodiments, the contacted surface may contain a biofilm, may not contain a biofilm, or contains only de minimus amounts of an established biofilm. In some embodiments, de novo biofilm formation on the surface is prevented according to any mechanisms as described herein.

[0280] In some embodiments, the contacted surface comprises a biofilm and the biofilm is disrupted or eradicated. In some embodiments, eradication comprises killing bacteria in the biofilm, including persister bacteria. In other embodiments, the present lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure not only kill bacteria within a biofilm, thus eradicating the biofilm, but also disrupt or destroy the biofilm matrix. This ability is advantageous since matrices, even in the absence of live bacteria, often become quickly re-infected.

EXAMPLES

Example 1. Activity of Gram-Negative (GN) Lysins and Lysin-AMP Polypeptide Constructs in Medium Supplemented with Human Serum

[0281] Materials and Methods

[0282] Gram-negative bacteria, e.g., *P. aeruginosa*, were cultured and tested in casamino acid (CAA) media (5 g/L casamino acids, Ameresco/VWR; 5.2 mM K_2HPO_4, Sigma-Aldrich, Inc., St. Louis, Mo.; 1 mMMgSO4, Sigma-Aldrich) supplemented with 150 mMNaCl, 2.5% human serum or 25% human serum (Type AB, male human serum, pooled from Sigma-Aldrich, Inc., referred to herein as CAA-HuS).

[0283] Determination of Minimal Inhibitory Concentrations (MIC)

[0284] MIC values were determined using a modification of the standard broth microdilution reference method defined by the Clinical and Laboratory Standards Institute (CLSI), CLSI. 2015. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-10th Edition, Clinical and Laboratory Standards Institute, Wayne, Pa., The modification was based on the replacement of Mueller Hinton Broth with CAA medium (with or without NaCl), supplemented with 2.5% human serum (Table 4) or 25% human serum (Table 5). MIC is the minimum concentration of lysin sufficient to suppress at least 80% of bacterial growth compared to control.

[0285] Results

[0286] Table 4 provides the molecular weight and isoelectric point of the GN lysin polypeptides. By comparing the sequences and components of the various polypeptides, the effect of a particular structural modification on isoelectric point (a higher pI favors outer membrane penetration) and activity (as assessed by MIC) can be determined.

[0287] For example, Table 4 shows the effects of single point mutations on GN316 (SEQ ID NO: 22). GN394 (SEQ ID NO: 48) has a lower pI and a higher activity in CAA but a lower activity in CAA with human serum. The activity reduction in human serum is less for GN396 (SEQ ID NO: 50), whereas GN408 (SEQ ID NO: 52) is substantially more potent both in the presence and absence of human serum. On the other hand, GN418 (SEQ ID NO: 54) loses activity in unsupplemented CAA media but gains potency in the presence of human serum.

[0288] The single point mutation in GN217 (SEQ ID NO: 8) improves its potency over GN37 both in the absence and presence of human serum. The modifications to GN37 (SEQ ID NO: 84) yielding GN218 (SEQ ID NO: 10), GN223 (SEQ ID NO: 12), GN239 (SEQ ID NO: 14) and GN243 (SEQ ID NO: 16) result in very strong activity in the presence of human serum. Similar observations can be made based on comparison of the sequence and components of other polypeptides.

[0289] Table 5 shows that additional selected lysins including GN178, GN122, GN76, GN218, GN11, GN75, GN14, GN93, GN328, GN7 and GN316 were active in CAA supplemented with human serum (25%) when tested against the carbepenam-resistant clinical isolate WC-453. In contrast, the activity of GN83 (and the control T4 lysozyme and control artilysin GN126) was repressed in this medium.

Example 2. Activity of GN Lysins and Lysin-AMP Polypeptide Constructs in the Presence of Divalent Cations

[0290] The activity of selected GN lysins and constructs in the presence of divalent cations was evaluated, and the impact of divalent cations at physiological concentrations was examined in the MIC assay format. Fold changes in MIC were measured in the presence of various cation concentrations (1.25 mM $CaCl_2$), 1.25 mM $CaCl_2$), 0.25 mM $CaCl_2$, 1.5 mM $MgCl_2$, 0.78 mM $MgCl_2$, 0.15 mM $MgCl_2$, and a combination of 1.25 mM $CaCl_2$) and 0.78 mM $MgCl_2$) supplemented into 25% CAA medium. The results are shown below in Table 6. It is noted that 25% CAA typically has 0.25 nM $MgSO_4$. *Pseudomonas aeruginosa* strain CFS-1292 (meropenem resistant) was used as the reporter strain. It was concluded that the GN lysins and constructs tested are active in the presence of physiological levels of calcium and magnesium.

TABLE 5

Sensitivity of selected lysins and constructs in human serum (25%).

Lysin	CAA	CAA/HuS
GN178	8	1
GN83	>128	>128
GN122	2	2
GN76	64	8
GN126	2	128
GN218	8	1
GN11	32	128
GN75	8	8
GN14	>128	32
GN93	128	8
GN328	8	2
GN7	>128	128
GN316	16	<0.0625
T4LZY	>128	>128

TABLE 4

Sensitivity of selected lysins or selected lysin-AMP polypeptide constructs in human serum (2.5%).

GN#	MW	pI	CAA MIC (mg/mL)	CAA/HuS MIC (mg/mL)
GN168 (SEQ ID NO: 2)	22299.78	11.6	8	N.D.
GN176 (SEQ ID NO: 4)	19370	9.8	8	N.D.
GN178 (SEQ ID NO: 6)	19290.04	9.7	8	4
GN217 (SEQ ID NO: 8)	13879.91	9.4	4	0.125
GN218 (SEQ ID NO: 10)	16038.43	9.8	8	1
GN223 (SEQ ID NO: 12)	18570.35	10.3	32	2
GN239 (SEQ ID NO: 14)	16836.42	10.2	4	0.25
GN243 (SEQ ID NO: 16)	18880.02	10.5	32	0.5
GN280 (SEQ ID NO: 18)	17928.9	10.2	4	0.5
GN281 (SEQ ID NO: 20)	18188.07	10.2	2	0.5
GN316 (SEQ ID NO: 22)	28672.72	8.7	16	0.125
GN329 (SEQ ID NO: 26)	20810.83	8.9	4	0.25
GN333 (SEQ ID NO: 28)	20918.79	8.9	8	0.06
GN349 (SEQ ID NO: 30)	34169.19	9.5	16	1
GN351 (SEQ ID NO: 32)	33866.76	9.9	8	0.125
GN352 (SEQ ID NO: 34)	33398.27	8.9	4	0.5
GN353 (SEQ ID NO: 36)	33485.42	8.9	4	0.25
GN357 (SEQ ID NO: 38)	30891.39	9.3	16	0.25
GN359 (SEQ ID NO: 40)	31094.67	8.7	8	0.25
GN369 (SEQ ID NO: 42)	30934.63	8.8	8	0.0625
GN370 (SEQ ID NO: 44)	19140.86	10.7	16	4
GN371 (SEQ ID NO: 46)	17530.95	8.7	>32	0.5
GN394 (SEQ ID NO: 48)	28659.62	7.5	8	0.5
GN396 (SEQ ID NO: 50)	28659.62	7.5	8	0.25
GN408 (SEQ ID NO: 52)	28653.66	7.8	2	0.125
GN418 (SEQ ID NO: 54)	28659.62	7.5	32	0.06
GN424 (SEQ ID NO: 56)	29118.75	8.4	N.D.	N.D.
GN425 (SEQ ID NO: 58)	29895.81	7.5	2	0.25
GN428 (SEQ ID NO: 60)	28814.89	8.9	8	0.125
GN93 (SEQ ID NO: 62)	22959.07	9.6	128	8
GN431 (SEQ ID NO: 64)	28715.73	8.5	8	0.0625
GN486 (SEQ ID NO: 66)	17.8	10.6	2	0.125
GN485 (SEQ ID NO: 68)	8.312	9.8	N.D	ND

TABLE 6

		Fold Increase (MIC) in presence of cations						
		25% CAA supplemented with:						
GN number	MIC in 25% CAA	2.5 mM $CaCl_2$ (high)	1.25 mM $CaCl_2$ (medium)	0.25 mM $CaCl_2$ (low)	1.5 mM MgCh (high)	0.78 mM $MgCl_2$ (medium)	0.15 mM $MgCl_2$ (low)	1.25 mM $CaCl_2$ 0.78 mM $MgCl_2$
	MIC (ug/mL)							
108	4	1	0.5	0.5	0.5	0.5	0.5	2
121	1-2	2	1-2	0.5	1	1-2	0.5	2
123	2	1	1	1	1	1	1	1
156	2	1	2	2	2	2	2	2
316	4	1	1	1	1	1	1	1
329	4	0.5	0.25	1	0.5	0.5	0.5	2
333	8	1	1	4	1	1	1	4
351	1	1	1-2	0.5	2	1-2	0.25	2
357	4	1	1	0.5	1	1	1	0.5
428	4	1	1-2	1	1	1-4	1	1-4
370	4	1	1-4	0.5	1	1-2	1	1-4
431	2	1	1	2	n.d.	1	1	1

Example 3. Time-Kill Assay of GN Lysins or Lysin-AMP Polypeptide Construct Activity

[0291] An overnight culture of the carbepenam-resistant clinical isolate *P. aeruginosa* strain WC-453 was diluted 1:50 into fresh CAA media and grown for 2.5 hours at 37° C. with agitation. Exponential phase bacteria were then pelleted and resuspended in 1/5 culture volume of 25 mM HEPES, pH 7.4 before a final adjustment to an optical density corresponding to a McFarland value of 0.5. The adjusted culture was then diluted 1:50 into either 25 mM HEPES pH 7.4 or CAA supplemented with 25% human serum and the GN lysins were added at a final concentration of 10 μg/ml. Control cultures were included with the addition of no lysin (i.e., buffer control), GN65, GN126 or GN81. All treatments were incubated at 37° C. with aeration. At time points before the addition of lysin (or buffer control) and at 1 hour and 3 hours intervals thereafter, culture samples were removed for quantitative plating on CAA agar plates.

[0292] As shown in Tables 7 and 8, below, bactericidal activity was observed for the majority of GN lysins tested in HEPES (Table 7) and CAA/HuS (Table 8) in the time-kill format, as defined by a CFU decrease of 3-Log_{10}, 3 hours after the addition of lysin. For CAA/HuS, Table 8 shows that GN83, GN121, GN75, GN14, GN76, GN93, GN316, GN329, GN333, GN351, GN357, GN428, GN370 and GN431 each demonstrated bactericidal activity at a 3-hour time point after addition at a concentration of 10 μg/mL.

TABLE 7

HEPES (Log_{10} CFU/mL)		
GN	1 hr	3 hr
83	<3.7	<3.7
121	<3.7	<3.7
75	5.7	<3.7
65	5.7	<3.7
126	<3.7	<3.7
7	7.5	6.2
11	6.7	<3.7
14	<3.7	<3.7

TABLE 7-continued

HEPES (Log_{10} CFU/mL)		
GN	1 hr	3 hr
40	7.0	5.7
43	6.4	<3.7
76	<3.7	<3.7
80	7.7	6.7
93	6.0	<3.7
122	7.7	5.4
81	7.4	6.5
Blank	7.7	7.2

TABLE 8

CAA/HuS (Log_{10} CFU/mL)		
GN	1 hr.	3 hr
83	5.7	<3.7
121	7.6	<3.7
75	5.9	<3.7
65	6.0	<3.7
126	6.6	<3.7
7	7.0	7.0
14	5.7	<3.7
40	6.6	6.7
43	6.9	7.0
76	5.7	<3.7
80	6.7	7.0
93	6.6	<3.7
122	6.7	6.7
81	6.7	7.0
316	5.1	<3.7
329	4.4	<3.7
333	4.9	<3.7
351	4.6	<3.7
357	5.0	<3.7
428	5.5	<3.7
370	4.0	<3.7
431	5.8	<3.7
Blank	7.7	7.2

Example 4. Selected Lysins and Constructs have Potent Antibiofilm Activity

[0293] Disruption of biofilms formed by *P. aeruginosa* strain ATCC 17646 was examined in the Minimal Biofilm Eradicating Concentration (MBEC) assay as described herein. All of the selected lysins or selected lysin-AMP polypeptide constructs that were tested exhibited antibiofilm activity as depicted in Table 9, below. T4LYZ, GN126 and GN65 were included as controls.

TABLE 9

Antibiofilm Activity	
Lysin	MBEC (μg/mL)
GN76	0.125
GN126	0.125
GN83	1
GN80	0.125
GN93	0.125
GN122	1
GN217	0.5
GN316	1
GN329	0.5
GN333	1
GN351	1
GN357	0.5
GN428	1
GN370	1
GN431	1
T4LYZ	>64

Example 5. Selected Lysins and Constructs are Active in Pulmonary Surfactant

[0294] Gram-negative bacteria, e.g., *P. aeruginosa*, were cultured and tested in CAA media, supplemented with a range of SURVANTA® concentrations (6.25%, 3.15%, 1.56%, 0.78%, 0.39%, 0.19% and 0.09% SURVANTA®) in the MIC assay format. 6.25% SURVANTA® corresponds to 1.5 mg/mL phospholipids. The physiological level of pulmonary surfactant in epithelial lining fluid is around 0.01 mg/mL.

[0295] Table 10 depicts the fold increases in MIC for selected GN lysins tested against *P. aeruginosa* isolate CFS-1292. As a positive control, the impact of SURVANTA® on daptomycin (DAP) activity against *Staphylococcus aureus* was also tested. The selected GN lysins and constructs were not inhibited by pulmonary surfactant over a wide range of concentrations, which are inhibitory to the activity of DAP.

TABLE 10

Activity of GN lysins over a range of SURVANTA ® concentrations							
GN	% SURVANTA ®						
Clone*	6.25	3.15	1.56	0.78	0.39	0.19	0.09
108	2	2	1	1	1	1	1
121	2	2	1-2	1-2	1	1	1
123	2	2	1	1	1	1	1
147	1	2	2	2	1	1	1
156	2	2	2	1	1	1	1
150	2	2	1	1	1	1	1

TABLE 10-continued

Activity of GN lysins over a range of SURVANTA ® concentrations							
GN	% SURVANTA ®						
Clone*	6.25	3.15	1.56	0.78	0.39	0.19	0.09
217	2	2	2	1	1	1	1
316	1	2	1	1	1	1	1
329	2	1	1	1	1	1	1
333	2	2	2	1	1	1	1
351	2	1-2	1-2	1	1	1	1
357	2	2	2	1	1	1	1
428	1	1-2	1	1	1	1	1
370	1-2	1-2	1-2	1	1	1	1
431	2	1	1	1	1	1	1
DAP**	256	128	128	64	64	32	32

Example 6. Further Characterization of GN121, GN351, GN370 and GN428 in Human Serum and Surfactant

[0296] GN121, GN351, GN370 and GN428 were further characterized for activity in human serum and pulmonary surfactant against a range of isolates. Gram-negative bacteria, e.g., *P. aeruginosa*, were cultured and tested in CAA media supplemented with 12.5% human serum (Type AB, male, pooled; Sigma-Aldrich) or 6.25% SURVANTA® and a range of *P. aeruginosa* isolates were evaluated using the MIC assay. 6.25% SURVANTA® corresponds to 1.5 mg/mL phospholipids.

[0297] Tables 11 and 12 show that GN121, GN351, GN370 and GN428 are active against a variety of *P. aeruginosa* isolates in human serum (Table 11) or SURVANTA® (Table 12). GN121, GN351, GN370 and GN428 demonstrated greater or comparable activity to that of the antibiotic meropenem in either human serum or SURVANTA®. As evident in Tables 11 and 12, the MIC values for the selected lysins ranged from 0.5 to 4 mg/mL (Table 11) or 0.5 to 2 mg/mL (Table 12). In contrast, the MIC values for meropenem were 32 mg/mL or greater against certain *P. aeruginosa* isolates, e.g., CFS 1559.

TABLE 11

Activity in human serum					
P. aeruginosa	Meropenem MIC	CAA + 12.5% Human Serum MIC (μg/mL)			
Strain	(μg/mL)	GN121	GN351	GN370	GN428
CFS 1292	32	1	1	2	2
CFS 1557 (PA19)	32	2	4	4	4
CFS 1558 (PA20)	16	0.5	1	0.5	2
CFS 1559 (PA21)	>32	1	2	2	2
CFS 1560 (PA22)	16	1	2	2	2
CFS 1561 (PA23)	16	1	2	2	2
CFS 1562 (PA24)	>32	1	2	2	2
CFS 1766 (ATCC 27853)	1	2	2	4	4
CFS 1539 (PA1)	16	0.5	0.5	1	1
CFS 1540 (PA2)	16	0.5	0.5	1	1
CFS 1541 (PA3)	8	0.5	0.5	1	1
CFS 1596 (PA26)	0.5	0.5	1	1	1
CFS 1597 (PA27)	1	0.5	0.5	0.5	0.5
CFS 1669 (PA41)	<0.25	1	1	2	2
CFS 1674 (PA46)	4	0.5	1	2	2
CFS 1675 (PA47)	4	0.5	0.5	1	1

TABLE 11-continued

Activity in human serum					
P. aeruginosa Strain	Meropenem MIC (μg/mL)	CAA + 12.5% Human Serum MIC (μg/mL)			
		GN121	GN351	GN370	GN428
CFS 1109 (ATCC 17646)	0.5	0.5	1	1	1

TABLE 12

Activity in pulmonary surfactant (SURVANTA ®)				
P. aeruginosa Strain	Fold change in MIC for CAA + 6.25% Human Serum			
	GN121	GN351	GN370	GN428
CFS 1292	1	2	1	1
CFS 1557 (PA19)	2	1	0.5	0.5
CFS 1558 (PA20)	2	2	1	1
CFS 1559 (PA21)	2	2	1	1
CFS 1560 (PA22)	2	2	1	1
CFS 1561 (PA23)	1	1	1	1
CFS 1562 (PA24)	2	1	0.5	1
CFS 1766 (ATCC 27853)	1	1	1	2
CFS 1539 (PA1)	1	1	0.5	0.5
CFS 1540 (PA2)	1	1	1	1
CFS 1541 (PA3)	2	2	1	1
CFS 1596 (PA26)	2	2	1	1
CFS 1597 (PA27)	2	1	0.5	0.5
CFS 1669 (PA41)	2	0.5	0.5	0.5
CFS 1674 (PA46)	2	2	0.5	1
CFS 1675 (PA47)	1	0.5	0.5	0.5
CFS 1109 (ATCC 17646)	2	1	1	1

Example 7. Bactericidal Activity of GN121, GN351, GN370 and GN428 Against *Pseudomonas aeruginosa* in Human Serum and Pulmonary Surfactant

[0298] Further characterization of the bacteriolytic activities of four anti-pseudomonal lysins described herein, GN121, GN351, GN370, and GN428, was evaluated using standard in vitro susceptibility testing formats that incorporate human serum or pulmonary surfactant. The mechanism of GN lysin action was further evaluated by fluorescence and transmission electron microscopy (TEM), as discussed below.

[0299] Materials and methods: MICs were determined by broth microdilution in media supplemented with human serum and pulmonary surfactant (SURVANTA®; Myoderm Clinical Supplies). Minimal biofilm eradicating concentrations (MBECs) were determined using standard methods. MBEC was measured using CAA supplemented with 12.5% human serum. Fluorescence microscopy was performed after LIVE/DEAD staining (ThermoFisher) and TEM was performed.

[0300] Results: The activity of the selected GN lysins in human serum and pulmonary surfactant (SURVANTA®) was observed. Lysin MIC values were determined in the standard AST format medium (25% Casamino Acid Medium with 0.25 mM $MgSO_4$) alone and in the presence of 12.5% human serum and 0.78% SURVANTA®. The SURVANTA® concentration of 0.78% represents a physiological level of pulmonary surfactant. *Pseudomonas aeruginosa* strain CFS-1292 (meropenem resistant) was used as the reporter strain. As shown in Table 13 below, it was concluded that GN121, GN351, GN428, and GN370 are active in human serum and pulmonary surfactant. Likewise, as confirmed in Table 14 below, the lysins exhibited a potent antibiofilm effect using 12.5% human serum, with MBEC values <1 μg/mL, similar to those observed for MICs.

TABLE 13

MIC values for lysins in media alone (25% CAA) and supplemented with human serum or pulmonary surfactant				
Clone	Gram-negative lysin	25% CAA MIC	MIC in human serum (12.5%) in CAA (μg/mL)	MIC in 0.78% Survanta ® (μg/mL)
1525	GN121	1	0.5	2
1799	GN351	1	0.0625	4
1876	GN428	4	0.125	4
1818	GN370	4	2	2

TABLE 14

MBEC values for lysins and lysin-AMP polypeptide constructs	
Lysin or Lysin-AMP polypeptide construct	MBEC (μg/mL) in CAA supplemented with 12.5% human serum
GN121	0.25
GN351	0.5
GN428	1
GN370	1

Example 8. Ability of GN Lysins to Destabilize Bacterial Outer Membrane

[0301] The ability of gram-negative lysins to destabilize the outer membrane of *P. aeruginosa* was evaluated through the use of an N-phenyl-1-napthyl amine (NPN) uptake assay. See Dassanayake, R. P. et al., "Antimicrobial activity of bovine NK-lysin-derived peptides on *Mycoplasma bovis*", PLOS One 2018; 9(1):e86364. Exponential *P. aeruginosa* (CFS 1292) was harvested, washed, and re-suspended in 5 mM 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) buffer and 5 mM glucose at pH 7.4. NPN was added to a final concentration of 10 mM. Gram-negative lysins, including GN121, GN351, GN428, and GN370, were added at a final concentration of 100 μg/well. Changes in fluorescence were recorded (excitation 1=350 nm; emission 1=420 nm) over two hours. The NPN incorporated into the membrane resulted in an increase in fluorescence. As shown in FIGS. **2**A and **2**B, the gram-negative lysins mediated disruption of the outer membrane of the bacterial cell wall. The data for each gram-negative lysin is shown below in Table 15.

TABLE 15

Fluorescence over time for *P. aeruginosa* exposed to NPN and gram-negative lysins

Time in	% RFU				
minutes	Buffer	GN121	GN351	GN428	GN370
5	100	370	381	194	205
10	100	500	406	242	217
20	100	528	407	271	213
40	100	530	386	250	198
60	100	565	383	183	193
100	100	557	338	137	184

Example 9. Microscopy Shows GN Lysin Bactericidality in Serum

[0302] *Pseudomonas aeruginosa* strain 1292 was treated for 15 minutes with GN121 (10 μg/mL) or a buffer control in 100% human serum. Samples were stained using the Live/Dead Cell Viability Kit (ThermoFisher) and examined by both differential interference contrast (DIC) and fluorescence microscopy. As depicted in FIG. **3**, which shows a series of photomicrographs showing microscopic analysis (×2000 magnification), there was an absence of dead bacteria in the untreated row and a reduction of live bacteria in the treated row.

Example 10. Synergy of GN Lysins and Meropenem in Human Serum

[0303] Standard checkerboard assays were performed to assess synergy of GN lysins with meropenem in the presence of human serum. *P. aeruginosa* strains CFS 1292, 1557 (PA19), 1558 (PA20) CFS 1559 (PA21), CFS 1560 (PA22), CFS 1561 (PA23), CFS 1562 (PA24), and CFS 1766 (ATCC 27853) were suspended in a solution of 25% CAA and 12.5% human serum, and synergy was evaluated by measuring the fractional inhibitory concentration index (FICI) values. FICI values less than or equal to 0.5 were consistent with potent synergy. As shown below in Table 16, all of GN121, GN351, GN370, and GN428 exhibited synergy with meropenem for each of the three *P. aeruginosa* strains evaluated.

TABLE 16

Synergy between meropenem and gram-negative lysins in human serum

Strain	Gram-negative lysin	FICI value (Run #1)	FICI value (Run #2)
CFS 1292	GN121	0.25	0.292
	GN351	0.1875	0.219
	GN370	0.1875	0.219
	GN428	0.1875	0.219
CFS 1557 (PA19)	GN121	0.375	0.427
	GN351	0.25	0.292
	GN370	0.1875	0.240
	GN428	0.15625	0.198
CFS 1558 (PA20)	GN121	0.125	0.156
	GN351	0.15625	0.177
	GN370	0.09375	0.109
	GN428	0.09375	0.135
CFS 1559 (PA21)	GN121	—	0.229
	GN351	—	0.177
	GN370	—	0.438
	GN428	—	0.396
CFS 1560 (PA22)	GN121	—	0.313
	GN351	—	0.323
	GN370	—	0.198
	GN428	—	0.229
CFS 1561 (PA23)	GN121	—	0.198
	GN351	—	0.240
	GN370	—	0.240
	GN428	—	0.323
CFS 1562 (PA24	GN121	—	0.214
	GN351	—	0.177
	GN370	—	0.240
	GN428	—	0.198
CFS 1766 (ATCC 27853)	GN121	—	0.229
	GN351	—	0.109
	GN370	—	0.156
	GN428	—	0.156

Example 11. Synergy Between Antibiotics and Lysins or Lysin-AMP Polypeptide Constructs

[0304] Synergy between GN76 (SEQ ID NO: 203), GN121 (SEQ ID NO: 175), GN123 (SEQ ID NO: 173), GN351 (SEQ TD NO: 32), GN370 (SEQ ID NO: 44) and GN428 (SEQ TD NO: 60) and 12 different antibiotics were examined in checkerboard assays using CAA medium, supplemented with 2.5% human serum as described herein, using the carbapenem-resistant clinical strain WC-452. Fractional inhibitor concentration index (FICI) values were determined for all combinations; values of <0.5 indicate synergy.

TABLE 17

Synergy between antibiotics and lysins or lysin-AMP polypeptide constructs

Antibiotic	GN76 (SEQ ID NO: 203) (MIC μg/mL)	GN121 (SEQ ID NO: 175) (MIC μg/mL)	GN123 (SEQ ID NO: 173) (MIC μg/mL)	GN351 (SEQ ID NO: 32) (MIC μg/mL)	GN370 (SEQ ID NO: 44) (MIC μg/mL)	GN428 (SEQ ID NO: 60) (MIC μg/mL)
Amikacin	0.281	0.375	0.250	0.250	0.125	0.281
Azithromycin	0.156	0.188	0.125	0.125	0.188	0.250
Aztreonam	0.281	0.625	0.375	0.125	0.188	0.156
Ciprofloxacin	0.281	0.313	0.375	0.375	0.281	0.125
Colistin	0.250	0.046	0.188	0.046	0.046	0.094
Fosfomycin	0.125	0.375	0.250	0.500	0.375	0.313
Gentamicin	0.313	0.375	0.375	0.125	0.250	0.250
Imipenem	0.254	0.375	0.188	0.156	0.094	0.188
Meropenem	0.375	0.313	0.125	0.188	0.125	0.188

TABLE 17-continued

Synergy between antibiotics and lysins or lysin-AMP polypeptide constructs

Antibiotic	GN76 (SEQ ID NO: 203) (MIC μg/mL)	GN121 (SEQ ID NO: 175) (MIC μg/mL)	GN123 (SEQ ID NO: 173) (MIC μg/mL)	GN351 (SEQ ID NO: 32) (MIC μg/mL)	GN370 (SEQ ID NO: 44) (MIC μg/mL)	GN428 (SEQ ID NO: 60) (MIC μg/mL)
Pipercillan	0.375	0.375	0.500	0.281	0.125	0.375
Rifampicin	0.281	0.313	0.156	0.250	0.250	0.500
Tobramycin	0.281	0.188	0.188	0.153	0.188	0.188
Antibiotic	GN76	GN121	GN123	GN351	GN370	GN428
Amikacin	0.281	0.375	0.250	0.250	0.125	0.281
Azithromycin	0.156	0.188	0.125	0.125	0.188	0.250
Aztreonam	0.281	0.625	0.375	0.125	0.188	0.156
Ciprofloxacin	0.281	0.313	0.375	0.375	0.281	0.125
Colistin	0.250	0.046	0.188	0.046	0.046	0.094
Fosfomycin	0.125	0.375	0.250	0.500	0.375	0.313
Gentamicin	0.313	0.375	0.375	0.125	0.250	0.250
Imipenem	0.254	0.375	0.188	0.156	0.094	0.188
Meropenem	0.375	0.313	0.125	0.188	0.125	0.188
Pipercillan	0.375	0.375	0.500	0.281	0.125	0.375
Rifampicin	0.281	0.313	0.156	0.250	0.250	0.500
Tobramycin	0.281	0.188	0.188	0.153	0.188	0.188

[0305] As indicated in Table 17, below, the foregoing lysins and lysin-AMP constructs are synergistic across a broad range of antibiotics. For imipenem, the synergy is consistent with resensitization to the carbapenem antibiotic.

Example 12. Resensitization of Carbapenem-Resistant Clinical Strains Using Antibiotics in Combination with GN Lysins

[0306] The ability of GN121 (SEQ ID NO: 175) or GN123 (SEQ ID NO: 173) to resensitize carbapenem-resistant *P. aeruginosa* strains to carbapenems was assessed by combining each of the foregoing lysins with two carbapenems, i.e., imipenem (IPM) or meropenem (MEM). Up to seven carbapenem-resistant isolates were assessed. Resensitization occurs in synergistic combinations in which the carbapenem MIC values fall below established breakpoints, e.g. a MIC value of <2 for carbapenem-sensitive isolates, a MIC value of 4 for intermediately sensitive carbapenem isolates and a MIC value of >8 for carbapenem-resistant isolates. See Clinical and Laboratory Standards Institute (CLSI), CLSI. 2019. M100 Performance Standards for Antimicrobial Susceptibility Testing; 29th Edition. Clinical and Laboratory Standards Institute, Wayne, Pa.

[0307] As indicated in Tables 18-21 synergistic combinations with GN123 (SEQ ID NO: 173) or GN121 (SEQ ID NO: 175) demonstrated reductions of IPM and MEM MICS to below breakpoint values for each of the seven carbapenems examined. These observations are consistent with resensitization.

TABLE 18

Gram-negative bacterial resensitization using a combination of IMIPENEM and GN123

	IMIPENEM MIC (μg/mL)		GN123 (μg/mL)		
Isolate	Alone	Combination	Alone	Combination	FICI
PA19	32 (R)	0.5 (S)	8	0.125	0.03
Analysis of additional CARBAPENEM^R isolates:					
PA20	16 (R)	1 (S)	16	2	0.188
PA21	32 (R)	0.5 (S)	8	1	0.141
PA22	16 (R)	2 (S)	16	1	0.188
PA23	8 (R)	0.25 (S)	8	2	0.281
PA24	32 (R)	2 (S)	16	2	0.188
WC-452	16 (R)	1 (S)	16	2	0.188

(R) = resistant
(S) = sensitive

TABLE 19

Gram-negative bacterial resensitization using a combination of MEROPENEM and GN123 (SEQ ID NO: 173)

	MEROPENEM MIC (μg/mL)		GN123 (μg/mL)		
Isolate	Alone	Combination	Alone	Combination	FICI
PA19	32 (R)	0.5 (S)	8	0.25	0.046
PA20	16 (R)	0.5 (S)	16	1	0.094
PA21	32 (R)	1 (S)	8	1	0.156
PA22	16 (R)	1 (S)	16	1	0.125
PA23	16 (R)	0.5 (S)	8	1	0.156
PA24	32 (R)	2 (S)	16	0.5	0.094
WC-452	16 (R)	1 (S)	16	1	0.125

(R) = resistant
(S) = sensitive

TABLE 20

Gram-negative bacterial resensitization using a combination of IMIPENEM and GN121 (SEQ ID NO: 175)

	Imipenem MIC (μg/mL)		GN121 (μg/mL)		
Isolate	Alone	Combination	Alone	Combination	FICI
PA19	32 (R)	1 (S)	1	0.125	0.155
PA20	16 (R)	0.5 (S)	1	0.25	0.265
PA21	32 (R)	1 (S)	1	0.125	0.155
PA22	32 (R)	2 (S)	2	0.25	0.188
PA23	16 (R)	0.125 (S)	1	0.25	0.257
PA24	32 (R)	1 (S)	1	0.125	0.155

(R) = resistant

(S) = sensitive

TABLE 21

Gram-negative bacterial resensitization using a combination of MEROPENEM and GN121 (SEQ ID NO: 175)

	Meropenem MIC (μg/mL)		GN121 (μg/mL)		
Isolate	Alone	Combination	Alone	Combination	FICI
PA19	32 (R)	1	2	0.5	0.281
PA20	16 (R)	1	2	0.5	0.313
PA21	32 (R)	2	1	0.125	0.188
PA22	16 (R)	1	1	0.25	0.313
PA23	16 (R)	2	2	0.5	0.375
PA24	32 (R)	1	1	0.125	0.156
WC-452	16 (R)	1	1	0.06	0.123

(R) = resistant

(S) = sensitive

Example 13. Resensitization of Carbapenem-Resistant Clinical Strains Using Antibiotics in Combination with Additional Lysins or Lysin-AMP Constructs

[0308] The ability of GN351 (SEQ ID NO: 32), GN370 (SEQ ID NO: 44) or GN428 (SEQ ID NO: 60) to resensitize carbapenem-resistant clinical strains to carbapenems was assessed by combining each of the foregoing lysins or lysin-AMP polypeptide constructs with IPM or MEM. WC-452, a carbapenem-resistant isolate, was assessed. As noted in Example 3, above, resensitization occurs in synergistic combinations in which the carbapenem MIC values fall below the previously described breakpoints.

[0309] As indicated in Table 22 synergistic combinations with GN351 (SEQ ID NO: 32), GN370 (SEQ ID NO: 44) or GN428 (SEQ ID NO: 60) demonstrated reductions of IPM and MEM MICS to below breakpoint values for WC-452. These observations are consistent with resensitization.

[0310] The findings herein indicate that the present lysins and lysin-AMP polypeptide constructs described can resensitize *P. aeruginosa* to carbapenem antibiotics, driving MICs below breakpoint values in vitro. This novel ability of lysins and lysin-AMP polypeptide constructs to resensitize antibiotic-resistant strains to conventional antibiotics indicates the benefit of these biologics as therapeutics to combat and reverse antimicrobial resistance.

TABLE 22

Gram-negative bacterial resensitization using combinations of MEM or IPM and GN351 (SEQ ID NO: 32), GN370 (SEQ ID NO: 44), or GN428 (SEQ ID NO: 60)

Combinations	Antibiotic MIC		Lysin MIC		
vs. WC-452	Alone	Combination	Alone	Combination	FICI
IPM + GN351	16 (R)	0.5 (S)	1	0.125	0.156
IPM + GN370	16 (R)	0.5 (S)	2	0.125	0.094
IPM + GN428	16 (R)	1 (S)	2	0.25	0.188
MEM + GN351	16 (R)	1 (S)	1	0.125	0.188
MEM + GN370	16 (R)	0.5 (S)	2	0.125	0.125
MEM + GN428	16 (R)	1 (S)	2	0.25	0.188

Example 14. Low Propensity for Resistance to GN Lysins

[0311] In another experiment, it was determined that Gram-negative bacteria did not develop resistance to GN121, GN351, GN370, and GN428 in a 21-day serial passage resistance assay. An analysis of bacterial resistance was performed using *P. aeruginosa* (strain WC-452) over 21 days of serial passage in the presence of a GN-lysin dilution series (in duplicate). Briefly, the broth microdilution MIC format was used in which 2-fold dilution ranges of GN lysin were cultured with the bacteria 5×10^6 CFU/ml starting concentration) in CAA broth for 18 hours at 37° C. The well with the highest concentration of GN lysin in which bacterial growth was seen was then used as the inoculum for the next day's passage, and the process was repeated over a 21 day period. The MIC at each daily time-point was recorded, and resistance was measured as a step-wise increase in MIC.

[0312] In the assay, GN121, GN351, GN370, and GN428 lysin MICs increased by up to 1-$\log_2$ dilutions (2-fold) over 18 days, which was comparable to passage control (absence of treatment). FIGS. **4**A-**4**D. In contrast, the Ciprofloxacin control increased 4-$\log_2$ dilutions (16-fold) over 18 days (FIG. **4**E). D'Lima et al. also found an increase in Ciprofloxacin MIC during serial passage. See D'Lima et al., 2012, *Antimicrobial Agents and Chemotherapy,* 56: 2753-2755, which reports an increase of Ciprofloxacin MIC of up to 32-fold over a 21 day serial passage. Our results are consistent with a low propensity for GN lysin resistance, which is similar to that observed with Gram-positive lysins. See, for example, PCT/US19/19638, which was filed on Feb. 26, 2019, and is herein incorporated by reference in its entirety.

Example 15. GN Lysins and Lysin-AM Constructs are not Hemolytic

[0313] The hemolytic activity of selected GN lysins and constructs was measured as the amount of hemoglobin released by the lysis of human erythrocytes (Lv et al., 2014, *PLoS One,* 9:e86364). Briefly, 3 milliliters of fresh human blood cells (hRBGs) obtained from pooled healthy donors in a polycarbonate tube containing heparin was centrifuged at 1,000×g for 5 minutes at 4° C. The erythrocytes obtained were washed three times with PBS solution (pH 7.2) and resuspended in PBS. A 50 μL volume of the erythrocyte solution was incubated with 50 μL of each GN lysin and or construct (in PBS) in a 2-fold dilution range (from 128 μg/ml to 0.25 μg/ml) for 1 hour at 37° C. Intact erythrocytes were pelleted by centrifugation at 1,000×g for 5 minutes at 4° C., and the supernatant was transferred to a new 96-well plate.

The release of hemoglobin was monitored by measuring the absorbance at 570 nm. As a negative control, hRBGs in PBS were treated as above with 0.1% Triton X-100.

[0314] Table 23 below shows the minimal hemolytic concentrations (MHCs), which result in >5% hemolysis compared to the Triton X-100 control. MHCs for AMPs with known hemolytic activity are shown for comparison. GN126 is also included for comparison. As indicated in the Table, the selected lysins demonstrate no hemolytic activity.

TABLE 23

Minimal Hemolytic Concentrations for selected lysins.

Lysin	MHC (μg/mL)
GN76	>128
GN126	>128
GN83	>128
GN75	>128
GN7	>128
GN11	>128
GN14	>128
GN217	>128
GN316	>128
GN329	>128
GN333	>128
GN351	>128
GN357	>128
GN428	>128
GN370	>128
GN431	>128
RR12	8
RR12Polar	4
RR12hydro	32

Example 16. GN Lysins and Constructs are Tolerated In Vivo

[0315] The in vivo tolerability of selected lysins was assessed in non-infected ICR mice (ca. 4-6 weeks old, 11-18 g, supplied by Charles River (Margate, UK)) by administering a single intravenous dose of each lysin to two mice at the starting doses as described in Table 24 below. The mice were monitored closely for 1 hour post dose and if there were no clinical signs of side-effects, another two mice were injected with a higher dose of each lysin (Table 24). Mice were monitored closely for 1 hour post dose and then at regular intervals until the end of study at 8 hours post dose.

TABLE 24

Study design for the tolerability study

GN lysin	Dose (mg/kg)	Dose Volume (mL/kg)	Route	% Survival
GN121	3 and 10	10	IV	100
GN150	30 and 85	10	IV	100
GN316	30 and 100	10	IV	100
GN370	30 and 100	10	IV	100
GN431	30 an 100	10	IV	100

[0316] Mice were monitored at a frequency appropriate for their clinical condition. Mouse weights were recorded on days −4, −1 and 0, both to ensure animals remained within ethical limits, and to allow accurate calculation of individual dosing volumes (adjusted according to the weight of each mouse).

[0317] The mice were euthanized at 8 hours post dose and a post mortem was performed. At the designated time of euthanasia, the clinical condition and body weight of all animals was assessed, then mice were euthanized by pentobarbitone overdose.

[0318] The starting doses of all lysins were well tolerated at 1 hour post dose so the higher dose of the lysins was administered in the second cohort of mice as described earlier. The second cohort of mice were monitored closely for 1 hour post dose and subsequently all mice were regularly monitored for any clinical signs of side-effects until 8 hours post dose. Both low and high doses of the lysins were well tolerated without any clinical observations and the study was ended by euthanizing the mice at 8 hours post dose. A post mortem was carried out on all mice which showed no morphological changes to the viscera. Accordingly, the selected lysins were all well tolerated in vivo at the highest dose levels tested when administered intravenously.

Example 17. GN370 is Active Against a Wide Range of Gram-Negative Bacteria

[0319] MIC values were determined using the methodology described above, i.e., the standard broth microdilution reference method defined by CLSI. MIC_{50} is the minimum concentration of peptide sufficient to suppress at least 50% of the bacterial growth compared to control, and MIC_{50} is the minimum concentration of peptide sufficient to suppress at least 90% of the bacterial growth compared to control, whereas the term MIC, as described above, refers to suppression of at least 80% bacterial growth.

[0320] An antibiotic-resistant isolate bank panel was chosen from the Center for Disease Control's strain lists for use in this range study. Specifically, a panel of *Pseudomonas aeruginosa* multi-drug-resistant (MDR) and extensively antibiotic-resistant (XDR) isolates were chosen to represent a diversity of antimicrobial susceptibility results for drugs that are used to treat infections. The strains are described, for example, at wwwn.cdc.gov/ARIsolateBank/Panel/PanelDetail?ID=12 for the *Pseudomonas aeruginosa* isolates. Lab strains PAO1 and ATCC 27853 were also tested. An additional 49 *Pseudomonas aeruginosa* isolates were obtained from Weill Cornell Medical College, New York and these were also assessed. Nine (9) isolates from *Acinetobacter baumannii* and eight (8) isolates from *Klebsiella pneumoniae* were also tested.

[0321] FIG. **5** and Tables 25 and 26 show the MIC, MIC_{50} and MIC_{50} values for the *Pseudomonas aeruginosa* isolates. GN370 was active against all tested *Pseudomonas aeruginosa* isolates including MDR and XDR isolates (MIC values ranging from 0.25-4). Surprisingly, as shown below in Table 26, GN370 was also active against *Acinetobacter baumannii* and *Klebsiella pneumoniae* (MTC values ranging from 0.5-1 and 0.25-4, respectively).

TABLE 25

Pseudomonas aeruginosa Panel

CDC Antibiotic-Resistant Bank No.	MIC GN370
0229	2
0230	1
0231	2
0232	2
0233	0.5

TABLE 25-continued

Pseudomonas aeruginosa Panel	
CDC Antibiotic-Resistant Bank No.	MIC GN370
0234	1
0235	2
0236	0.5
0237	0.5
0238	1
0239	2
0240	2
0241	2
0242	0.5
0243	0.25
0244	2
0245	2
0246	1
0247	1
0248	1
0249	1
0250	1
0251	1
0252	1
0253	0.5
0254	1
0255	1
0256	0.5
0257	0.5
0258	1
0259	1
0260	ng
0261	1
0262	1
0263	0.5
0264	0.5
0265	2
0266	2
0267	2
0268	2
0269	2
0270	1
0271	1
0272	2
0763	1
0764	1
0765	1
0766	0.25
0767	1
0768	ng

TABLE 25-continued

Pseudomonas aeruginosa Panel	
CDC Antibiotic-Resistant Bank No.	MIC GN370
0769	2
0770	0.5
0771	2
0772	0.5
0773	1

TABLE 26

GN370 active against a range of genera

Strain	n	MIC_{50}	MIC_{90}	Range
P. aeruginosa	104	1	2	0.25-4
A. baumannii	9	1	1	0.5-1
K. pneumoniae	8	2	4	0.25-4

Example 18. Rat Toxicity Study

[0322] Experimental Design, Phase 1

[0323] A rat toxicity study of GN370 was conducted in two phases (Phase 1 and Phase 2). The dose escalation phase (Phase 1) of the study was conducted to determine the maximum tolerated dose (MTD) of GN370. During Phase 1, GN370 and control/vehicle (25 mM Tris, 50 mM Sodium Chloride, pH 8.0) were administered once to groups of male Sprague Dawley rats (250 g to 325 g at the onset of treatment, 7-8 weeks of age) by intravenous infusion over a period of 2 hours via the tail vein in an escalating dose fashion as described in the Table below.

[0324] The infusion rate for the animals of Groups 1 and 4 was 5 mL/kg/hour (10 mL/kg) over a two hour period. The infusion rate for Groups 2 and 3 was 2.5 mL/kg/hour (5 mL/kg), also over a two hour period. A stepwise approach was taken to ensure that each dose level used was tolerated prior to higher dose levels being tested. As such, a minimum 24 hour observation period was allowed between successive doses. All surviving animals were observed for 3, 7 or 14 days post-dose, following which they were euthanized and subjected to a necropsy examination (Study days 3, 7 or 14, post-dose).

TABLE 27

Phase 1 Design

Group Numbers[a]	Group Designation	Dose Level (mg/kg)	Dose Concentration (mg/mL)	Dose Volume (mL/kg	Number of Main Animals (Male)	Days of Euthanasia
1	Control*	0	0	10	5	4
					3	8
					3	15
2	GN370 Low Dose	10	2	5	5	4
					3	8
					3	15
3	GN370 Mid Dose	50	10	5	5	4
					3	8
					3	15
4	GN370 High Dose	100	10	10	5	4
					3	8
					3	15

*The Control animals received the control/vehicle item alone

[a]= Each dose was followed by a 24-hour observation period

[0325] Experimental Design, Phase 2

[0326] For Phase 2, GN370 and control/vehicle were administered to groups of rats by intravenous infusion over a period of 2 hours via tail vein for 4 consecutive days as described in the table below. The infusion rate for animals in Groups 5 and 8 was 10 mL/kg/hour (20 mL/kg) over a period of 2 hours. The infusion rate for the Group 6 animals was 2.5 mL/kg/hour (5 mL/kg), and the infusion rate for the Group 7 animals was 5 mL/kg/hour (10 mL/kg) over a period of 2 hours.

[0327] The infusion period for Group 8 was stopped on day 2 due to the effects described in the results below. On day 3, three toxicokinetic (TK) animals were infused for a period of 4 hours and subsequently dosed on days 4 and 5. The infusion rate was 5 mL/kg/hour (20 mL/kg).

[0328] All surviving animals in Groups 5, 6, and 7 were observed for 3, 7 or 14 days after the last dosing (4^{th} dose), following which they were euthanized and subjected to a necropsy examination at days 7, 11 or 18, respectively. The three TK rats with the extended 4 hour infusion period were euthanized on day 8, considered as main animals, and accordingly subjected to a necropsy examination.

TABLE 28

Phase 2 Design

Group Numbers	Group Designation	Dose Level (mg/kg/day)	Dose Concentration (mg/mL)	Dose Volume (mL/kg	Number of Main Animals (Male)	Number ofTK Animals (Male)	Days of Euthan asia
5	Control	0	0	20	—	3	5
					5	—	7
					3	—	11
					3	—	18
6	GN370	25	5	5	—	6	5
	Low Dose				5	—	7
					3	—	11
					3	—	18
7	GN370	75	75	10	—	6	5
	Mid Dose				5	—	7
					3	—	11
					3	—	18
8	GN370	200	10	20	—	6	5*
	High Dose				5	—	3
					3	—	9
					3	—	16

*3 TK animals were euthanized on Day 8 and considerec as main animals

[0329] Necropsy Procedures

[0330] The main animals were euthanized on completion of their respective observation periods following an overnight period without food. The animals were anesthetized with Isoflurane to allow for collection of blood samples for clinical pathology evaluation followed by exsanguination. Blood samples were collected from the abdominal aorta at termination. Urine was collected over a period of approximately 12 to 18 hours by placing individual rats on a wire mesh cage with a collection tray under the case or by placing the animals in metabolic cages.

[0331] For each animal, the necropsy consisted of an external examination, including reference to all clinically-recorded lesions, as well as a detailed internal examination. Organs were dissected, trimmed free of fat and weighted.

[0332] Upon completion of the gross pathology examination and selected organ weighing in both study phases, the tissues and organs were retained. Neutral buffered 10% formalin was used for fixation and preservation. For Phase 1 and 2, histopathological examination is being performed on vehicle and high dose groups (on going).

[0333] Toxicokinetic Procedures

[0334] TK animals were euthanized on Day 5 and discarded without further examination following completion of sample collection. Samples were collected as follows. A series of blood samples (approximately 0.3 mL each) were collected from two cohorts of 3 TK rats/group/time-point relative to dosing on Day 1 and 4 of Phase 2 as indicated in the table below.

[0335] Control animals were bled at predose and 5 minutes after infusion. Each rat (unanesthetized) was bled by jugular venipuncture (as an alternate bleeding technique, the animals were bled from the sublingual vein), and the samples were collected into tubes containing the anticoagulant K_2EDTA. The tubes were placed on wet ice pending processing.

[0336] Following collection, the samples were centrifuged (2500 rpm for 10 minutes at approximately 4° C. within approximately 30 minutes of collection. The resulting plasma was recovered, split into 2 aliquots of approximately equal volume and stored frozen (<60° C.) in labelled tubes. The plasma samples are analyzed for GN370 concentration using ELISA (ongoing). Non-compartmental analysis for the GN370 in the plasma data set will be performed using PHOENIX® WINNONLIN® software using default parameters.

[0337] Toxicokinetic parameters including Terminal elimination half-life (Tin) and Area under the plasma drug concentration time curve from the time of dosing to the last quantifiable concentration ($AUC_{0\text{-}Tlast}$) will also be assessed.

TABLE 29

		Sample Collection								
		Toxicokinetic time point (relative to end of dosing)								
Group No.	No. of animals	Predose	5 min.	15 min.	30 min.	1 hour	2 hours	4 hours	6 hours	24 hours
6	3+	√		√		√		√		√
	3#		√		√		√		√	
7	3+	√		√		√		√		√
	3#		√		√		√		√	
8	3+	√		√		√		√		√
	3#		√		√		√		√	

+3 animals with the lowest identification numbers.

#3 animals with the highest identification numbers.

[0338] In addition to the above, laboratory investigations (hematology, coagulation, clinical chemistry analyses and urinalysis will be performed on all main animals at termination (both Phase 1 and Phase 2). Hematology parameters, e.g., red blood cell count, white blood cell count, coagulation parameters, e.g. prothrombin time and activated partial thromboplastin time and clinical chemistry parameters, e.g. glucose levels, total protein, will be determined from the blood samples. A urinalysis will also be conducted to assess e.g. glucose, ketone and protein levels.

[0339] Results

[0340] The Phase 1 single dose escalation study conducted as described above revealed no macroscopic findings or clinical signs of toxicity at up to 100 mg/kg GN370. The Phase 2 repeat dose study (4 days) did not reveal any clinical signs of toxicity at either 25 mg/kg or 75 mg/kg dosages. On dosing day 2, as noted above, the infusion was stopped after 1.75 hours in animals dosed at 200 mg/kg due to "swollen" nose/face. In three TK rats, as also noted above, the infusion period was extended to 4 hours (200 mg/kg) and no clinical signs or macroscopic findings indicating toxicity were observed.

Example 19. Efficacy of GN370 in Rabbit Pulmonary Model

[0341] Establishment of Model

[0342] A rabbit pulmonary model was established for use in assessing the efficacy of the GN370 lysin alone and in combination with an antibiotic (meropenem). Initially, the lowest bacterial inoculum that established robust bioburdens of *P. aeruginosa* isolate CFS 1558 (PA20) in all target tissues without excess mortality was determined. A comparison of the bioburden in target tissue at inoculums of 6×10^8 CFU, 3×10^9 CFU and 8×10^9 CFU is shown below. 3×10^9 CFU of the *P. aeruginosa* isolate was used to challenge the rabbits during the efficacy study described below.

TABLE 30

Bacterial Burden after administration of *Pseudomonas* inoculum

	Organ			
Treatment*	Lung 1	Lung 2	Kidneys	Spleen
Control 6×10^8 CFU (5)	3.24 ± 0.47	3.40 ± 1.12	1.18 ± 0.71	1.24 ± 0.71
Control 3×10^9 CFU (3)	7.77 ± 0.92	6.15 ± 0.43	5.22 ± 0.34	4.19 ± 0.40
Control 8×10^9 CFU (3)	8.51 ± 0.13	8.09 ± 0.93	6.94 ± 0.55	6.94 ± 0.70

*Number of animals in parentheses; rabbits sacrificed 5-6 hours post-endobronchial challenge.

[0343] The dosage of meropenem resulting in a static effect was also determined, i.e. a non-bactericidal effect (<2 $\log_{10}$ CFU/g reduction in lung and other target tissue counts versus untreated controls). To determine this dosage, the rabbits were treated with 10 mg/kg, 20 mg/kg, 30 mg/kg and 40 mg/kg of meropenem (three times a day, subcutaneous administration for two days). Meropenem therapy was started 5-6 hours after induction of pneumonia and the animals were sacrificed at 18-24 hours after the last antibiotic dose. As indicated in the table below, 20 mg/kg established a static effect.

TABLE 31

Bacterial Burden after treatment with Meropenem

	Organ			
Treatment*	Lung 1	Lung 2	Kidneys	Spleen
Control 3×10^9 CFU	8.06 ± 0.63	6.47 ± 0.47	4.43 ± 0.45	4.72 ± 0.62
Meropenem 10 mg/kg (4)	7.39 ± 0.34	7.42 ± 0.64	4.36 ± 0.43	4.01 ± 0.10
Meropenem 20 mg/kg (3)	6.85 ± 1.09	6.97 ± 1.19	4.51 ± 0.73	4.74 ± 0.57
Meropenem 25 mg/kg (6)	4.55 ± 1.65	3.73 ± 1.03	2.06 ± 0.58	2.15 ± 0.78
Meropenem 30 mg/kg (8)	4.83 ± 1.19	4.42 ± 1.14	2.24 ± 0.64	1.97 ± 0.63
Meropenem 40 mg/kg (5)	4.66 ± 0.11	2.95 ± 1.19	2.34 ± 0.65	1.93 ± 0.47

*Number of animals in parentheses; rabbits sacrificed 18-24 hours after last antibiotic dose.

[0344] Efficacy of GN370

[0345] The rabbit pulmonary model described above was used to assess the efficacy of the GN370 lysin alone and in combination with an antibiotic (meropenem). The rabbits were infected intratracheally with *P. aeruginosa* isolate CFS 1558 (PA20) (3×10^9 CFU). Treatment commenced 6 hours post-infection. The treatment groups are shown in Table 32 below. The rabbits were sacrificed 18-24 hours after the last dose of meropenem and the bacterial burden (CFU/gram) in the lung, spleen and kidneys was assessed.

[0346] Only 40% of the infected rabbits treated with the vehicle survived through the end of the study. None of the rabbits treated with a GN370 lysin dosage of 30 mg/kg survived after 24 hours. 40% of rabbits survived 24 hours after treatment with a 30 mg/kg dosage of lysin+meropenem.

[0347] As shown in Table 33, bacterial density in all three tissues (lung, kidney, and spleen) from animals treated with GN-370 (10 mg/kg) in addition to meropenem was decreased compared to meropenem or GN370 alone, demonstrating synergy. In addition, GN370 split doses (over a 24 h period), i.e. 3×3.33 mg/kg (total dose of 10 mg/kg) and

3×10 mg/kg (total dose of 30 mg/kg) were tested. The results indicate that a single dose of GN370 at 10 mg/kg+meropenem was more effective than the split dose of 3×3.33 mg/kg+meropenem. However, splitting the 30 mg/kg in 3×10 mg/kg+meropenem was synergistic and provided significant bacterial burden reduction. There was a paradoxical increase in counts when the single lysin dose was increased to 30 mg/kg in combination with meropenam associated with excess early mortality. Normal (uninfected) rabbits given 30 mg/kg of lysin intravenously suffered no ill acute effects or subacute mortalities.

[0348] This example provides evidence that GN lysins and constructs of the instant disclosure may be used alone or in combination with antibiotics, such as meropenem, to treat pulmonary infections, such as pneumonia (including HAP and/or VAP) and cystic fibrosis exacerbations.

TABLE 32

Treatment Groups in Rabbit Pulmonary Model

Treatment	N	Route	Dosage amount	Frequency of Dosages
6 hours untreated (pre-therapy control)	10	N/A	N/A	N/A
Meropenem	10	Subcutaneous (SC)	20 mg/kg	Every 8 hours (3 doses)
GN370	10	Intravenous (IV)	3 mg/kg	1 dose
Meropenem + GN370	10	SC/IV	20 mg/kg + 3 mg/kg	Every 8 hours (3 doses)/1 dose
GN370	10	IV	10 mg/kg	1 dose
Meropenem + GN370	10	SC/IV	20 mg/kg + 10 mg/kg	Every 8 hours (3 doses)/1 dose
GN370	10	IV	30 mg/kg	1 dose
Meropenem + GN370	10	SC/IV	20 mg/kg + 30 mg/kg	Every 8 hours (3 doses)/1 dose
Meropenem + GN370	9	SC/IV	20 mg/kg + 10 mg/kg	Every 8 hours (3 doses)/Every 8 hours (3 doses)
GN370	10	IV	10 mg/kg	Every 8 hours (3 doses)
Meropenem + GN370	10	SC/IV	20 mg/kg + 3.3 mg/kg	Every 8 hours (3 doses)/Every 8 hours (3 doses)
GN370	10	IV	3.3 mg/kg	Every 8 hours (3 doses)

TABLE 33

Bacterial Burden Reduction with GN370 alone or combined with meropenem

	Organ			
Treatment	Lung 1	Lung 2	Kidneys	Spleen
6 hours untreated (pre-therapy control)	7.28 ± 095	7.35 ± 1.12	4.61 ± 0.71	4.77 ± 0.83
Vehicle (N = 10; 6 out of 10 rabbits died at 24 h post-infection)	7.67 ± 0.57	7.92 ± 0.43	5.77 ± 1.14	5.81 ± 0.73
meropenem (20 mg/kg × 3 doses)	6.08 ± 0.86	6.17 ± 0.93	4.22 ± 0.69	3.74 ± 0.54
GN370 (3 mg/kg, 1 dose)	6.45 ± 1.05	6.59 ± 0.97	4.91 ± 1.11	5.20 ± 1.11
meropenem (20 mg/kg) + GN370 (3 mg/kg, 1 dose)	6.06 ± 1.22	6.27 ± 1.08	4.05 ± 1.11	4.16 ± 0.92
GN370 (10 mg/kg, 1 dose)	6.84 ± 0.88	5.65 ± 1.35	3.86 ± 0.87	3.90 ± 0.50
meropenem (20 mg/kg) + GN370 (10 mg/kg, 1 dose)	3.77 ± 1.48	4.07 ± 1.50	2.26 ± 1.05	2.26 ± 1.18
GN370 (30 mg/kg, 1 dose)	7.97 ± 0.43	7.79 ± 0.50	5.34 ± 0.48	5.25 ± 0.35
meropenem (20 mg/kg) + GN370 (30 mg/kg, 1 dose)	6.79 ± 0.95	6.70 ± 1.14	4.37 ± 0.78	4.41 ± 0.84
meropenem (20 mg/kg) + GN370 (10 mg/kg × 3 dose)	3.80 ± 1.14	3.60 ± 1.20	3.33 ± 1.00	3.00 ± 0.88
GN370 (10 mg/kg × 3 dose)	6.92 ± 1.61	6.57 ± 1.50	5.22 ± 1.20	5.35 ± 0.32
meropenem (20 mg/kg) + GN370 (3.3 mg/kg × 3 dose)	5.58 ± 1.64	4.99 ± 0.90	4.30 ± 0.98	4.78 ± 0.63
GN370 (3.3 mg/kg × 3 dose)	7.11 ± 1.40	7.34 ± 1.40	5.38 ± 0.74	5.79 ± 0.65

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FEATURE Location/Qualifiers
REGION 1..172
note = Synthetic Construct
source 1..172
mol_type = protein
organism = synthetic construct
SEQUENCE: 4
MSFNVTPKFK RWQLYFRGRM WTAGGTAGGR TSQRGIDLIK SFEGLRLSAY QDSVGVWTIG 60
YGTTRGVTRY MTITVEQAER MLSNDIQRFE PELDRLAKVP LNQNQWDALM SFVYNLGAAN 120
LASSTLLDLL NKGDYQGAAD QFPHWVNAGG KRLDGLVKRR AAERALFLEP LS 172

SEQ ID NO: 5 moltype = DNA length = 582
FEATURE Location/Qualifiers

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misc_feature            1..582
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            28..558
                        note = GN178 lysin
source                  1..582
                        mol_type = other DNA
                        organism = synthetic construct
CDS                     28..558
SEQUENCE: 5
gtttaacttt aagaaggaga attcaccatg ccaccaattt ttagcaaact ggcgggcaaa  60
aaaattaaaa acctgctgat tagcggcctg aaaggcggta gcggcagcgg tagcggtagc  120
ggcagcccgc gtacatccca acgaggcatc gacctcatca aatccttcga gggcctgcgc  180
ctgtccgctt accaggactc ggtgggtgtc tggaccatag gttacggcac cactcggggc  240
gtcacccgct acatgacgat caccgtcgag caggccgagc ggatgctgtc gaacgacatt  300
cagcgcttcg agccagagct agacaggctg gcgaaggtgc cactgaacca gaaccagtgg  360
gatgccctga tgagcttcgt gtacaacctg ggcgcggcca atctggcgtc gtccacgctg  420
ctcgacctgc tgaacaaggg tgactaccag ggagcagcgg accagttccc gcattgggtg  480
aatgcgggcg gtaagcgctt ggatggtctg gttaagcgtc gagcagccga gcgtgcgctg  540
ttcctggagc cactatcgtg ataaaagctt ggctgttttg gc                     582

SEQ ID NO: 6            moltype = AA  length = 177
FEATURE                 Location/Qualifiers
REGION                  1..177
                        note = Synthetic Construct
source                  1..177
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 6
MPPIFSKLAG KKIKNLLISG LKGGSGSGSG SGSPRTSQRG IDLIKSFEGL RLSAYQDSVG  60
VWTIGYGTTR GVTRYMTITV EQAERMLSND IQRFEPELDR LAKVPLNQNQ WDALMSFVYN  120
LGAANLASST LLDLLNKGDY QGAADQFPHW VNAGGKRLDG LVKRRAAERA LFLEPLS     177

SEQ ID NO: 7            moltype = DNA  length = 429
FEATURE                 Location/Qualifiers
misc_feature            1..429
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            28..405
                        note = GN217 lysin
source                  1..429
                        mol_type = other DNA
                        organism = synthetic construct
CDS                     28..405
SEQUENCE: 7
gtttaacttt aagaaggaga attcaccatg acctacaccc tgtctaaacg ttctctggac  60
aacctgaaag gtgttcaccc ggacctggtt gctgttgttc accgtgctat ccagctgacc  120
ccggttgact tcgctgttat cgaaggtctg cgttctgttt ctcgtcagaa agaactggtt  180
gctgctggtg cttctaaaac catgaactct cgtcacctga ccggtcacgc tgttgacctg  240
gctgcttacg ttaacggtat ccattgggac tggccgctgt acgacgctat cgctgttgct  300
gttaaagctg ctgctaaaga actgggtgtt gctatcgttt ggggtggtga ctggaccacc  360
ttcaaagacg gtccgcactt cgaactggac cgttctaaat accgttaata aaagcttggc  420
tgttttggc                                                          429

SEQ ID NO: 8            moltype = AA  length = 126
FEATURE                 Location/Qualifiers
REGION                  1..126
                        note = Synthetic Construct
source                  1..126
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 8
MTYTLSKRSL DNLKGVHPDL VAVVHRAIQL TPVDFAVIEG LRSVSRQKEL VAAGASKTMN  60
SRHLTGHAVD LAAYVNGIHW DWPLYDAIAV AVKAAAKELG VAIVWGGDWT TFKDGPHFEL  120
DRSKYR                                                             126

SEQ ID NO: 9            moltype = DNA  length = 501
FEATURE                 Location/Qualifiers
misc_feature            1..501
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            1..501
                        note = GN218 lysin
source                  1..501
                        mol_type = other DNA
                        organism = synthetic construct
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CDS 28..477
SEQUENCE: 9
gtttaacttt aagaaggaga attcaccatg acctacaccc tgtctaaacg ttctctggac 60
aacctgaaag gtgttcaccc ggacctggtt gctgttgttc accgtgctat ccagctgacc 120
ccggttgact tcgctgttat cgaaggtctg cgttctgttt ctcgtcagaa agaactggtt 180
gctgctggtg cttctaaaac catgaactct cgtcacctga ccggtcacgc tgttgacctg 240
gctgcttacg ttaacggtat ccgttgggac tggccgctgt acgacgctat cgctgttgct 300
gttaaagctg ctgctaaaga actgggtgtt gctatcgttt ggggtggtga ctggaccacc 360
ttcaaagacg gtccgcactt cgaactggac cgttctaaat acggcggtgg ctctggaggt 420
ggtgggtccg gcggtggctc tcgcctgaaa aaaattggca aagtgctgaa atggatttaa 480
taaaagcttg gctgttttgg c 501

SEQ ID NO: 10 moltype = AA length = 150
FEATURE Location/Qualifiers
REGION 1..150
note = Synthetic Construct
source 1..150
mol_type = protein
organism = synthetic construct
SEQUENCE: 10
MTYTLSKRSL DNLKGVHPDL VAVVHRAIQL TPVDFAVIEG LRSVSRQKEL VAAGASKTMN 60
SRHLTGHAVD LAAYVNGIRW DWPLYDAIAV AVKAAAKELG VAIVWGGDWT TFKDGPHFEL 120
DRSKYGGGSG GGGSGGGSRL KKIGKVLKWI 150

SEQ ID NO: 11 moltype = DNA length = 573
FEATURE Location/Qualifiers
misc_feature 1..573
note = Description of Artificial Sequence: Synthetic polynucleotide
misc_feature 28..549
note = GN223 lysin
source 1..573
mol_type = other DNA
organism = synthetic construct
CDS 28..549
SEQUENCE: 11
gtttaacttt aagaaggaga attcaccatg acctacaccc tgtctaaacg ttctctggac 60
aacctgaaag gtgttcaccc ggacctggtt gctgttgttc accgtgctat ccagctgacc 120
ccggttgact tcgctgttat cgaaggtctg cgttctgttt ctcgtcagaa agaactggtt 180
gctgctggtg cttctaaaac catgaactct cgtcacctga ccggtcacgc tgttgacctg 240
gctgcttacg ttaacggtat ccgttgggac tggccgctgt acgacgctat cgctgttgct 300
gttaaagctg ctgctaaaga actgggtgtt gctatcgttt ggggtggtga ctggaccacc 360
ttcaaagacg gtccgcactt cgaactggac cgttctaaat accgtccacc aggcggtggc 420
tctggaggtg gtgggtccgg cggtggctct tcgaagaagg cgtcgaggaa gagttttact 480
aagggtgccg ttaaggttca taagaaaaat gttcctactc gtgttcctat gcgtggcggt 540
attaggcttt aataaaagct tggctgtttt ggc 573

SEQ ID NO: 12 moltype = AA length = 174
FEATURE Location/Qualifiers
REGION 1..174
note = Synthetic Construct
source 1..174
mol_type = protein
organism = synthetic construct
SEQUENCE: 12
MTYTLSKRSL DNLKGVHPDL VAVVHRAIQL TPVDFAVIEG LRSVSRQKEL VAAGASKTMN 60
SRHLTGHAVD LAAYVNGIRW DWPLYDAIAV AVKAAAKELG VAIVWGGDWT TFKDGPHFEL 120
DRSKYRPPGG GSGGGGSGGG SSKKASRKSF TKGAVKVHKK NVPTRVPMRG GIRL 174

SEQ ID NO: 13 moltype = DNA length = 519
FEATURE Location/Qualifiers
misc_feature 1..519
note = Description of Artificial Sequence: Synthetic polynucleotide
misc_feature 28..495
note = GN239 lysin
source 1..519
mol_type = other DNA
organism = synthetic construct
CDS 28..495
SEQUENCE: 13
gtttaacttt aagaaggaga attcaccatg acctacaccc tgtctaaacg ttctctggac 60
aacctgaaag gtgttcaccc ggacctggtt gctgttgttc accgtgctat ccagctgacc 120
ccggttgact tcgctgttat cgaaggtctg cgttctgttt ctcgtcagaa agaactggtt 180
gctgctggtg cttctaaaac catgaactct cgtcacctga ccggtcacgc tgttgacctg 240
gctgcttacg ttaacggtat ccgttgggac tggccgctgt acgacgctat cgctgttgct 300

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gttaaagctg ctgctaaaga actgggtgtt gctatcgttt ggggtggtga ctggaccacc  360
ttcaaagacg gtccgcactt cgaactggac cgttctaaat acggcggtgg ctctggaggt  420
ggtgggtccg gcggtggctc tcgtaaaaaa acccgtaaac gtctgaaaaa aatcggtaaa  480
gttctgaaat ggatctaata aaagcttggc tgttttggc                         519

SEQ ID NO: 14          moltype = AA  length = 156
FEATURE                Location/Qualifiers
REGION                 1..156
                       note = Synthetic Construct
source                 1..156
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 14
MTYTLSKRSL DNLKGVHPDL VAVVHRAIQL TPVDFAVIEG LRSVSRQKEL VAAGASKTMN  60
SRHLTGHAVD LAAYVNGIRW DWPLYDAIAV AVKAAAKELG VAIVWGGDWT TFKDGPHFEL  120
DRSKYGGGSG GGGSGGGSRK KTRKRLKKIG KVLKWI                           156

SEQ ID NO: 15          moltype = DNA  length = 570
FEATURE                Location/Qualifiers
misc_feature           1..570
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           28..546
                       note = GN243 lysin
source                 1..570
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..546
SEQUENCE: 15
gtttaacttt aagaaggaga attcaccatg acctacaccc tgtctaaacg ttctctggac  60
aacctgaaag gtgttcaccc ggacctggtt gctgttgttc accgtgctat ccagctgacc  120
ccggttgact tcgctgttat cgaaggtctg cgttctgttt ctcgtcagaa agaactggtt  180
gctgctggtg cttctaaaac catgaactct cgtcacctga ccggtcacgc tgttgacctg  240
gctgcttacg ttaacggtat ccgttgggac tggccgctgt acgacgctat cgctgttgct  300
gttaaagctg ctgctaaaga actgggtgtt gctatcgttt ggggtggtga ctggaccacc  360
ttcaaagacg gtccgcactt cgaactggac cgttctaaat accgtaaaaa aacccgtaaa  420
cgtctgaaaa aaatcggtaa agttctgaaa tggatcccac caggcggtgg ctctggaggt  480
ggtgggtccg gcggtggctc tacccgcaaa cgcctgaaaa aaattggcaa agtgctgaaa  540
tggatttaat aaaagcttgg ctgttttggc                                   570

SEQ ID NO: 16          moltype = AA  length = 173
FEATURE                Location/Qualifiers
REGION                 1..173
                       note = Synthetic Construct
source                 1..173
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 16
MTYTLSKRSL DNLKGVHPDL VAVVHRAIQL TPVDFAVIEG LRSVSRQKEL VAAGASKTMN  60
SRHLTGHAVD LAAYVNGIRW DWPLYDAIAV AVKAAAKELG VAIVWGGDWT TFKDGPHFEL  120
DRSKYRKKTR KRLKKIGKVL KWIPPGGGSG GGGSGGGSTR KRLKKIGKVL KWI        173

SEQ ID NO: 17          moltype = DNA  length = 528
FEATURE                Location/Qualifiers
misc_feature           1..528
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           28..504
                       note = GN280 lysin
source                 1..528
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..504
SEQUENCE: 17
gtttaacttt aagaaggaga attcaccatg aaactcagcg aaaaacgagc actgttcacc  60
cagctgcttg cccagttaat tctttgggca ggaactcagg atcgagtgtc agtagccttg  120
gatcaagtga aaaggacaca ggctgaagct gatgccaatg ctaagtctgg agcaggcatt  180
aggaactctc tccatctact gggattagcc ggtgatctta tcctctacaa ggatggtaaa  240
tacatggata agagcgagga ttataagttc ctgggagatt actggaagag tctccatcct  300
ctttgtcggt ggggcggaga ttttaaaagc cgtcctgatg gtaatcattt ctccttggaa  360
cacgaaggag tgcaacgtaa aaaaacccgt aaacgtctga aaaaaatcgg taaagttctg  420
aaatggatcc caccaaccgc gggcggcacc gcgggcggca cccgcaaacg cctgaaaaaa  480
attggcaaag tgctgaaatg gatttaataa aagcttggct gttttggc               528

SEQ ID NO: 18          moltype = AA  length = 159
FEATURE                Location/Qualifiers
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REGION                  1..159
                        note = Synthetic Construct
source                  1..159
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 18
MKLSEKRALF TQLLAQLILW AGTQDRVSVA LDQVKRTQAE ADANAKSGAG IRNSLHLLGL  60
AGDLILYKDG KYMDKSEDYK FLGDYWKSLH PLCRWGGDFK SRPDGNHFSL EHEGVQRKKT  120
RKRLKKIGKV LKWIPPTAGG TAGGTRKRLK KIGKVLKWI                         159

SEQ ID NO: 19           moltype = DNA  length = 543
FEATURE                 Location/Qualifiers
misc_feature            1..543
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            1..543
                        note = GN281 lysin
source                  1..543
                        mol_type = other DNA
                        organism = synthetic construct
CDS                     28..519
SEQUENCE: 19
gtttaacttt aagaaggaga attcaccatg aaactcagcg aaaaacgagc actgttcacc  60
cagctgcttg cccagttaat tctttgggca ggaactcagg atcgagtgtc agtagccttg  120
gatcaagtga aaaggacaca ggctgaagct gatgccaatg ctaagtctgg agcaggcatt  180
aggaactctc tccatctact gggattagcc ggtgatctta tcctctacaa ggatggtaaa  240
tacatggata agagcgagga ttataagttc ctgggagatt actggaagag tctccatcct  300
ctttgtcggt ggggcggaga ttttaaaagc cgtcctgatg gtaatcattt ctccttggaa  360
cacgaaggag tgcaacgtaa aaaaacccgt aaacgtctga aaaaaatcgg taaagttctg  420
aaatggatcg gcggtggctc tggaggtggt gggtccggcg gtggctctcc accaacccgc  480
aaacgcctga aaaaaattgg caaagtgctg aaatggattt aataaaagct tggctgtttt  540
ggc                                                                543

SEQ ID NO: 20           moltype = AA  length = 164
FEATURE                 Location/Qualifiers
REGION                  1..164
                        note = Synthetic Construct
source                  1..164
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 20
MKLSEKRALF TQLLAQLILW AGTQDRVSVA LDQVKRTQAE ADANAKSGAG IRNSLHLLGL  60
AGDLILYKDG KYMDKSEDYK FLGDYWKSLH PLCRWGGDFK SRPDGNHFSL EHEGVQRKKT  120
RKRLKKIGKV LKWIGGGSGG GGSGGGSPPT RKRLKKIGKV LKWI                   164

SEQ ID NO: 21           moltype = DNA  length = 852
FEATURE                 Location/Qualifiers
misc_feature            1..852
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            1..852
                        note = GN316 lysin
source                  1..852
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 21
gaattcacca tgggatccca tcatcaccac catcatggtg ccattttaaa gattggcagc  60
aaaggtctgg aagttaagaa tcttcagacc agtctcaaca aaatcgggtt caatctggtt  120
gccgatggca tatttggtaa agcgactgac aacgccgtca gggcagttca ggcaggtgcc  180
ggactggtcg ttgatggtat tgctggcccc aagaccatgt atgcgattcg caacgcaggg  240
gagtctcatc aggatcatct gactgaggct gacttgattg acgctgctcg tgaattgtct  300
gttgaccttg ctagcatcaa ggcagtcaac caagtagaat cgcgcggtac tggcttcacc  360
aagtctggta agatcaagac attgtttgaa cgccacatca tgtacaaaaa gctgaatgcc  420
aagttcggtc aggcaaaagc caatgctctg gcccagcttt acccgacgtt ggttaacgcc  480
aaagccgggg gatacacagg tggggacgcg gagttggaac gactccatgg tgcaatagcg  540
atcgataaag attgcgccta cgagagcgct tcctacgggt tattccagat catggggttc  600
aactgcgtta tttgtggata tgacaatgcc gaggagatgt tcaacgactt tctcactggt  660
gaacgtgctc agctcatggc atttgtcaag ttcatcaagg ctgacgccaa tctgtggaaa  720
gcattgaagg acaagaattg ggctgagttt gctcggcgtt acaatggccc ggcgtatgca  780
cagaaccagt acgacaccaa gctggctgca gcatacaaat cattcagtta gtaaaagctt  840
ggctgttttg gc                                                      852

SEQ ID NO: 22           moltype = AA  length = 264
FEATURE                 Location/Qualifiers
REGION                  1..264
                        note = Description of Artificial Sequence: Synthetic
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                     polypeptide
REGION               1..264
                     note = MISC_FEATURE - GN316 lysin
source               1..264
                     mol_type = protein
                     organism = synthetic construct
SEQUENCE: 22
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFS                                         264

SEQ ID NO: 23        moltype = DNA  length = 879
FEATURE              Location/Qualifiers
misc_feature         1..879
                     note = Description of Artificial Sequence: Synthetic
                      polynucleotide
misc_feature         1..879
                     note = modified GN316 lysin
source               1..879
                     mol_type = other DNA
                     organism = synthetic construct
SEQUENCE: 23
gaattcacca tgggatccca tcatcaccac catcatggtg ccggatccca tcatcaccac  60
catcatggta ttttaaagat tggcagcaaa ggtctggaag ttaagaatct tcagaccagt  120
ctcaacaaaa tcgggttcaa tctggttgcc gatggcatat ttggtaaagc gactgacaac  180
gccgtcaggg cagttcaggc aggtgccgga ctggtcgttg atggtattgc tggccccaag  240
accatgtatg cgattcgcaa cgcaggggag tctcatcagg atcatctgac tgaggctgac  300
ttgattgacg ctgctcgtga attgtctgtt gaccttgcta gcatcaaggc agtcaaccaa  360
gtagaatcgc gcggtactgg cttcaccaag tctggtaaga tcaagacatt gtttgaacgc  420
cacatcatgt acaaaaagct gaatgccaag ttcggtcagg caaaagccaa tgctctggcc  480
cagctttacc cgacgttggt taacgccaaa gccgggggat acacaggtgg ggacgcggag  540
ttggaacgac tccatggtgc aatagcgatc gataaagatt gcgcctacga gagcgcttcc  600
tacgggttat tccagatcat ggggttcaac tgcgttattt gtggatatga caatgccgag  660
gagatgttca acgactttct cactggtgaa cgtgctcagc tcatggcatt tgtcaagttc  720
atcaaggctg acgccaatct gtggaaagca ttgaaggaca agaattgggc tgagtttgct  780
cggcgttaca atggcccggc gtatgcacag aaccagtacg acaccaagct ggctgcagca  840
tacaaatcat tcagttagta aaagcttggc tgttttggc                          879

SEQ ID NO: 24        moltype = AA  length = 273
FEATURE              Location/Qualifiers
REGION               1..273
                     note = Description of Artificial Sequence: Synthetic
                      polypeptide
REGION               1..273
                     note = MISC_FEATURE - modified GN316 lysin
source               1..273
                     mol_type = protein
                     organism = synthetic construct
SEQUENCE: 24
MGSHHHHHHG AILKIGSKGL EVKNLQTSLN KIGFNLVADG IFGKATDNAV RAVQAGAGLV  60
VDGIAGPKTM YAIRNAGESH QDHLTEADLI DAARELSVDL ASIKAVNQVE SRGTGFTKSG  120
KIKTLFERHI MYKKLNAKFG QAKANALAQL YPTLVNAKAG GYTGGDAELE RLHGAIAIDK  180
DCAYESASYG LFQIMGFNCV ICGYDNAEEM FNDFLTGERA QLMAFVKFIK ADANLWKALK  240
DKNWAEFARR YNGPAYAQNQ YDTKLAAAYK SFS                               273

SEQ ID NO: 25        moltype = DNA  length = 612
FEATURE              Location/Qualifiers
misc_feature         28..588
                     note = GN329
source               1..612
                     mol_type = other DNA
                     organism = Pseudomonas phage KPP10
CDS                  28..588
SEQUENCE: 25
gtttaacttt aagaaggaga attcaccatg atcaccgaca gagagtatca gcaagctgct  60
gagatgttgg gagtagatgt cccagcgatc aaggcagtga ccaaggtgga ggccccggta  120
gggggcttcc agcctacagg agagccaacg atcctctacg agcgtcacca gatgtaccga  180
cagctccagg ccaaagggct cccaacggaa ggtcatcccc cagacctggt aaataaggta  240
gctggtgggt atggaaaata cagcgagcaa cacgctaaac tggcccgtgc cgtaaagatc  300
gacagggaca gcgccctgga gtcctgctcc tgggggatgt tccagatcat gggctaccac  360
tggaagctga tggggtaccc tacccttcaa gctttcgtaa acgccatgta cgccagcgaa  420
ggagcccaga tggacgcctt ctgccggttc atcaaggcac aacccaccac gcatgctgcc  480
ttgaaagccc atgattgggc caagtttgcc agactgtaca acggtccagg ctacgccaag  540
aacaagtatg acgtgaaatt ggagaaagca tatgctgaag ctagtggctg ataaaagctt  600
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ggctgttttg gc                                                          612

SEQ ID NO: 26          moltype = AA  length = 187
FEATURE                Location/Qualifiers
source                 1..187
                       mol_type = protein
                       organism = Pseudomonas phage KPP10
SEQUENCE: 26
MITDREYQQA AEMLGVDVPA IKAVTKVEAP VGGFQPTGEP TILYERHQMY RQLQAKGLPT  60
EGHPPDLVNK VAGGYGKYSE QHAKLARAVK IDRDSALESC SWGMFQIMGY HWKLMGYPTL  120
QAFVNAMYAS EGAQMDAFCR FIKAQPTTHA ALKAHDWAKF ARLYNGPGYA KNKYDVKLEK  180
AYAEASG                                                            187

SEQ ID NO: 27          moltype = DNA  length = 609
FEATURE                Location/Qualifiers
misc_feature           28..585
                       note = GN333 lysin
source                 1..609
                       mol_type = other DNA
                       organism = Delftia sp.
CDS                    28..585
                       protein_id = 227
                       translation = MALTEQDFQSAADDLGVDVASVKAVTKVESRGSGFLLSGVPKILFE
                        RHWMFKLLKRKLGRDPEINDVCNPKAGGYLGGQAEHERLDKAVKMDRDCALQSASWGLF
                        QIMGFHWEALGYASVQAFVNAQYASEGSQLNTFVRFIKTNPAIHKALKSKDWAEFARRY
                        NGPDYKKNNYDVKLAEAYQSFK
SEQUENCE: 27
gtttaacttt aagaaggaga attcaccatg gctctaactg agcaagactt ccaatcggct  60
gccgatgatc tcggagtcga tgttgccagt gtaaaggccg tcactaaagt agagagtcgt  120
gggagcggct ttctactttc tggcgtccct aagattctat tcgaaaggca ctggatgttc  180
aagcttctca aaaggaagct aggtcgtgac cctgaaataa acgacgtttg caaccctaaa  240
gctggaggat acctcggcgg acaagcggag cacgaacgtc tagataaagc agtcaagatg  300
gatagagact gcgcacttca aagtgcctct tggggcctat tccagattat gggattccat  360
tgggaggcac taggttatgc gagtgttcag gcatttgtca atgcccagta cgctagcgag  420
ggatcgcaac taaacacttt tgtgcgcttc atcaagacca acccggcaat tcacaaagct  480
ttaaagtcta aggactgggc agaattcgca agaaggtata acgggccgga ttacaagaaa  540
aacaactacg atgttaagct agcagaagcc tatcaatcct tcaagtaata aaagcttggc  600
tgttttggc                                                          609

SEQ ID NO: 28          moltype = AA  length = 186
FEATURE                Location/Qualifiers
source                 1..186
                       mol_type = protein
                       organism = Delftia sp.
SEQUENCE: 28
MALTEQDFQS AADDLGVDVA SVKAVTKVES RGSGFLLSGV PKILFERHWM FKLLKRKLGR  60
DPEINDVCNP KAGGYLGGQA EHERLDKAVK MDRDCALQSA SWGLFQIMGF HWEALGYASV  120
QAFVNAQYAS EGSQLNTFVR FIKTNPAIHK ALKSKDWAEF ARRYNGPDYK KNNYDVKLAE  180
AYQSFK                                                             186

SEQ ID NO: 29          moltype = DNA  length = 984
FEATURE                Location/Qualifiers
misc_feature           1..984
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           28..957
                       note = GN349 lysin
source                 1..984
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..957
SEQUENCE: 29
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg  60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc  120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc  180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat  240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt  300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt  360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt  420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg  480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa  540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt  600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct  660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag  720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag  780
tacgacacca agctggctgc agcatacaaa tcattcagta ccgcgggcgg caccgcgggc  840
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ggcgcacgaa gatacagact ttcgcgacgc agaagtcgac gacttttttc aagaactgca  900
ttaagaatgc atcgaagaaa tagacttcga agaattatgc gtggcggcat taggttttag  960
taataaaagc ttggctgttt tggc                                        984

SEQ ID NO: 30          moltype = AA  length = 310
FEATURE                Location/Qualifiers
REGION                 1..310
                       note = Synthetic Construct
source                 1..310
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 30
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFSTAGGTA GGARRYRLSR RRSRRLFSRT ALRMHRRNRL  300
RRIMRGGIRF                                                        310

SEQ ID NO: 31          moltype = DNA  length = 984
FEATURE                Location/Qualifiers
misc_feature           1..984
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           28..957
                       note = GN351 lysin
source                 1..984
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..957
SEQUENCE: 31
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg  60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc  120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc  180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat  240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt  300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt  360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt  420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg  480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa  540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt  600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct  660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag  720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag  780
tacgacacca agctggctgc agcatacaaa tcattcagta ccgcgggcgg caccgcgggc  840
ggcgctcgtt cccgtagacg tatgtctaag cgttcttccc gccgttcgtt ccgcaagtat  900
gcgaagtcgc ataagaagaa ctttaaagcc cgctcaatgc gtggcggtat ccgtttatga  960
taataaaagc ttggctgttt tggc                                        984

SEQ ID NO: 32          moltype = AA  length = 310
FEATURE                Location/Qualifiers
REGION                 1..310
                       note = Synthetic Construct
source                 1..310
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 32
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFSTAGGTA GGARSRRRMS KRSSRRSFRK YAKSHKKNFK  300
ARSMRGGIRL                                                        310

SEQ ID NO: 33          moltype = DNA  length = 981
FEATURE                Location/Qualifiers
misc_feature           1..981
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           1..981
                       note = GN352 lysin28
source                 1..981
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..954
SEQUENCE: 33
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gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg  60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc  120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc  180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat  240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt  300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt  360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt  420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg  480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa  540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt  600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct  660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag  720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag  780
tacgacacca agctggctgc agcatacaaa tcattcagta ccgcgggcgg caccgcgggc  840
ggcaaacgta gaaaaatgac aagaaaaggt tctaagcgtc tttttactgc aactgctgat  900
aaaactaaat ctatcaatac tgccccgccg ccaatgcgtg gcggtatccg gttgtagtaa  960
taaaagcttg gctgttttgg c                                            981

SEQ ID NO: 34          moltype = AA  length = 309
FEATURE                Location/Qualifiers
REGION                 1..309
                       note = Synthetic Construct
source                 1..309
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 34
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFSTAGGTA GGKRRKMTRK GSKRLFTATA DKTKSINTAP  300
PPMRGGIRL                                                          309

SEQ ID NO: 35          moltype = DNA  length = 978
FEATURE                Location/Qualifiers
misc_feature           1..978
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           28..951
                       note = GN353 lysin
source                 1..978
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..951
SEQUENCE: 35
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg  60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc  120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc  180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat  240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt  300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt  360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt  420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg  480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa  540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt  600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct  660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag  720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag  780
tacgacacca agctggctgc agcatacaaa tcattcagta ccgcgggcgg caccgcgggc  840
ggcagaaagc gaatgtctaa gcgtgttgac aagaaggtgt tccgtcgtac tgccgcatct  900
gccaagaaga ttaacattga ccccaagatt taccgtggag gtattcgcct atgataataa  960
aagcttggct gttttggc                                                978

SEQ ID NO: 36          moltype = AA  length = 308
FEATURE                Location/Qualifiers
REGION                 1..308
                       note = Synthetic Construct
source                 1..308
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 36
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFSTAGGTA GGRKRMSKRV DKKVFRRTAA SAKKINIDPK  300
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IYRGGIRL 308

SEQ ID NO: 37 moltype = DNA length = 903
FEATURE Location/Qualifiers
misc_feature 1..903
note = Description of Artificial Sequence: Synthetic polynucleotide
misc_feature 28..879
misc_feature 28..879
note = GN357 lysin
source 1..903
mol_type = other DNA
organism = synthetic construct
CDS 28..879
SEQUENCE: 37
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg 60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc 120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc 180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat 240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt 300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt 360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt 420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg 480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa 540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt 600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct 660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag 720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag 780
tacgacacca agctggctgc agcatacaaa tcattcagta ccgcgggcgg caccgcgggc 840
ggccgccgcc tgattcgcct gtggctgcgc ctgctgcgct aataaaagct tggctgtttt 900
ggc 903

SEQ ID NO: 38 moltype = AA length = 284
FEATURE Location/Qualifiers
REGION 1..284
note = Synthetic Construct
source 1..284
mol_type = protein
organism = synthetic construct
SEQUENCE: 38
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT 60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH 120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY 180
GLFQIMGFNC VICGYDNAEE MFNDPLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR 240
RYNGPAYAQN QYDTKLAAAY KSFSTAGGTA GGRRLIRLWL RLLR 284

SEQ ID NO: 39 moltype = DNA length = 912
FEATURE Location/Qualifiers
misc_feature 1..912
note = Description of Artificial Sequence: Synthetic polynucleotide
misc_feature 28..888
note = GN359 lysin
source 1..912
mol_type = other DNA
organism = synthetic construct
CDS 28..888
SEQUENCE: 39
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg 60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc 120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc 180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat 240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt 300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt 360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt 420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg 480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa 540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt 600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct 660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag 720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag 780
tacgacacca agctggctgc agcatacaaa tcattcagta ccgcgggcgg caccgcgggc 840
ggcacccgca aacgcctgaa aaaaattggc aaagtgctga aatggattta ataaaagctt 900
ggctgttttg gc 912

SEQ ID NO: 40 moltype = AA length = 287

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FEATURE                 Location/Qualifiers
REGION                  1..287
                        note = Synthetic Construct
source                  1..287
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 40
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFSTAGGTA GGTRKRLKKI GKVLKWI                287

SEQ ID NO: 41           moltype = DNA  length = 897
FEATURE                 Location/Qualifiers
misc_feature            1..897
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            28..873
                        note = GN369 lysin
source                  1..897
                        mol_type = other DNA
                        organism = synthetic construct
CDS                     28..873
SEQUENCE: 41
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg  60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc  120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc  180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat  240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt  300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt  360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt  420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg  480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa  540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt  600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct  660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag  720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag  780
tacgacacca agctggctgc agcatacaaa tcattcagtc gtaaaaaaac ccgtaaacgt  840
ctgaaaaaaa tcggtaaagt tctgaaatgg atctagtaaa agcttggctg ttttggc     897

SEQ ID NO: 42           moltype = AA  length = 282
FEATURE                 Location/Qualifiers
REGION                  1..282
                        note = Synthetic Construct
source                  1..282
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 42
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFSRKKTRK RLKKIGKVLK WI                     282

SEQ ID NO: 43           moltype = DNA  length = 558
FEATURE                 Location/Qualifiers
misc_feature            1..558
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            28..534
                        note = GN370 lysin
source                  1..558
                        mol_type = other DNA
                        organism = synthetic construct
CDS                     28..534
SEQUENCE: 43
gtttaacttt aagaaggaga attcaccatg atcgaccgtt tcattcgtct gaatccgacc  60
catggtccgc gtcgtccgcg tcgtccgggt cgtcgtgctc cggttcgtac atcccaacga  120
ggcatcgacc tcatcaaatc cttcgagggc ctgcgcctgt ccgcttacca ggactcggtg  180
ggtgtctgga ccataggtta cggcaccact cggggcgtca cccgctacat gacgatcacc  240
gtcgagcagg ccgagcggat gctgtcgaac gacattcagc gcttcgagcc agagctagac  300
aggctggcga aggtgccact gaaccagaac cagtgggatg ccctgatgag cttcgtgtac  360
aacctgggcg cggccaatct ggcgtcgtcc acgctgctcg acctgctgaa caagggtgac  420
taccagggag cagcggacca gttcccgcat tgggtgaatg cgggcggtaa gcgcttggat  480
ggtctggtta agcgtcgagc agccgagcgt gcgctgttcc tggagccact atcgtgataa  540
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aagcttggct gttttggc                                                  558

SEQ ID NO: 44          moltype = AA  length = 169
FEATURE                Location/Qualifiers
REGION                 1..169
                       note = Synthetic Construct
source                 1..169
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 44
MIDRFIRLNP THGPRRPRRP GRRAPVRTSQ RGIDLIKSFE GLRLSAYQDS VGVWTIGYGT  60
TRGVTRYMTI TVEQAERMLS NDIQRFEPEL DRLAKVPLNQ NQWDALMSFV YNLGAANLAS  120
STLLDLLNKG DYQGAADQFP HWVNAGGKRL DGLVKRRAAE RALFLEPLS              169

SEQ ID NO: 45          moltype = DNA  length = 516
FEATURE                Location/Qualifiers
misc_feature           1..516
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           28..492
                       note = GN371lysin
source                 1..516
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..492
SEQUENCE: 45
gtttaacttt aagaaggaga attcaccatg atcgaccgtt tcattcgtct gaatccgacc  60
catcgtacat cccaacgagg catcgacctc atcaaatcct tcgagggcct gcgcctgtcc  120
gcttaccagg actcggtggg tgtctggacc ataggttacg gcaccactcg gggcgtcacc  180
cgctacatga cgatcaccgt cgagcaggcc gagcggatgc tgtcgaacga cattcagcgc  240
ttcgagccag agctagacag gctggcgaag gtgccactga accagaacca gtgggatgcc  300
ctgatgagct tcgtgtacaa cctgggcgcg gccaatctgg cgtcgtccac gctgctcgac  360
ctgctgaaca agggtgacta ccagggagca gcggaccagt tcccgcattg ggtgaatgcg  420
ggcggtaagc gcttggatgg tctggttaag cgtcgagcag ccgagcgtgc gctgttcctg  480
gagccactat cgtgataaaa gcttggctgt tttggc                            516

SEQ ID NO: 46          moltype = AA  length = 155
FEATURE                Location/Qualifiers
REGION                 1..155
                       note = Synthetic Construct
source                 1..155
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 46
MIDRFIRLNP THRTSQRGID LIKSFEGLRL SAYQDSVGVW TIGYGTTRGV TRYMTITVEQ  60
AERMLSNDIQ RFEPELDRLA KVPLNQNQWD ALMSFVYNLG AANLASSTLL DLLNKGDYQG  120
AADQFPHWVN AGGKRLDGLV KRRAAERALF LEPLS                             155

SEQ ID NO: 47          moltype = DNA  length = 846
FEATURE                Location/Qualifiers
misc_feature           1..846
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           28..819
                       note = GN394 lysin
source                 1..846
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..819
SEQUENCE: 47
gtttaacttt aagaaggaga attcaccatg gccatttttaa agattggcag caaaggtctg  60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc  120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc  180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat  240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt  300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt  360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt  420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg  480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa  540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt  600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct  660
cagctcatgg catttgtcga cttcatcaag gctgacgcca atctgtggaa agcattgaag  720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag  780
tacgacacca agctggctgc agcatacaaa tcattcagtt agtaataaaa gcttggctgt  840
tttggc                                                             846
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SEQ ID NO: 48 moltype = AA length = 264
FEATURE Location/Qualifiers
REGION 1..264
note = Synthetic Construct
source 1..264
mol_type = protein
organism = synthetic construct
SEQUENCE: 48
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT 60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH 120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY 180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVDFI KADANLWKAL KDKNWAEFAR 240
RYNGPAYAQN QYDTKLAAAY KSFS 264

SEQ ID NO: 49 moltype = DNA length = 846
FEATURE Location/Qualifiers
misc_feature 1..846
note = Description of Artificial Sequence: Synthetic polynucleotide
misc_feature 28..819
note = GN396 lysin
source 1..846
mol_type = other DNA
organism = synthetic construct
CDS 28..819
SEQUENCE: 49
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg 60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc 120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc 180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat 240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt 300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt 360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt 420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg 480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa 540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt 600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct 660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggga cgcattgaag 720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag 780
tacgacacca agctggctgc agcatacaaa tcattcagtt agtaataaaa gcttggctgt 840
tttggc 846

SEQ ID NO: 50 moltype = AA length = 264
FEATURE Location/Qualifiers
REGION 1..264
note = Synthetic Construct
source 1..264
mol_type = protein
organism = synthetic construct
SEQUENCE: 50
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT 60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH 120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY 180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWDAL KDKNWAEFAR 240
RYNGPAYAQN QYDTKLAAAY KSFS 264

SEQ ID NO: 51 moltype = DNA length = 846
FEATURE Location/Qualifiers
misc_feature 1..846
note = Description of Artificial Sequence: Synthetic polynucleotide
misc_feature 28..819
note = GN408 lysin
source 1..846
mol_type = other DNA
organism = synthetic construct
CDS 28..819
SEQUENCE: 51
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg 60
gaagttaaga atcttcagac cagtctcaac aaaatcgggt tcaatctggt tgccgatggc 120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc 180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat 240
caggatcatc tgactgaggc tgacttgatt gacgctgctc atgaattgtc tgttgacctt 300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt 360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt 420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg 480

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ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa  540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt  600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct  660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag  720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag  780
tacgacacca agctggctgc agcatacaaa tcattcagtt agtaataaaa gcttggctgt  840
tttggc                                                            846

SEQ ID NO: 52          moltype = AA  length = 264
FEATURE                Location/Qualifiers
REGION                 1..264
                       note = Synthetic Construct
source                 1..264
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 52
MAILKIGSKG LEVKNLQTSL NKIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAAHELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFS                                        264

SEQ ID NO: 53          moltype = DNA  length = 846
FEATURE                Location/Qualifiers
misc_feature           1..846
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           28..819
                       note = GN418 lysin
source                 1..846
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    28..819
SEQUENCE: 53
gtttaacttt aagaaggaga attcaccatg gccattttaa agattggcag caaaggtctg  60
gaagttaaga atcttcagac cagtctcaac gacatcgggt tcaatctggt tgccgatggc  120
atatttggta aagcgactga caacgccgtc agggcagttc aggcaggtgc cggactggtc  180
gttgatggta ttgctggccc caagaccatg tatgcgattc gcaacgcagg ggagtctcat  240
caggatcatc tgactgaggc tgacttgatt gacgctgctc gtgaattgtc tgttgacctt  300
gctagcatca aggcagtcaa ccaagtagaa tcgcgcggta ctggcttcac caagtctggt  360
aagatcaaga cattgtttga acgccacatc atgtacaaaa agctgaatgc caagttcggt  420
caggcaaaag ccaatgctct ggcccagctt tacccgacgt tggttaacgc caaagccggg  480
ggatacacag gtggggacgc ggagttggaa cgactccatg gtgcaatagc gatcgataaa  540
gattgcgcct acgagagcgc ttcctacggg ttattccaga tcatggggtt caactgcgtt  600
atttgtggat atgacaatgc cgaggagatg ttcaacgact ttctcactgg tgaacgtgct  660
cagctcatgg catttgtcaa gttcatcaag gctgacgcca atctgtggaa agcattgaag  720
gacaagaatt gggctgagtt tgctcggcgt tacaatggcc cggcgtatgc acagaaccag  780
tacgacacca agctggctgc agcatacaaa tcattcagtt agtaataaaa gcttggctgt  840
tttggc                                                            846

SEQ ID NO: 54          moltype = AA  length = 264
FEATURE                Location/Qualifiers
REGION                 1..264
                       note = Synthetic Construct
source                 1..264
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 54
MAILKIGSKG LEVKNLQTSL NDIGFNLVAD GIFGKATDNA VRAVQAGAGL VVDGIAGPKT  60
MYAIRNAGES HQDHLTEADL IDAARELSVD LASIKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLNAKF GQAKANALAQ LYPTLVNAKA GGYTGGDAEL ERLHGAIAID KDCAYESASY  180
GLFQIMGFNC VICGYDNAEE MFNDFLTGER AQLMAFVKFI KADANLWKAL KDKNWAEFAR  240
RYNGPAYAQN QYDTKLAAAY KSFS                                        264

SEQ ID NO: 55          moltype = DNA  length = 858
FEATURE                Location/Qualifiers
misc_feature           28..834
                       note = GN424 lysin
source                 1..858
                       mol_type = other DNA
                       organism = Burkholderia pseudomultivorans
CDS                    28..834
SEQUENCE: 55
gtttaacttt aagaaggaga attcaccatg aataccttc gtttcaacag tcgcggcgcc  60
gaagtcggcg tgctgcagca acggctcgtg cgcgccggct atccgatcga cgtcacgcat  120
ctctatgacg aagcgacgga gcaggccgtg aaggcgttgc aggcagcggc cggaatcgtc  180
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gtcgacggaa tcgccggccc gaacacctat gccgtgttgt cggccggcca gcgcgaccgc  240
aagcacttga ccgaagcgga catcgcccgc gccgcagaca agctcggtgt ctcgccggca  300
tgcgtccgcg ccgtcaacga agtcgagtca cgcggctcgg gctttctggc ggacggccgg  360
cccgtgattc tcttcgagcg gcacgtgatg tacaaccgcc tcgtcgcggc gaagcgtgcc  420
gtcgacgcag cgagcgcagc gcagcgcttt ccgaacgtcg tcagcgcgaa gccgggcgga  480
taccagggcg gcgcagccga atatgtgcga ctcgacaccg ccgcgcgcat cgatgcggca  540
atcgcgtacg aatcggcgag ctggggcgca tttcaggtga tgggctatca ctgggaacgc  600
ctgggctact cgagcatcga cgagttcgtt gcccggatgg agacgagcga aggcgaacag  660
ctcgacgcgt ttgtgcggtt cgtcgccgcc gactcgtcgc tgcgcacggc gctgaaaaac  720
cggaagtggg ctgcattcgc gaagggctac aacggcccgg actatgcgcg caacctctac  780
gacgcgaagc tcgcccaggc gtacgaacgg tatgccggca cgaaggcggc cgcgtgataa  840
aagcttggct gttttggc                                                858

SEQ ID NO: 56          moltype = AA  length = 269
FEATURE                Location/Qualifiers
source                 1..269
                       mol_type = protein
                       organism = Burkholderia pseudomultivorans
SEQUENCE: 56
MNTLRFNSRG AEVGVLQQRL VRAGYPIDVT HLYDEATEQA VKALQAAAGI VVDGIAGPNT  60
YAVLSAGQRD RKHLTEADIA RAADKLGVSP ACVRAVNEVE SRGSGFLADG RPVILFERHV  120
MYNRLVAAKR AVDAASAAQR FPNVVSAKPG GYQGGAAEYV RLDTAARIDA AIAYESASWG  180
AFQVMGYHWE RLGYSSIDEF VARMETSEGE QLDAFVRFVA ADSSLRTALK NRKWAAPAKG  240
YNGPDYARNL YDAKLAQAYE RYAGTKAAA                                    269

SEQ ID NO: 57          moltype = DNA  length = 864
FEATURE                Location/Qualifiers
misc_feature           28..840
                       note = GN425 lysin
source                 1..864
                       mol_type = other DNA
                       organism = Pseudomonas flexibilis
CDS                    28..840
SEQUENCE: 57
gtttaacttt aagaaggaga attcaccatg accctgcgcc tcgatgacgt cggcctcgac  60
gtgctccatc tgcagaagcg cctcaacgag ctgggcgcga atccgcggct gctgcccgat  120
ggccagttcg gcgaggtcac cgagcgcgcc gtgcgggcct tccagcaacg tgccggcctg  180
gtggtcgatg gcgtggccgg acccaagacg atggccgccc tgtccggcca ttccaccagc  240
cgcctgctcg gccagcgcga cctgcaacgc gccgccgacc gcttgggcgt gccgctggcc  300
agcgtcatgg ccctcaatgc cgtggaaagt cgcggcgagg gcttcgccgc caatggccgg  360
ccggtgatcc tgttcgagcg gcacgtgatg cacgaacgct tgcaggtcaa cggcctgagc  420
gaagccgagg cggacgccct ggcggcacgc caccccggcc tggtgagtcg ccggccaggc  480
ggctacgtcg gcgacaccgc cgagcatcag cgcctggcca atgcccgcct gttgcatgac  540
accgctgccc tggaatccgc cagttgggga ctgttccagg tgatgggcta ccactggcag  600
gccctgggct acgacaccac ccaggacttc accgagcgca tggcccgcca cgaagccgag  660
cacctggaag cgttcgtgcg cttcatcgaa gccgatccgg cactgcacaa ggcactcaag  720
ggccgtaagt gggccgagtt cgcccgccgc tacaacggcc cggcctacgc ccgcaatttg  780
tacgacgtga agctggctcg ggcattcgag caattcagcg acgcactgca ggccgccgca  840
tgataaaagc ttggctgttt tggc                                          864

SEQ ID NO: 58          moltype = AA  length = 271
FEATURE                Location/Qualifiers
source                 1..271
                       mol_type = protein
                       organism = Pseudomonas flexibilis
SEQUENCE: 58
MTLRLDDVGL DVLHLQKRLN ELGANPRLLP DGQFGEVTER AVRAFQQRAG LVVDGVAGPK  60
TMAALSGHST SRLLGQRDLQ RAADRLGVPL ASVMALNAVE SRGEGFAANG RPVILFERHV  120
MHERLQVNGL SEAEADALAA RHPGLVSRRP GGYVGDTAEH QRLANARLLH DTAALESASW  180
GLFQVMGYHW QALGYDTTQD FTERMARHEA EHLEAFVRFI EADPALHKAL KGRKWAEFAR  240
RYNGPAYARN LYDVKLARAF EQFSDALQAA A                                 271

SEQ ID NO: 59          moltype = DNA  length = 843
FEATURE                Location/Qualifiers
misc_feature           28..819
                       note = GN428 lysin
source                 1..843
                       mol_type = other DNA
                       organism = Escherichia virus
CDS                    28..819
SEQUENCE: 59
gtttaacttt aagaaggaga attcaccatg gccattctaa aacttggcaa ccgaggttct  60
gaagtcaaag cacttcaaca aagcctcaac aaaatcggtt tctctcttac agccgatggc  120
atatttggta aggcaacaga gaatgccgtc aaatccgttc aggcaggtgc tggattggtt  180
attgatggta ttgctgggcc aaagaccttc tatgctatcc gcaacgctgg agacgctcac  240
caggaacatc tgaccgaagc ggacttggtt gacgcagcac gtgaacttgg tgttgagctg  300
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gccagtatga aagcggtgaa ccaggtagaa tcccgtggta cgggttttac caaaactggc  360
aagatcaaaa ctctgtttga gcgccacatc atgtacaaaa aggtgacggc caaattcggg  420
caagcaagag ccaatgctct gtaccaactc tacccaacat tggttaaccc caattctggc  480
gggtatatcg gcggagacgc ggagttggaa cgccttcagg gtgcaatcgc ccttgacgag  540
gactgcgctt acgagagtgc ttcctacggc ctattccaga tcatggggtt caactgccaa  600
atctgtggct attcaaatgc caaagagatg ttcactgatt tcctgactgg tgaacgcgct  660
catcttctgg catttgtcaa gttcatcaag gctgatgcca atatgtggaa agccctgaag  720
aacaagaatt gggccgagtt tgctcgtcgg tacaatggtc cggcatatgc gaaaaaccag  780
tatgatacta aactggcggc agcatacaag agtttctgtt aataaaagct tggctgtttt  840
ggc                                                               843

SEQ ID NO: 60          moltype = AA  length = 264
FEATURE                Location/Qualifiers
source                 1..264
                       mol_type = protein
                       organism = Escherichia virus
SEQUENCE: 60
MAILKLGNRG SEVKALQQSL NKIGFSLTAD GIFGKATENA VKSVQAGAGL VIDGIAGPKT  60
FYAIRNAGDA HQEHLTEADL VDAARELGVE LASMKAVNQV ESRGTGFTKT GKIKTLFERH  120
IMYKKVTAKF GQARANALYQ LYPTLVNPNS GGYIGGDAEL ERLQGAIALD EDCAYESASY  180
GLFQIMGFNC QICGYSNAKE MFTDFLTGER AHLLAFVKFI KADANMWKAL KNKNWAEFAR  240
RYNGPAYAKN QYDTKLAAAY KSFC                                        264

SEQ ID NO: 61          moltype = DNA  length = 660
FEATURE                Location/Qualifiers
misc_feature           1..660
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           13..639
                       note = GN93 lysin
source                 1..660
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    13..639
SEQUENCE: 61
ggagaattca ccatgaaatt ctttaagttc tttaagtttt ttaaagccgg cgcaggagct  60
ggtgcaggag ctggtgcagg agctggtgca ggagctagca ataacgaact tccttgggta  120
gccgaagccc gaaagtatat cggccttcgc gaagacactt cgaagacttc gcataacccg  180
aaacttcttg ccatgcttga ccgcatgggc gaattttcca acgaatcccg cgcttggtgg  240
cacgacgacg aaacgccttg gtgcggactg ttcgtcggct attgcttggg cgttgccggg  300
cgctacgtcg tccgcgaatg gtacagggcg cgggcatggg aagccccgca gcttacgaag  360
cttgaccggc ccgcatacgg cgcgcttgtg accttcacgc gaagcggcgg cggccacgtc  420
ggttttattg tgggcaagga tgcgcgcgga aatcttatgg ttcttggcgg taatcagtcg  480
aacgccgtaa gtatcgcacc gttcgcagta tcccgcgtaa ccggctattt ctggccgtcg  540
ttctggcgaa acaagaccgc agttaaaagc gttccgtttg aagaacgtta ttcgctgccg  600
ctgttgaagt cgaacggcga actttcgacg aatgaagcgt aataagcttg gctgttttgg  660

SEQ ID NO: 62          moltype = AA  length = 209
FEATURE                Location/Qualifiers
REGION                 1..209
                       note = Synthetic Construct
source                 1..209
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 62
MKFFKFFKFF KAGAGAGAGA GAGAGAGASN NELPWVAEAR KYIGLREDTS KTSHNPKLLA  60
MLDRMGEFSN ESRAWWHDDE TPWCGLFVGY CLGVAGRYVV REWYRARAWE APQLTKLDRP  120
AYGALVTFTR SGGGHVGFIV GKDARGNLMV LGGNQSNAVS IAPFAVSRVT GYFWPSFWRN  180
KTAVKSVPFE ERYSLPLLKS NGELSTNEA                                   209

SEQ ID NO: 63          moltype = DNA  length = 843
FEATURE                Location/Qualifiers
misc_feature           28..819
                       note = GN431 lysin
source                 1..843
                       mol_type = other DNA
                       organism = Dickeya phage phiD3
CDS                    28..819
SEQUENCE: 63
gtttaacttt aagaaggaga attcaccatg gccattctaa aacttggcaa ccgtggcact  60
gaagtgaagg cacttcagga tagcctcaac aaaatcggct tcaccctcgt cgctgacggc  120
atctttggta aggcaacaga gaacgctgtc aagaccgttc aggcgggtgc ggggcttgtc  180
attgatggta tcgtgggtcc aaagacctcc tatgctattc gcaacgccgg ggaagcgcat  240
caggatcacc tgactgaggc tgaccttatc gaggcggcca atcagctggg cgtcgacctc  300
gcttctgtga aggcagtcaa ccaggttgaa tcccgtggca caggcttcac caagtcaggc  360
aagatcaaga cattgttcga gcgtcacatc atgtataaga aactgatggc aaagttcgga  420
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caggctcgag cgaatgccat gggtcagatg tatccgactc tggtcagccc ggttgcaggc  480
gggtacacgg gaggtgacgc agaattggat cgactccacg cagcgatcaa catcgacgag  540
gattgtgcgt acgagagcgc ttcatacggc ctcttccaga tcatgggctt caactgccag  600
gtctgcgggt atgccaacgc caaggagatg ttcaatgact tcctgacggg agaacgtgct  660
cacctgatgg cattcgtgaa gttcatcaag gctgatgcca agctctggca ggctctgaag  720
gacaagaatt gggctgagtt cgcgcggcgc tataatggtc cggcgtatac caagaaccag  780
tacgacacga agctcgcagc agcatacaac agcttcaatt aataaaagct tggctgtttt  840
ggc                                                                843

SEQ ID NO: 64          moltype = AA  length = 264
FEATURE                Location/Qualifiers
source                 1..264
                       mol_type = protein
                       organism = Dickeya phage phiD3
SEQUENCE: 64
MAILKLGNRG TEVKALQDSL NKIGFTLVAD GIFGKATENA VKTVQAGAGL VIDGIVGPKT  60
SYAIRNAGEA HQDHLTEADL IEAANQLGVD LASVKAVNQV ESRGTGFTKS GKIKTLFERH  120
IMYKKLMAKF GQARANAMGQ MYPTLVSPVA GGYTGGDAEL DRLHAAINID EDCAYESASY  180
GLFQIMGFNC QVCGYANAKE MFNDFLTGER AHLMAFVKFI KADAKLWQAL KDKNWAEFAR  240
RYNGPAYTKN QYDTKLAAAY NSFN                                         264

SEQ ID NO: 65          moltype = DNA  length = 510
FEATURE                Location/Qualifiers
misc_feature           1..510
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           10..510
                       note = GN486 lysin
source                 1..510
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    10..510
SEQUENCE: 65
gaattcacca tgggatccca tcatcaccac catcatggtg gtccgcgtcg tccgcgtcgt  60
ccgggtcgtc gtgctccggt tcgtacctct cagcgtggta tcgacctgat caaatctttc  120
gaaggtctgc gtctgtctgc ttaccaggac tctgttggtg tttggaccat cggttacggt  180
accacccgtg gtgttacccg ttacatgacc atcaccgttg aacaggctga acgtatgctg  240
tctaacgaca tccagcgttt cgaaccggaa ctggaccgtc tggctaaagt tccgctgaac  300
cagaaccagt gggacgctct gatgtctttc gtttacaacc tgggtgctgc taacctggct  360
tcttctaccc tgctgaaact gctgaacaaa ggtgactacc agggtgctgc tgaccagttc  420
ccgcgttggg ttaacgctgg tggtaaacgt ctggacggtc tggttaaacg tcgtgctgct  480
gaacgtgctc tgttcctgga accgctgtct                                   510

SEQ ID NO: 66          moltype = AA  length = 167
FEATURE                Location/Qualifiers
REGION                 1..167
                       note = Synthetic Construct
source                 1..167
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 66
MGSHHHHHHG GPRRPRRPGR RAPVRTSQRG IDLIKSFEGL RLSAYQDSVG VWTIGYGTTR  60
GVTRYMTITV EQAERMLSND IQRFEPELDR LAKVPLNQNQ WDALMSFVYN LGAANLASST  120
LLKLLNKGDY QGAADQFPRW VNAGGKRLDG LVKRRAAERA LFLEPLS                167

SEQ ID NO: 67          moltype = DNA  length = 219
FEATURE                Location/Qualifiers
misc_feature           1..219
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           1..216
                       note = GN485 lysin
source                 1..219
                       mol_type = other DNA
                       organism = synthetic construct
CDS                    1..216
SEQUENCE: 67
atgccgggtc tgtctggttt catccgtaac gctgacaccc cggttacctc tctgggttct  60
gctggtcacg ttcacgttcc ggaaggtccg ctgatccgta tcaacccgga ctgcctgctg  120
ggtaccccgt tcaaattctt caagttcttc aagttcttca agttctttaa gttctttaag  180
tttttcaagt tcttcaagaa cgaatgcgtt ctgctgtaa                          219

SEQ ID NO: 68          moltype = AA  length = 72
FEATURE                Location/Qualifiers
REGION                 1..72
                       note = Synthetic Construct
```

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```
source                  1..72
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 68
MPGLSGFIRN ADTPVTSLGS AGHVHVPEGP LIRINPDCLL GTPFKFFKFF KFFKFFKFFK  60
FFKFFKNECV LL                                                      72

SEQ ID NO: 69           moltype = DNA  length = 132
FEATURE                 Location/Qualifiers
source                  1..132
                        mol_type = other DNA
                        organism = Chlamydia phage 2
SEQUENCE: 69
atgaggttaa aaatggcacg aagaagatac agacttccgc gacgtagaag tcgaagactt  60
ttttcaagaa ctgcattgag gatgcatcca agaaataggc ttcgaagaat tatgcgtggc  120
ggcattaggt tc                                                      132

SEQ ID NO: 70           moltype = AA  length = 44
FEATURE                 Location/Qualifiers
source                  1..44
                        mol_type = protein
                        organism = Chlamydia phage 2
SEQUENCE: 70
MRLKMARRRY RLPRRRSRRL FSRTALRMHP RNRLRRIMRG GIRF                   44

SEQ ID NO: 71           moltype = DNA  length = 24
FEATURE                 Location/Qualifiers
misc_feature            1..24
                        note = Description of Artificial Sequence: Synthetic
                         oligonucleotide
misc_feature            1..24
                        note = linker
source                  1..24
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 71
accgcgggcg gcaccgcggg cggc                                         24

SEQ ID NO: 72           moltype = AA  length = 8
FEATURE                 Location/Qualifiers
REGION                  1..8
                        note = Description of Artificial Sequence: Synthetic peptide
REGION                  1..8
                        note = MISC_FEATURE - linker
source                  1..8
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 72
TAGGTAGG                                                           8

SEQ ID NO: 73           moltype = DNA  length = 435
FEATURE                 Location/Qualifiers
misc_feature            1..435
                        note = GN4
source                  1..435
                        mol_type = other DNA
                        organism = Pseudomonas phage PAJU2
SEQUENCE: 73
atgcgtacat cccaacgagg catcgacctc atcaaatcct tcgagggcct gcgcctgtcc  60
gcttaccagg actcggtggg tgtctggacc ataggttacg gcaccactcg gggcgtcacc  120
cgctacatga cgatcaccgt cgagcaggcc gagcggatgc tgtcgaacga cattcagcgc  180
ttcgagccag agctagacag gctggcgaag gtgccactga accagaacca gtgggatgcc  240
ctgatgagct tcgtgtacaa cctgggcgcg gccaatctgg cgtcgtccac gctgctcaag  300
ctgctgaaca agggtgacta ccagggagca gcggaccagt tcccgcgctg ggtgaatgcg  360
ggcggtaagc gcttggatgg tctggttaag cgtcgagcag ccgagcgtgc gctgttcctg  420
gagccactat cgtga                                                   435

SEQ ID NO: 74           moltype = AA  length = 144
FEATURE                 Location/Qualifiers
REGION                  1..144
                        note = MISC_FEATURE - GN4
source                  1..144
                        mol_type = protein
                        organism = Pseudomonas phage PAJU2
SEQUENCE: 74
MRTSQRGIDL IKSFEGLRLS AYQDSVGVWT IGYGTTRGVT RYMTITVEQA ERMLSNDIQR  60
```

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FEPELDRLAK VPLNQNQWDA LMSFVYNLGA ANLASSTLLK LLNKGDYQGA ADQFPRWVNA  120
GGKRLDGLVK RRAAERALFL EPLS                                        144

SEQ ID NO: 75          moltype = DNA  length = 63
FEATURE                Location/Qualifiers
source                 1..63
                       mol_type = other DNA
                       organism = Penaeus chinensis
SEQUENCE: 75
atgagcttta acgtgacccc gaaatttaaa cgctggcagc tgtattttcg cggccgcatg  60
tgg                                                               63

SEQ ID NO: 76          moltype = AA  length = 21
FEATURE                Location/Qualifiers
source                 1..21
                       mol_type = protein
                       organism = Penaeus chinensis
SEQUENCE: 76
MSFNVTPKFK RWQLYFRGRM W                                           21

SEQ ID NO: 77          moltype = DNA  length = 438
FEATURE                Location/Qualifiers
misc_feature           1..438
                       note = Description of Artificial Sequence: Synthetic
                        polynucleotide
misc_feature           1..438
                       note = Modified GN4 lysin, GN146
source                 1..438
                       mol_type = other DNA
                       organism = synthetic construct
SEQUENCE: 77
atgcgtacat cccaacgagg catcgacctc atcaaatcct tcgagggcct gcgcctgtcc  60
gcttaccagg actcggtggg tgtctggacc ataggttacg gcaccactcg gggcgtcacc  120
cgctacatga cgatcaccgt cgagcaggcc gagcggatgc tgtcgaacga cattcagcgc  180
ttcgagccag agctagacag gctggcgaag gtgccactga accagaacca gtgggatgcc  240
ctgatgagct tcgtgtacaa cctgggcgcg gccaatctgg cgtcgtccac gctgctcgac  300
ctgctgaaca agggtgacta ccagggagca gcggaccagt tcccgcattg ggtgaatgcg  360
ggcggtaagc gcttggatgg tctggttaag cgtcgagcag ccgagcgtgc gctgttcctg  420
gagccactat cgtgataa                                               438

SEQ ID NO: 78          moltype = AA  length = 144
FEATURE                Location/Qualifiers
REGION                 1..144
                       note = Description of Artificial Sequence: Synthetic
                        polypeptide
REGION                 1..144
                       note = MISC_FEATURE - Modified GN4 lysin, GN146
source                 1..144
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 78
MRTSQRGIDL IKSFEGLRLS AYQDSVGVWT IGYGTTRGVT RYMTITVEQA ERMLSNDIQR  60
FEPELDRLAK VPLNQNQWDA LMSFVYNLGA ANLASSTLLD LLNKGDYQGA ADQFPHWVNA  120
GGKRLDGLVK RRAAERALFL EPLS                                        144

SEQ ID NO: 79          moltype = DNA  length = 57
FEATURE                Location/Qualifiers
source                 1..57
                       mol_type = other DNA
                       organism = Pelophylax esculentus
SEQUENCE: 79
atttttagca aactggcggg caaaaaaatt aaaaacctgc tgattagcgg cctgaaa     57

SEQ ID NO: 80          moltype = AA  length = 19
FEATURE                Location/Qualifiers
source                 1..19
                       mol_type = protein
                       organism = Pelophylax esculentus
SEQUENCE: 80
IFSKLAGKKI KNLLISGLK                                              19

SEQ ID NO: 81          moltype = DNA  length = 36
FEATURE                Location/Qualifiers
misc_feature           1..36
                       note = Description of Artificial Sequence: Synthetic
                        oligonucleotide
```

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```
misc_feature            1..36
                        note = BBa_K1485002
source                  1..36
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 81
ggcggtagcg gcagcggtag cggtagcggc agcccg                              36

SEQ ID NO: 82           moltype = AA  length = 12
FEATURE                 Location/Qualifiers
REGION                  1..12
                        note = Description of Artificial Sequence: Synthetic peptide
REGION                  1..12
                        note = MISC_FEATURE - BBa_K1485002
source                  1..12
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 82
GGSGSGSGSG SP                                                        12

SEQ ID NO: 83           moltype = DNA  length = 381
FEATURE                 Location/Qualifiers
misc_feature            1..381
                        note = GN37
source                  1..381
                        mol_type = other DNA
                        organism = Micavibrio aeruginosavorus
SEQUENCE: 83
atgacataca ccctgagcaa aagaagcctg gataacctaa aaggcgttca tcccgatctg  60
gttgccgttg tccatcgcgc catccagctt acaccggttg atttcgcggt gatcgaaggc  120
ctgcgctccg tatcccgcca aaaggaactg gtggccgccg gcgccagcaa gaccatgaac  180
agccgacacc tgacaggcca tgcggttgat ctagccgctt acgtcaatgg catccgctgg  240
gactggcccc tgtatgacgc catcgccgtg gctgtgaaag ccgcagcaaa ggaattgggt  300
gtggccatcg tgtggggcgg tgactggacc acgtttaagg atggcccgca ctttgaactg  360
gatcggagca aatacagatg a                                           381

SEQ ID NO: 84           moltype = AA  length = 126
FEATURE                 Location/Qualifiers
source                  1..126
                        mol_type = protein
                        organism = Micavibrio aeruginosavorus
SEQUENCE: 84
MTYTLSKRSL DNLKGVHPDL VAVVHRAIQL TPVDFAVIEG LRSVSRQKEL VAAGASKTMN  60
SRHLTGHAVD LAAYVNGIRW DWPLYDAIAV AVKAAAKELG VAIVWGGDWT TFKDGPHFEL  120
DRSKYR                                                               126

SEQ ID NO: 85           moltype = DNA  length = 39
FEATURE                 Location/Qualifiers
misc_feature            1..39
                        note = Description of Artificial Sequence: Synthetic
                         oligonucleotide
misc_feature            1..39
                        note = IGEM linker (BBA_K1486037)
source                  1..39
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 85
ggcggtggct ctggaggtgg tgggtccggc ggtggctct                           39

SEQ ID NO: 86           moltype = AA  length = 13
FEATURE                 Location/Qualifiers
REGION                  1..13
                        note = Description of Artificial Sequence: Synthetic peptide
REGION                  1..13
                        note = MISC_FEATURE - IGEM linker (BBA_K1486037)
source                  1..13
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 86
GGGSGGGGSG GGS                                                       13

SEQ ID NO: 87           moltype = DNA  length = 36
FEATURE                 Location/Qualifiers
source                  1..36
                        mol_type = other DNA
                        organism = Sus scrofa
```

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```
SEQUENCE: 87
cgcctgaaaa aaattggcaa agtgctgaaa tggatt                          36

SEQ ID NO: 88          moltype = AA  length = 12
FEATURE                Location/Qualifiers
source                 1..12
                       mol_type = protein
                       organism = Sus scrofa
SEQUENCE: 88
RLKKIGKVLK WI                                                    12

SEQ ID NO: 89          moltype = DNA  length = 102
FEATURE                Location/Qualifiers
misc_feature           1..102
                       note = Description of Unknown: Gokushovirinae sequence
misc_feature           1..102
                       note = gkh2
misc_feature           1..102
                       note = Description of Unknown: Gokushovirinae sequence
source                 1..102
                       mol_type = other DNA
                       organism = unidentified
SEQUENCE: 89
atgtcgaaga aggcgtcgag gaagagtttt actaagggtg ccgttaaggt tcataagaaa  60
aatgttccta ctcgtgttcc tatgcgtggc ggtattaggc tt                    102

SEQ ID NO: 90          moltype = AA  length = 34
FEATURE                Location/Qualifiers
REGION                 1..34
                       note = Description of Unknown: Gokushovirinae sequence
source                 1..34
                       mol_type = protein
                       organism = unidentified
SEQUENCE: 90
MSKKASRKSF TKGAVKVHKK NVPTRVPMRG GIRL                            34

SEQ ID NO: 91          moltype = DNA  length = 54
FEATURE                Location/Qualifiers
source                 1..54
                       mol_type = other DNA
                       organism = Sus scrofa
SEQUENCE: 91
cgtaaaaaaa cccgtaaacg tctgaaaaaa atcggtaaag ttctgaaatg gatc       54

SEQ ID NO: 92          moltype = AA  length = 18
FEATURE                Location/Qualifiers
source                 1..18
                       mol_type = protein
                       organism = Sus scrofa
SEQUENCE: 92
RKKTRKRLKK IGKVLKWI                                              18

SEQ ID NO: 93          moltype = DNA  length = 45
FEATURE                Location/Qualifiers
source                 1..45
                       mol_type = other DNA
                       organism = Sus scrofa
SEQUENCE: 93
acccgcaaac gcctgaaaaa aattggcaaa gtgctgaaat ggatt                 45

SEQ ID NO: 94          moltype = AA  length = 15
FEATURE                Location/Qualifiers
source                 1..15
                       mol_type = protein
                       organism = Sus scrofa
SEQUENCE: 94
TRKRLKKIGK VLKWI                                                 15

SEQ ID NO: 95          moltype = DNA  length = 348
FEATURE                Location/Qualifiers
source                 1..348
                       mol_type = other DNA
                       organism = Pseudomonas phage PaP2
SEQUENCE: 95
atgaaactca gcgaaaaacg agcactgttc acccagctgc ttgcccagtt aattctttgg  60
gcaggaactc aggatcgagt gtcagtagcc ttggatcaag tgaaaaggac acaggctgaa  120
```

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```
gctgatgcca atgctaagtc tggagcaggc attaggaact ctctccatct actgggatta  180
gccggtgatc ttatcctcta caaggatggt aaatacatgg ataagagcga ggattataag  240
ttcctgggag attactggaa gagtctccat cctctttgtc ggtggggcgg agattttaaa  300
agccgtcctg atggtaatca tttctccttg gaacacgaag gagtgcaa               348

SEQ ID NO: 96          moltype = AA  length = 116
FEATURE                Location/Qualifiers
source                 1..116
                       mol_type = protein
                       organism = Pseudomonas phage PaP2
SEQUENCE: 96
MKLSEKRALF TQLLAQLILW AGTQDRVSVA LDQVKRTQAE ADANAKSGAG IRNSLHLLGL  60
AGDLILYKDG KYMDKSEDYK FLGDYWKSLH PLCRWGGDFK SRPDGNHFSL EHEGVQ      116

SEQ ID NO: 97          moltype = DNA  length = 30
FEATURE                Location/Qualifiers
misc_feature           1..30
                       note = Description of Artificial Sequence: Synthetic
                        oligonucleotide
misc_feature           1..30
                       note = linker
source                 1..30
                       mol_type = other DNA
                       organism = synthetic construct
SEQUENCE: 97
ccaccaaccg cgggcggcac cgcgggcggc                                   30

SEQ ID NO: 98          moltype = AA  length = 10
FEATURE                Location/Qualifiers
REGION                 1..10
                       note = Description of Artificial Sequence: Synthetic peptide
source                 1..10
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 98
PPTAGGTAGG                                                         10

SEQ ID NO: 99          moltype = DNA  length = 27
FEATURE                Location/Qualifiers
misc_feature           1..27
                       note = Description of Artificial Sequence: Synthetic
                        oligonucleotide
misc_feature           1..27
                       note = purification tag GSHHHHHHG
source                 1..27
                       mol_type = other DNA
                       organism = synthetic construct
SEQUENCE: 99
ggatcccatc atcaccacca tcatggt                                      27

SEQ ID NO: 100         moltype = AA  length = 9
FEATURE                Location/Qualifiers
REGION                 1..9
                       note = Description of Artificial Sequence: Synthetic peptide
source                 1..9
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 100
GSHHHHHHG                                                          9

SEQ ID NO: 101         moltype = DNA  length = 120
FEATURE                Location/Qualifiers
source                 1..120
                       mol_type = other DNA
                       organism = Chlamydia phage 4
SEQUENCE: 101
atggcacgaa gatacagact ttcgcgacgc agaagtcgac gacttttttc aagaactgca  60
ttaagaatgc atcgaagaaa tagacttcga agaattatgc gtggcggcat taggttttag  120

SEQ ID NO: 102         moltype = AA  length = 39
FEATURE                Location/Qualifiers
source                 1..39
                       mol_type = protein
                       organism = Chlamydia phage 4
SEQUENCE: 102
MARRYRLSRR RSRRLFSRTA LRMHRRNRLR RIMRGGIRF                         39
```

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```
SEQ ID NO: 103          moltype = DNA  length = 126
FEATURE                 Location/Qualifiers
source                  1..126
                        mol_type = other DNA
                        organism = Escherichia coli
SEQUENCE: 103
atggctcgtt cccgtagacg tatgtctaag cgttcttccc gccgttcgtt ccgcaagtat  60
gcgaagtcgc ataagaagaa ctttaaagcc cgctcaatgc gtggcggtat ccgtttatga  120
taataa                                                            126

SEQ ID NO: 104          moltype = AA  length = 39
FEATURE                 Location/Qualifiers
source                  1..39
                        mol_type = protein
                        organism = Escherichia coli
SEQUENCE: 104
MARSRRRMSK RSSRRSFRKY AKSHKKNFKA RSMRGGIRL                        39

SEQ ID NO: 105          moltype = DNA  length = 114
FEATURE                 Location/Qualifiers
source                  1..114
                        mol_type = other DNA
                        organism = Chlamydia trachomatis
SEQUENCE: 105
aaacgtagaa aaatgacaag aaaaggttct aagcgtcttt ttactgcaac tgctgataaa  60
actaaatcta tcaatactgc cccgccgcca atgcgtggcg gtatccggtt gtag        114

SEQ ID NO: 106          moltype = AA  length = 37
FEATURE                 Location/Qualifiers
source                  1..37
                        mol_type = protein
                        organism = Chlamydia trachomatis
SEQUENCE: 106
KRRKMTRKGS KRLFTATADK TKSINTAPPP MRGGIRL                           37

SEQ ID NO: 107          moltype = DNA  length = 114
FEATURE                 Location/Qualifiers
source                  1..114
                        mol_type = other DNA
                        organism = Oscillibacter sp. PC13
SEQUENCE: 107
atgagaaagc gaatgtctaa gcgtgttgac aagaaggtgt tccgtcgtac tgccgcatct  60
gccaagaaga ttaacattga ccccaagatt taccgtggag gtattcgcct atga        114

SEQ ID NO: 108          moltype = AA  length = 37
FEATURE                 Location/Qualifiers
source                  1..37
                        mol_type = protein
                        organism = Oscillibacter sp. PC13
SEQUENCE: 108
MRKRMSKRVD KKVFRRTAAS AKKINIDPKI YRGGIRL                           37

SEQ ID NO: 109          moltype = DNA  length = 36
FEATURE                 Location/Qualifiers
misc_feature            1..36
                        note = Description of Artificial Sequence: Synthetic
                         oligonucleotide
misc_feature            1..36
                        note = RR12
source                  1..36
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 109
cgccgcctga ttcgcctgtg gctgcgcctg ctgcgc                            36

SEQ ID NO: 110          moltype = AA  length = 12
FEATURE                 Location/Qualifiers
REGION                  1..12
                        note = Description of Artificial Sequence: Synthetic peptide
source                  1..12
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 110
RRLIRLWLRL LR                                                      12
```

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```
SEQ ID NO: 111          moltype = DNA  length = 12
FEATURE                 Location/Qualifiers
misc_feature            1..12
                        note = Description of Artificial Sequence: Synthetic
                         oligonucleotide
misc_feature            1..12
                        note = structure moiety
source                  1..12
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 111
atgatcgacc gt                                                 12

SEQ ID NO: 112          moltype = AA  length = 4
FEATURE                 Location/Qualifiers
REGION                  1..4
                        note = Description of Artificial Sequence: Synthetic peptide
source                  1..4
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 112
MIDR                                                          4

SEQ ID NO: 113          moltype = DNA  length = 12
FEATURE                 Location/Qualifiers
misc_feature            1..12
                        note = Description of Artificial Sequence: Synthetic
                         oligonucleotide
misc_feature            1..12
                        note = moiety (outer membrane binding peptide from PMID:
                         22628248)
source                  1..12
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 113
ttcattcgtc tg                                                 12

SEQ ID NO: 114          moltype = AA  length = 4
FEATURE                 Location/Qualifiers
REGION                  1..4
                        note = Description of Artificial Sequence: Synthetic peptide
source                  1..4
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 114
FIRL                                                          4

SEQ ID NO: 115          moltype = DNA  length = 12
FEATURE                 Location/Qualifiers
misc_feature            1..12
                        note = Description of Artificial Sequence: Synthetic
                         oligonucleotide
misc_feature            1..12
                        note = structure moiety
source                  1..12
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 115
aatccgaccc at                                                 12

SEQ ID NO: 116          moltype = AA  length = 4
FEATURE                 Location/Qualifiers
REGION                  1..4
                        note = Description of Artificial Sequence: Synthetic peptide
source                  1..4
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 116
NPTH                                                          4

SEQ ID NO: 117          moltype = DNA  length = 477
FEATURE                 Location/Qualifiers
misc_feature            1..477
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            1..477
```

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```
                     note = GN202 lysin
source               1..477
                     mol_type = other DNA
                     organism = synthetic construct
SEQUENCE: 117
ggtccgcgtc gtccgcgtcg tccgggtcgt cgtgctccgg ttcgtacatc ccaacgaggc  60
atcgacctca tcaaatcctt cgagggcctg cgcctgtccg cttaccagga ctcggtgggt  120
gtctggacca taggttacgg caccactcgg ggcgtcaccc gctacatgac gatcaccgtc  180
gagcaggccg agcggatgct gtcgaacgac attcagcgct tcgagccaga gctagacagg  240
ctggcgaagg tgccactgaa ccagaaccag tgggatgccc tgatgagctt cgtgtacaac  300
ctgggcgcgg ccaatctggc gtcgtccacg ctgctcgacc tgctgaacaa gggtgactac  360
cagggagcag cggaccagtt cccgcattgg gtgaatgcgg gcggtaagcg cttggatggt  420
ctggttaagc gtcgagcagc cgagcgtgcg ctgttcctgg agccactatc gtgataa     477

SEQ ID NO: 118        moltype = AA  length = 158
FEATURE               Location/Qualifiers
REGION                1..158
                      note = Description of Artificial Sequence: Synthetic
                       polypeptide
source                1..158
                      mol_type = protein
                      organism = synthetic construct
SEQUENCE: 118
MGPRRPRRPG RRAPVRTSQR GIDLIKSFEG LRLSAYQDSV GVWTIGYGTT RGVTRYMTIT  60
VEQAERMLSN DIQRFEPELD RLAKVPLNQN QWDALMSFVY NLGAANLASS TLLDLLNKGD  120
YQGAADQFPH WVNAGGKRLD GLVKRRAAER ALFLEPLS                          158

SEQ ID NO: 119        moltype = DNA  length = 30
FEATURE               Location/Qualifiers
misc_feature          1..30
                      note = Description of Artificial Sequence: Synthetic
                       oligonucleotide
misc_feature          1..30
                      note = cationic peptide
source                1..30
                      mol_type = other DNA
                      organism = synthetic construct
SEQUENCE: 119
aaattcttta agttctttaa gttttttaaa                                    30

SEQ ID NO: 120        moltype = AA  length = 10
FEATURE               Location/Qualifiers
REGION                1..10
                      note = Description of Artificial Sequence: Synthetic peptide
source                1..10
                      mol_type = protein
                      organism = synthetic construct
SEQUENCE: 120
KFFKFFKFFK                                                          10

SEQ ID NO: 121        moltype = DNA  length = 54
FEATURE               Location/Qualifiers
misc_feature          1..54
                      note = Description of Artificial Sequence: Synthetic
                       oligonucleotide
misc_feature          1..54
                      note = linker
source                1..54
                      mol_type = other DNA
                      organism = synthetic construct
SEQUENCE: 121
gccggcgcag gagctggtgc aggagctggt gcaggagctg gtgcaggagc tagc         54

SEQ ID NO: 122        moltype = AA  length = 18
FEATURE               Location/Qualifiers
REGION                1..18
                      note = Description of Artificial Sequence: Synthetic peptide
source                1..18
                      mol_type = protein
                      organism = synthetic construct
SEQUENCE: 122
AGAGAGAGAG AGAGAGAS                                                 18

SEQ ID NO: 123        moltype = DNA  length = 543
FEATURE               Location/Qualifiers
misc_feature          1..543
```

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```
                     note = Description of Artificial Sequence: Synthetic
                      polynucleotide
misc_feature         1..543
                     note = GN14 lysin
source               1..543
                     mol_type = other DNA
                     organism = synthetic construct
SEQUENCE: 123
aataacgaac ttccttgggt agccgaagcc cgaaagtata tcggccttcg cgaagacact  60
tcgaagactt cgcataaccc gaaacttctt gccatgcttg accgcatggg cgaattttcc  120
aacgaatccc gcgcttggtg gcacgacgac gaaacgcctt ggtgcggact gttcgtcggc  180
tattgcttgg gcgttgccgg gcgctacgtc gtccgcgaat ggtacagggc gcgggcatgg  240
gaagccccgc agcttacgaa gcttgaccgg cccgcatacg gcgcgcttgt gaccttcacg  300
cgaagcggcg gcggccacgt cggttttatt gtgggcaagg atgcgcgcgg aaatcttatg  360
gttcttggcg gtaatcagtc gaacgccgta agtatcgcac cgttcgcagt atcccgcgta  420
accggctatt tctggccgtc gttctggcga aacaagaccg cagttaaaag cgttccgttt  480
gaagaacgtt attcgctgcc gctgttgaag tcgaacggcg aactttcgac gaatgaagcg  540
taa                                                               543

SEQ ID NO: 124       moltype = AA  length = 180
FEATURE              Location/Qualifiers
REGION               1..180
                     note = Description of Artificial Sequence: Synthetic
                      polypeptide
source               1..180
                     mol_type = protein
                     organism = synthetic construct
SEQUENCE: 124
NNELPWVAEA RKYIGLREDT SKTSHNPKLL AMLDRMGEFS NESRAWWHDD ETPWCGLFVG  60
YCLGVAGRYV VREWYRARAW EAPQLTKLDR PAYGALVTFT RSGGGHVGFI VGKDARGNLM  120
VLGGNQSNAV SIAPFAVSRV TGYFWPSFWR NKTAVKSVPF EERYSLPLLK SNGELSTNEA  180

SEQ ID NO: 125       moltype = DNA  length = 471
FEATURE              Location/Qualifiers
misc_feature         1..471
                     note = Description of Artificial Sequence: Synthetic
                      polynucleotide
misc_feature         1..471
                     note = GN156
source               1..471
                     mol_type = other DNA
                     organism = synthetic construct
SEQUENCE: 125
ggtccgcgtc gtccgcgtcg tccgggtcgt cgtgctccgg ttcgtacctc tcagcgtggt  60
atcgacctga tcaaatcttt cgaaggtctg cgtctgtctg cttaccagga ctctgttggt  120
gtttggacca tcggttacgg taccacccgt ggtgttaccc gttacatgac catcaccgtt  180
gaacaggctg aacgtatgct gtctaacgac atccagcgtt tcgaaccgga actggaccgt  240
ctggctaaag ttccgctgaa ccagaaccag tgggacgctc tgatgtcttt cgtttacaac  300
ctgggtgctg ctaacctggc ttcttctacc ctgctgaaac tgctgaacaa aggtgactac  360
cagggtgctg ctgaccagtt cccgcgttgg gttaacgctg gtggtaaacg tctggacggt  420
ctggttaaac gtcgtgctgc tgaacgtgct ctgttcctgg aaccgctgtc t           471

SEQ ID NO: 126       moltype = AA  length = 157
FEATURE              Location/Qualifiers
REGION               1..157
                     note = Description of Artificial Sequence: Synthetic
                      polypeptide
source               1..157
                     mol_type = protein
                     organism = synthetic construct
SEQUENCE: 126
GPRRPRRPGR RAPVRTSQRG IDLIKSFEGL RLSAYQDSVG VWTIGYGTTR GVTRYMTITV  60
EQAERMLSND IQRFEPELDR LAKVPLNQNQ WDALMSFVYN LGAANLASST LLKLLNKGDY  120
QGAADQFPRW VNAGGKRLDG LVKRRAAERA LFLEPLS                          157

SEQ ID NO: 127       moltype = AA  length = 39
FEATURE              Location/Qualifiers
REGION               1..39
                     note = Description of Artificial Sequence: Synthetic
                      polypeptide
REGION               1..39
                     note = MISC_FEATURE - PGN4
source               1..39
                     mol_type = protein
                     organism = synthetic construct
SEQUENCE: 127
```

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NKGDYQGAAD QFPRWVNAGG KRLDGLVKRR ASQSRESQC                          39

SEQ ID NO: 128          moltype = AA  length = 42
FEATURE                 Location/Qualifiers
REGION                  1..42
                        note = Description of Artificial Sequence: Synthetic
                         polypeptide
REGION                  1..42
                        note = MISC_FEATURE - FGN4-1
source                  1..42
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 128
NKGDYQGAAD QFPRWVNAGG KRLDGLVKRR AAERALFLEP LS                      42

SEQ ID NO: 129          moltype = AA  length = 31
FEATURE                 Location/Qualifiers
REGION                  1..31
                        note = Description of Artificial Sequence: Synthetic
                         polypeptide
REGION                  1..31
                        note = MISC_FEATURE - FGN4-2
source                  1..31
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 129
NKGDYQGAAD QFPRWVNAGG KRLDGLVKRR A                                  31

SEQ ID NO: 130          moltype = DNA  length = 54
FEATURE                 Location/Qualifiers
misc_feature            1..54
                        note = Description of Artificial Sequence: Synthetic
                         oligonucleotide
misc_feature            1..54
                        note = RI18
source                  1..54
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 130
cgtaaaaaaa cccgtaaacg tctgaaaaaa atcggtaaag ttctgaaatg gatc         54

SEQ ID NO: 131          moltype = AA  length = 18
FEATURE                 Location/Qualifiers
REGION                  1..18
                        note = Description of Artificial Sequence: Synthetic peptide
source                  1..18
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 131
RKKTRKRLKK IGKVLKWI                                                18

SEQ ID NO: 132          moltype = DNA  length = 111
FEATURE                 Location/Qualifiers
source                  1..111
                        mol_type = other DNA
                        organism = Chlamydia virus Chp1
SEQUENCE: 132
atggttcgta gaagacgttt gagaagaaga ataagtagaa gaatttttag aagaacagta  60
gctagagttg gtagaaggcg aaggtctttt cgtggtggta ttagatttta a           111

SEQ ID NO: 133          moltype = AA  length = 36
FEATURE                 Location/Qualifiers
source                  1..36
                        mol_type = protein
                        organism = Chlamydia virus Chp1
SEQUENCE: 133
MVRRRRLRRR ISRRIFRRTV ARVGRRRRSF RGGIRF                            36

SEQ ID NO: 134          moltype = DNA  length = 108
FEATURE                 Location/Qualifiers
source                  1..108
                        mol_type = other DNA
                        organism = Chlamydia virus CPAR39
SEQUENCE: 134
ttgtgcaaaa aagtgtgcaa aaaatgccca aaaaaagggc caaaaaatgc ccccaaaatc  60
ggagcatttt acgagagaaa aacacctaga cttaaacagt ctacttga               108
```

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```
SEQ ID NO: 135         moltype = AA  length = 35
FEATURE                Location/Qualifiers
source                 1..35
                       mol_type = protein
                       organism = Chlamydia virus CPAR39
SEQUENCE: 135
MCKKVCKKCP KKGPKNAPKI GAFYERKTPR LKQST                              35

SEQ ID NO: 136         moltype = DNA  length = 135
FEATURE                Location/Qualifiers
source                 1..135
                       mol_type = other DNA
                       organism = Chlamydia phage 3
SEQUENCE: 136
atgaggttaa aaatggcacg aagaagatac agacttccgc gacgtagaag tcgaagactt  60
ttttcaagaa ctgcattaag gatgcatcca agaaataggc ttcgaagaat tatgcgtggc  120
ggcattaggt tctag                                                   135

SEQ ID NO: 137         moltype = AA  length = 44
FEATURE                Location/Qualifiers
source                 1..44
                       mol_type = protein
                       organism = Chlamydia phage 3
SEQUENCE: 137
MRLKMARRRY RLPRRRSRRL FSRTALRMHP RNRLRRIMRG GIRF                    44

SEQ ID NO: 138         moltype = DNA  length = 117
FEATURE                Location/Qualifiers
source                 1..117
                       mol_type = other DNA
                       organism = Chlamydia trachomatis
SEQUENCE: 138
atgaaacgta gaaaaatgac aagaaaaggt tctaagcgtc tttttactgc aactgctgat  60
aaaactaaat ctatcaatac tgccccgccg ccaatgcgtg gcggtatccg gttgtaa      117

SEQ ID NO: 139         moltype = AA  length = 38
FEATURE                Location/Qualifiers
source                 1..38
                       mol_type = protein
                       organism = Chlamydia trachomatis
SEQUENCE: 139
MKRRKMTRKG SKRLFTATAD KTKSINTAPP PMRGGIRL                           38

SEQ ID NO: 140         moltype = DNA  length = 120
FEATURE                Location/Qualifiers
source                 1..120
                       mol_type = other DNA
                       organism = Chlamydia trachomatis
SEQUENCE: 140
atgtctaaaa agcgttctcg catgtctcgc cgccgttcta agaagttgtt ctcgaaaacg  60
gctctccgca cgaagagtgt caacacccgt ccgcctatgc gcggagggtt ccggttctga  120

SEQ ID NO: 141         moltype = AA  length = 39
FEATURE                Location/Qualifiers
source                 1..39
                       mol_type = protein
                       organism = Chlamydia trachomatis
SEQUENCE: 141
MSKKRSRMSR RRSKKLFSKT ALRTKSVNTR PPMRGGFRF                          39

SEQ ID NO: 142         moltype = DNA  length = 123
FEATURE                Location/Qualifiers
source                 1..123
                       mol_type = other DNA
                       organism = Chlamydia trachomatis
SEQUENCE: 142
atgtctcttc gtcgtcataa gctttctcgt aaggcgtcta agcgtatttt tcgtaaaggt  60
gcatcacgca cgaagacttt gaatactcgt gctacgccta tgcgcggcgg tttccgtatt  120
taa                                                                123

SEQ ID NO: 143         moltype = AA  length = 40
FEATURE                Location/Qualifiers
source                 1..40
                       mol_type = protein
                       organism = Chlamydia trachomatis
```

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SEQUENCE: 143
MSLRRHKLSR KASKRIFRKG ASRTKTLNTR ATPMRGGFRI                          40

SEQ ID NO: 144         moltype = DNA  length = 117
FEATURE                Location/Qualifiers
source                 1..117
                       mol_type = other DNA
                       organism = Chlamydia trachomatis
SEQUENCE: 144
gtgaaacgtc gtaaactgtc caaaaagaaa tctcgcaaga ttttcactcg cggtgctgta  60
aatgtgaaaa agcgtaacct tcgcgctcgc ccaatgcgcg gcggtttccg gatctaa     117

SEQ ID NO: 145         moltype = AA  length = 38
FEATURE                Location/Qualifiers
source                 1..38
                       mol_type = protein
                       organism = Chlamydia trachomatis
SEQUENCE: 145
MKRRKLSKKK SRKIFTRGAV NVKKRNLRAR PMRGGFRI                           38

SEQ ID NO: 146         moltype = DNA  length = 114
FEATURE                Location/Qualifiers
source                 1..114
                       mol_type = other DNA
                       organism = Chlamydia trachomatis
SEQUENCE: 146
atggctaaaa aaatgactaa aggcaaggat cgtcaggttt ttcgtaaaac cgctgatcgt  60
actaagaaac tcaatgttag accgttgtta tatcgaggag gtatcagatt atga        114

SEQ ID NO: 147         moltype = AA  length = 37
FEATURE                Location/Qualifiers
source                 1..37
                       mol_type = protein
                       organism = Chlamydia trachomatis
SEQUENCE: 147
MAKKMTKGKD RQVFRKTADR TKKLNVRPLL YRGGIRL                            37

SEQ ID NO: 148         moltype = DNA  length = 120
FEATURE                Location/Qualifiers
source                 1..120
                       mol_type = other DNA
                       organism = Chlamydia trachomatis
SEQUENCE: 148
atggcaggaa aaaaaatggt atcaaaagga aaagatagac agattttccg aaaaactgct  60
gatcgcacta aaaaaatgaa tgtgcgcccg ctattatatc gtggaggtat tagattatga  120

SEQ ID NO: 149         moltype = AA  length = 39
FEATURE                Location/Qualifiers
source                 1..39
                       mol_type = protein
                       organism = Chlamydia trachomatis
SEQUENCE: 149
MAGKKMVSKG KDRQIFRKTA DRTKKMNVRP LLYRGGIRL                          39

SEQ ID NO: 150         moltype = DNA  length = 126
FEATURE                Location/Qualifiers
source                 1..126
                       mol_type = other DNA
                       organism = Marine gokushovirus
SEQUENCE: 150
atgagaagac caagaaaaat gaactataaa aaatcaaaaa gaatgttttc acgcacagca  60
gcgagaacac acagaaaaaa ctctctaaga ggtagccgac ctatgagagg cggaatacgt  120
ctttaa                                                             126

SEQ ID NO: 151         moltype = AA  length = 41
FEATURE                Location/Qualifiers
source                 1..41
                       mol_type = protein
                       organism = Marine gokushovirus
SEQUENCE: 151
MRRPRKMNYK KSKRMFSRTA ARTHRKNSLR GSRPMRGGIR L                       41

SEQ ID NO: 152         moltype = DNA  length = 108
FEATURE                Location/Qualifiers
misc_feature           1..108
                       note = Description of Unknown: Bacteria; environmental
```

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```
                     sample sequence
source               1..108
                     mol_type = other DNA
                     organism = unidentified
SEQUENCE: 152
atgaaaatgc gtaagcggac ggacaagcga gtgtttaccc gcaccgctgc taagtccaag  60
aaagtgaaca ttgccccgaa aatttttaga ggaggtatcc gtctgtga               108

SEQ ID NO: 153       moltype = AA  length = 35
FEATURE              Location/Qualifiers
REGION               1..35
                     note = Description of Unknown: Bacteria; environmental
                      sample sequence
source               1..35
                     mol_type = protein
                     organism = unidentified
SEQUENCE: 153
MKMRKRTDKR VFTRTAAKSK KVNIAPKIFR GGIRL                             35

SEQ ID NO: 154       moltype = DNA  length = 120
FEATURE              Location/Qualifiers
source               1..120
                     mol_type = other DNA
                     organism = Escherichia sp.
SEQUENCE: 154
atggctcgtt ctcgccgtcg tatgtccaag cgttcttccc gtcgttcgtt ccgtaagtac  60
gcaaagacgc ataaacgtaa ctttaaagcc cgctctatgc gtggtggaat tcgtctttga  120

SEQ ID NO: 155       moltype = AA  length = 39
FEATURE              Location/Qualifiers
source               1..39
                     mol_type = protein
                     organism = Escherichia sp.
SEQUENCE: 155
MARSRRRMSK RSSRRSFRKY AKTHKRNFKA RSMRGGIRL                         39

SEQ ID NO: 156       moltype = DNA  length = 144
FEATURE              Location/Qualifiers
source               1..144
                     mol_type = other DNA
                     organism = Cognatishimia maritima
SEQUENCE: 156
atggaaagcc cgaacagccg cagccagctg ggcattaccc tgtatctgct gagcaccatt  60
tttccggatg cgtgctttcg ctatcgccgc gaactgccgt atccgctggt gatttggggc  120
gtggcgaccc tgtgcctgca gtaa                                         144

SEQ ID NO: 157       moltype = AA  length = 47
FEATURE              Location/Qualifiers
source               1..47
                     mol_type = protein
                     organism = Cognatishimia maritima
SEQUENCE: 157
MESPNSRSQL GITLYLLSTI FPDACFRYRR ELPYPLVIWG VATLCLQ                47

SEQ ID NO: 158       moltype = DNA  length = 114
FEATURE              Location/Qualifiers
misc_feature         1..114
                     note = Description of Unknown: Bacteria; environmental
                      sample sequence
source               1..114
                     mol_type = other DNA
                     organism = unidentified
SEQUENCE: 158
atgagacgtc gtcgtctatc ccgcagaact tcccgccgtt ttttccgtaa aggacttaag  60
gttcgccgtc gtaacctccg cgcgagaccc atgagaggcg gattcagaat ttga        114

SEQ ID NO: 159       moltype = AA  length = 37
FEATURE              Location/Qualifiers
REGION               1..37
                     note = Description of Unknown: Bacteria; environmental
                      sample sequence
source               1..37
                     mol_type = protein
                     organism = unidentified
SEQUENCE: 159
MRRRRLSRRT SRRFFRKGLK VRRRNLRARP MRGGFRI                           37
```

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SEQ ID NO: 160          moltype = DNA  length = 120
FEATURE                 Location/Qualifiers
misc_feature            1..120
                        note = Description of Unknown: Bacteria; environmental
                         sample sequence
source                  1..120
                        mol_type = other DNA
                        organism = unidentified
SEQUENCE: 160
atggcacgac gcaagaagat gaaaggcaag cgggataaac gggtgtttaa gcagacagcc  60
aacaaaacca aggctatcaa catcagccca aaaaacatga gaggggtac gagactgtga  120

SEQ ID NO: 161          moltype = AA  length = 39
FEATURE                 Location/Qualifiers
REGION                  1..39
                        note = Description of Unknown: Bacteria; environmental
                         sample sequence
source                  1..39
                        mol_type = protein
                        organism = unidentified
SEQUENCE: 161
MARRKKMKGK RDKRVFKQTA NKTKAINISP KNMRGGTRL                        39

SEQ ID NO: 162          moltype = DNA  length = 162
FEATURE                 Location/Qualifiers
source                  1..162
                        mol_type = other DNA
                        organism = Marine gokushovirus
SEQUENCE: 162
atgttaactg tgtggagtga cacccctacc ataaaaagga gaaaagacat gtatagaaag  60
agaatgtcaa gaaagaaaag taaaaaggtt tttgcaaaaa ccgcaatgaa agtaaataaa  120
agaaaccacg ttaaacctat gcgtggtgga tatagaatat aa                     162

SEQ ID NO: 163          moltype = AA  length = 53
FEATURE                 Location/Qualifiers
source                  1..53
                        mol_type = protein
                        organism = Marine gokushovirus
SEQUENCE: 163
MLTVWSDTPT IKRRKDMYRK RMSRKKSKKV FAKTAMKVNK RNHVKPMRGG YRI         53

SEQ ID NO: 164          moltype = DNA  length = 120
FEATURE                 Location/Qualifiers
source                  1..120
                        mol_type = other DNA
                        organism = Marine gokushovirus
SEQUENCE: 164
atgatgaagt acagaaaaaa aatgagcgct aaaagtagcc gaaagcaatt tacaaaaggc  60
gccatgaaag tgaagggtaa aaacttcaca aaaccaatgc gcggaggcat ccgtctatag  120

SEQ ID NO: 165          moltype = AA  length = 39
FEATURE                 Location/Qualifiers
source                  1..39
                        mol_type = protein
                        organism = Marine gokushovirus
SEQUENCE: 165
MMKYRKKMSA KSSRKQFTKG AMKVKGKNFT KPMRGGIRL                        39

SEQ ID NO: 166          moltype = DNA  length = 117
FEATURE                 Location/Qualifiers
source                  1..117
                        mol_type = other DNA
                        organism = Marine gokushovirus
SEQUENCE: 166
atgcgacgtt acaatgtaaa taaaggtaaa tctgctaaga agtttcgaaa gcaggtaagt  60
aagacgaagg ttgcaaacct acgttctaat ccaatgcgag gtggttggag actctaa     117

SEQ ID NO: 167          moltype = AA  length = 38
FEATURE                 Location/Qualifiers
source                  1..38
                        mol_type = protein
                        organism = Marine gokushovirus
SEQUENCE: 167
MRRYNVNKGK SAKKFRKQVS KTKVANLRSN PMRGGWRL                         38
```

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SEQ ID NO: 168          moltype = DNA  length = 87
FEATURE                 Location/Qualifiers
source                  1..87
                        mol_type = other DNA
                        organism = Spiroplasma virus SpV4
SEQUENCE: 168
atggcttatc gtggttttaa aacgagtcgt gttgtaaaac atagagtacg tagaagatgg  60
tttaatcata gaagacgtta tagatag                                      87

SEQ ID NO: 169          moltype = AA  length = 28
FEATURE                 Location/Qualifiers
source                  1..28
                        mol_type = protein
                        organism = Spiroplasma virus SpV4
SEQUENCE: 169
MAYRGFKTSR VVKHRVRRRW FNHRRRYR                                     28

SEQ ID NO: 170          moltype = DNA  length = 117
FEATURE                 Location/Qualifiers
source                  1..117
                        mol_type = other DNA
                        organism = Spiroplasma virus SpV4
SEQUENCE: 170
gtgagacgca aggttaagaa cacaaagcgt catcagtgga ggttgactca ttctgcacgt  60
tcaattaaac gtgctaatat aatgccgtca aatcctcgtg gtggacgtcg tttttag     117

SEQ ID NO: 171          moltype = AA  length = 38
FEATURE                 Location/Qualifiers
source                  1..38
                        mol_type = protein
                        organism = Spiroplasma virus SpV4
SEQUENCE: 171
MRRKVKNTKR HQWRLTHSAR SIKRANIMPS NPRGGRRF                          38

SEQ ID NO: 172          moltype = DNA  length = 798
FEATURE                 Location/Qualifiers
source                  1..798
                        mol_type = other DNA
                        organism = Pseudomonas phage PhiPA3
SEQUENCE: 172
atgacattac tgaagaaagg cgacaagggt gacgccgtaa aacaactaca gcagaaactc  60
aaagaccttg ggtataccct gggtgtcgat ggcaacttcg gtaatggcac cgatactgtc  120
gttcgttctt tccaaaccaa aatgaagctt agtgttgatg gtgtggttgg taatggtact  180
atgagtacta ttgactctac tctagcaggc attaaagcgt ggaagactag tgtacctttc  240
cctgcgacga acaaatcccg agcaatggca atgccaacgt tgactgaaat aggtcgactg  300
acaaacgttg atcctaaatt gctagcgaca ttctgttcta tcgaaagcgc gtttgattac  360
acagctaaac cctacaagcc cgatggcaca gtgtacagct ccgccgaagg ttggttccag  420
ttcctggatg caacatggga tgacgaagtg cgtaaacacg gtaagcaata tagcttccct  480
gttgatcctg gtcgttcttt gcgtaaagat ccacgggcta atggcttgat gggcgctgag  540
ttcctcaaag ggaatgctgc tattctgcgg ccagtactgg gtcatgaacc gagcgacaca  600
gatctttatc tagcccattt catgggagca ggtggcgcaa aacagttcct tatggccgat  660
caaaataaat tggctgccga attgttccct ggtccagcta aggctaatcc taacatcttc  720
tataaatccg gaaatattgc ccgcacttta gcagaggtct atgcagtcct cgatgctaag  780
gtagccaagc atagagct                                                798

SEQ ID NO: 173          moltype = AA  length = 266
FEATURE                 Location/Qualifiers
source                  1..266
                        mol_type = protein
                        organism = Pseudomonas phage PhiPA3
SEQUENCE: 173
MTLLKKGDKG DAVKQLQQKL KDLGYTLGVD GNFGNGTDTV VRSFQTKMKL SVDGVVGNGT  60
MSTIDSTLAG IKAWKTSVPF PATNKSRAMA MPTLTEIGRL TNVDPKLLAT FCSIESAFDY  120
TAKPYKPDGT VYSSAEGWFQ FLDATWDDEV RKHGKQYSFP VDPGRSLRKD PRANGLMGAE  180
FLKGNAAILR PVLGHEPSDT DLYLAHFMGA GGAKQFLMAD QNKLAAELFP GPAKANPNIF  240
YKSGNIARTL AEVYAVLDAK VAKHRA                                       266

SEQ ID NO: 174          moltype = DNA  length = 435
FEATURE                 Location/Qualifiers
misc_feature            1..435
                        note = Description of Artificial Sequence: Synthetic
                         polynucleotide
misc_feature            1..435
                        note = GN37 and RI18
source                  1..435
                        mol_type = other DNA
```

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                     organism = synthetic construct
SEQUENCE: 174
atgacataca ccctgagcaa aagaagcctg gataacctaa aaggcgttca tcccgatctg  60
gttgccgttg tccatcgcgc catccagctt acaccggttg atttcgcggt gatcgaaggc  120
ctgcgctccg tatcccgcca aaaggaactg gtggccgccg gcgccagcaa gaccatgaac  180
agccgacacc tgacaggcca tgcggttgat ctagccgctt acgtcaatgg catccgctgg  240
gactggcccc tgtatgacgc catcgccgtg gctgtgaaag ccgcagcaaa ggaattgggt  300
gtggccatcg tgtggggcgg tgactggacc acgtttaagg atggcccgca ctttgaactg  360
gatcggagca aatacagatg acgtaaaaaa acccgtaaac gtctgaaaaa aatcggtaaa  420
gttctgaaat ggatc                                                   435

SEQ ID NO: 175         moltype = AA  length = 144
FEATURE                Location/Qualifiers
REGION                 1..144
                       note = Description of Artificial Sequence: Synthetic
                        polypeptide
source                 1..144
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 175
MTYTLSKRSL DNLKGVHPDL VAVVHRAIQL TPVDFAVIEG LRSVSRQKEL VAAGASKTMN  60
SRHLTGHAVD LAAYVNGIRW DWPLYDAIAV AVKAAAKELG VAIVWGGDWT TFKDGPHFEL  120
DRSKYRRKKT RKRLKKIGKV LKWI                                         144

SEQ ID NO: 176         moltype = DNA  length = 120
FEATURE                Location/Qualifiers
source                 1..120
                       mol_type = other DNA
                       organism = Escherichia sp.
SEQUENCE: 176
atggctcgtt ctcgtcgtcg tatgtctaaa cgttcttctc gtcgttcttt tcgtaaatat  60
gctaaaactc ataaaaaaaa ttttaaagct cgttctatgc gtggaggaat tcgtttataa  120

SEQ ID NO: 177         moltype = AA  length = 39
FEATURE                Location/Qualifiers
source                 1..39
                       mol_type = protein
                       organism = Escherichia sp.
SEQUENCE: 177
MARSRRRMSK RSSRRSFRKY AKTHKKNFKA RSMRGGIRL                         39

SEQ ID NO: 178         moltype = DNA  length = 117
FEATURE                Location/Qualifiers
source                 1..117
                       mol_type = other DNA
                       organism = Escherichia coli
SEQUENCE: 178
atggcgcgca gccgccgccg catgagcaaa cgcagcagcc gccgcagctt tcgcaaatat  60
gcgaaaagcc ataaaaaaaa ctttaaagcg cgcagcatgc gcggcggcat tcgcctg     117

SEQ ID NO: 179         moltype = AA  length = 39
FEATURE                Location/Qualifiers
source                 1..39
                       mol_type = protein
                       organism = Escherichia coli
SEQUENCE: 179
MARSRRRMSK RSSRRSFRKY AKSHKKNFKA RSMRGGIRL                         39

SEQ ID NO: 180         moltype = DNA  length = 117
FEATURE                Location/Qualifiers
source                 1..117
                       mol_type = other DNA
                       organism = Alces alces faeces associated microvirus MP12
                        5423
SEQUENCE: 180
atggcaaaga aaattagaaa caaagcacgt gatagacgta tcttcacaag aacagcttca  60
cgcatgcaca aggcaaaccg cacaccaaga tttatgagag gcggtattag gttatga     117

SEQ ID NO: 181         moltype = AA  length = 38
FEATURE                Location/Qualifiers
source                 1..38
                       mol_type = protein
                       organism = Alces alces faeces associated microvirus MP12
                        5423
SEQUENCE: 181
MAKKIRNKAR DRRIFTRTAS RMHKANRTPR FMRGGIRL                          38
```

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SEQ ID NO: 182          moltype = DNA  length = 117
FEATURE                 Location/Qualifiers
misc_feature            1..117
                        note = Description of Unknown: Gokushovirinae environmental
                         samplesequence
source                  1..117
                        mol_type = other DNA
                        organism = unidentified
SEQUENCE: 182
atgcgtcgta aaaaaatgtc acgcggtaaa tcaaaaaaac tctttcgccg aacagcaaaa  60
cgcgttcatc gaaaaaacct acgagctcgc ccaatgcgtg gcggcatacg catgtag     117

SEQ ID NO: 183          moltype = AA  length = 38
FEATURE                 Location/Qualifiers
REGION                  1..38
                        note = Description of Unknown: Gokushovirinae environmental
                         samplesequence
source                  1..38
                        mol_type = protein
                        organism = unidentified
SEQUENCE: 183
MRRKKMSRGK SKKLFRRTAK RVHRKNLRAR PMRGGIRM                          38

SEQ ID NO: 184          moltype = DNA  length = 120
FEATURE                 Location/Qualifiers
misc_feature            1..120
                        note = Description of Unknown: Gokushovirinae environmental
                         samplesequence
source                  1..120
                        mol_type = other DNA
                        organism = unidentified
SEQUENCE: 184
atggcgaagc gacacaaaat cccgcaacgc gcgtcacaac attccttcac gcgccatgcg  60
caaaaggtcc accctaagaa cgttccccgc ctgccaatgc gaggcggtat ccgtctctaa  120

SEQ ID NO: 185          moltype = AA  length = 39
FEATURE                 Location/Qualifiers
REGION                  1..39
                        note = Description of Unknown: Gokushovirinae environmental
                         samplesequence
source                  1..39
                        mol_type = protein
                        organism = unidentified
SEQUENCE: 185
MAKRHKIPQR ASQHSFTRHA QKVHPKNVPR LPMRGGIRL                         39

SEQ ID NO: 186          moltype = DNA  length = 114
FEATURE                 Location/Qualifiers
misc_feature            1..114
                        note = Description of Unknown: uncultured bacterium sequence
source                  1..114
                        mol_type = other DNA
                        organism = unidentified
SEQUENCE: 186
atgcgtaaaa aaatgcacaa atcattagac aagcgagtgt ttaaccgcac tgcaaaaaaa  60
tcaaaaaaaa taaatgttaa tcctgtagtt tatcgtggag gtattagatt atga        114

SEQ ID NO: 187          moltype = AA  length = 37
FEATURE                 Location/Qualifiers
REGION                  1..37
                        note = Description of Unknown: uncultured bacterium sequence
source                  1..37
                        mol_type = protein
                        organism = unidentified
SEQUENCE: 187
MRKKMHKSLD KRVFNRTAKK SKKINVNPVV YRGGIRL                           37

SEQ ID NO: 188          moltype = DNA  length = 117
FEATURE                 Location/Qualifiers
source                  1..117
                        mol_type = other DNA
                        organism = Marine gokushovirus
SEQUENCE: 188
atgcgacgtt acaatgtaaa taaaggtaaa tctgctaaga agtttcgaaa gcaggtaagt  60
aagacgaagg ttgcaaacct acgttctaat ccaatgcgag gtggttggag actctaa     117
```

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SEQ ID NO: 189          moltype = AA  length = 38
FEATURE                 Location/Qualifiers
source                  1..38
                        mol_type = protein
                        organism = Marine gokushovirus
SEQUENCE: 189
MRRYNVNKGK SAKKFRKQVS KTKVANLRSN PMRGGWRL                          38

SEQ ID NO: 190          moltype = DNA  length = 126
FEATURE                 Location/Qualifiers
source                  1..126
                        mol_type = other DNA
                        organism = Richelia intracellularis HH01
SEQUENCE: 190
atgcgtccag ttaaaagatc aagagtaaat aaggcccgat ctgcaggcaa gtttcgtaag  60
caggtcggta aaacaaagat ggcaaatctg cgtagtaatc cgatgcgcgg cggatggcgg  120
ctgtga                                                             126

SEQ ID NO: 191          moltype = AA  length = 41
FEATURE                 Location/Qualifiers
source                  1..41
                        mol_type = protein
                        organism = Richelia intracellularis HH01
SEQUENCE: 191
MRPVKRSRVN KARSAGKFRK QVGKTKMANL RSNPMRGGWR L                      41

SEQ ID NO: 192          moltype = DNA  length = 126
FEATURE                 Location/Qualifiers
source                  1..126
                        mol_type = other DNA
                        organism = Gokushovirinae Fen7875_21
SEQUENCE: 192
atgaagccat tgaagcgtaa gccggttcag aaggcgcggt cagcagccaa gttccgtcga  60
aatgtgtcta ccgttaaggc tgccaatatg gcggtgaagc cgatgcgcgg cggttggcgg  120
ttctga                                                             126

SEQ ID NO: 193          moltype = AA  length = 41
FEATURE                 Location/Qualifiers
source                  1..41
                        mol_type = protein
                        organism = Gokushovirinae Fen7875_21
SEQUENCE: 193
MKPLKRKPVQ KARSAAKFRR NVSTVKAANM AVKPMRGGWR F                      41

SEQ ID NO: 194          moltype = DNA  length = 135
FEATURE                 Location/Qualifiers
source                  1..135
                        mol_type = other DNA
                        organism = Mycobacterium phage BabyRay
SEQUENCE: 194
atgaccaaga gagacatcga gtaccggaaa gctttggggc tcaacccatc tgagccgctc  60
ccgaagattg tgggtgccgt cacccgccac ggggccactc tgaaacgccc acgggtcacc  120
gcactggccc gatag                                                   135

SEQ ID NO: 195          moltype = AA  length = 44
FEATURE                 Location/Qualifiers
source                  1..44
                        mol_type = protein
                        organism = Mycobacterium phage BabyRay
SEQUENCE: 195
MTKRDIEYRK ALGLNPSEPL PKIVGAVTRH GATLKRPRVT ALAR                   44

SEQ ID NO: 196          moltype = DNA  length = 117
FEATURE                 Location/Qualifiers
source                  1..117
                        mol_type = other DNA
                        organism = Bdellovibrio phage phiMH2K
SEQUENCE: 196
atgaaaagaa aaccaatgag ccgcaaggcc tctcaaaaaa ccttcaaaaa gaacacaggc  60
gttcaacgca tgaaccatct caacccacgc gccatgcgtg gtggcattag actataa     117

SEQ ID NO: 197          moltype = AA  length = 38
FEATURE                 Location/Qualifiers
source                  1..38
                        mol_type = protein
```

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                     organism = Bdellovibrio phage phiMH2K
SEQUENCE: 197
MKRKPMSRKA SQKTFKKNTG VQRMNHLNPR AMRGGIRL                          38

SEQ ID NO: 198         moltype = DNA  length = 168
FEATURE                Location/Qualifiers
source                 1..168
                       mol_type = other DNA
                       organism = Pseudomonas phage PP7
SEQUENCE: 198
ttgtcgtcaa ccttgtgccg ctgggccgtt aaggccctgc ggtgtacccg tgtgtataag  60
gagtttatat ggaaaccctt agtagcgctc agttacgtga cgttgtatct tctgagctcg  120
gtcttcctgt cccaactcag ctaccccatc gggagctggg cggtgtag               168

SEQ ID NO: 199         moltype = AA  length = 55
FEATURE                Location/Qualifiers
source                 1..55
                       mol_type = protein
                       organism = Pseudomonas phage PP7
SEQUENCE: 199
MSSTLCRWAV KALRCTRVYK EFIWKPLVAL SYVTLYLLSS VFLSQLSYPI GSWAV       55

SEQ ID NO: 200         moltype = DNA  length = 108
FEATURE                Location/Qualifiers
source                 1..108
                       mol_type = other DNA
                       organism = Acinetobacter phage AP205
SEQUENCE: 200
atgaagaaaa ggacaaaagc cttgcttccc tatgcggttt tcatcatact cagctttcaa  60
ctaacattgt tgactgcctt gtttatgtat taccattata ccttttag               108

SEQ ID NO: 201         moltype = AA  length = 35
FEATURE                Location/Qualifiers
source                 1..35
                       mol_type = protein
                       organism = Acinetobacter phage AP205
SEQUENCE: 201
MKKRTKALLP YAVFIILSFQ LTLLTALFMY YHYTF                             35

SEQ ID NO: 202         moltype = DNA  length = 558
FEATURE                Location/Qualifiers
source                 1..558
                       mol_type = other DNA
                       organism = Acinetobacter phage vB_AbaP_CEB1
SEQUENCE: 202
atgattctga ctaaagatgg gtttggtatt atccgtaatg aactattcgg aggtaagtta  60
gatcaaactc aagtagatgc aataaacttt attgtagaga aagctactga gtctggttta  120
tcttatccag aggcagccta tttactagct accatctatc atgagactgg tctaccaagc  180
ggttatcgaa ctatgcaacc tattaaagaa gctggttctg ataactacct tcgatctaag  240
aagtactacc cgtacattgg ttatggttat gtacagttaa cttggaagga gaactatgga  300
cggattggta aacttattgg aattgaccta attaagaatc ctgagaaagc gctagaacct  360
ttaattgcta ttcagattgc tatcaaaggc atgttgaatg gttggttcac aggtgttgga  420
ttccgacgta aacgtccagt tagtaaatac aacaaacagc agtacatagc tgcgcgtaat  480
atcattaatg ggaaagataa ggctgagctt atagcgaagt acgctattat ctttgaacgc  540
gctctacgga gcttataa                                                558

SEQ ID NO: 203         moltype = AA  length = 185
FEATURE                Location/Qualifiers
source                 1..185
                       mol_type = protein
                       organism = Acinetobacter phage vB_AbaP_CEB1
SEQUENCE: 203
MILTKDGFGI IRNELFGGKL DQTQVDAINF IVEKATESGL SYPEAAYLLA TIYHETGLPS  60
GYRTMQPIKE AGSDNYLRSK KYYPYIGYGY VQLTWKENYG RIGKLIGIDL IKNPEKALEP  120
LIAIQIAIKG MLNGWFTGVG FRRKRPVSKY NKQQYIAARN IINGKDKAEL IAKYAIIFER  180
ALRSL                                                              185

SEQ ID NO: 204         moltype = AA  length = 36
FEATURE                Location/Qualifiers
REGION                 1..36
                       note = MISC_FEATURE - PMAP-36
source                 1..36
                       mol_type = protein
                       organism = Sus scrofa
SEQUENCE: 204
GRFRRLRKKT RKRLKKIGKV LKWIPPIVGS IPLGCG                            36
```

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SEQ ID NO: 205          moltype = DNA  length = 519
FEATURE                 Location/Qualifiers
misc_feature            1..519
                        note = GOS_4958713 hypothetical protein GOS_4958713,
                         partial [marinemetagenome]
source                  1..519
                        mol_type = other DNA
                        organism = unidentified
SEQUENCE: 205
atgaccccat ttgaccacgc cctcgagctc accctcggat tggagggtgg atactccaat  60
catttaatgg accgtggcgg agagaccatg tgcggtataa cggaggccgt agcacggagg  120
cacggatggg agggtgagat gcgagaccta cccatcgaaa tggtccggca tatttacaag  180
gtggattatt gggacccatt gatgggtgat tacctgggag aacacaaccc ggagctcgcg  240
gaggaattat ttgatacggc cgttaattgt ggcgtgggtt ttgcgtccaa gattctccaa  300
aagagcatca acgtattaaa ccgcaaccgg accgaggaca ttgcggagga tggccaaatc  360
ggtccacaaa ccctcaaggc tttacgggat ttggctcggc gtgattatga ttatttactc  420
gagtgttgca agattctcca gggtaaccat tatataagcc tagcccatcg cgaccccacc  480
caacggatat tcattcgagg atggttgacc agggtatga                          519

SEQ ID NO: 206          moltype = AA  length = 172
FEATURE                 Location/Qualifiers
REGION                  1..172
                        note = GOS_4958713 hypothetical protein GOS_4958713,
                         partial [marinemetagenome]
source                  1..172
                        mol_type = protein
                        organism = unidentified
SEQUENCE: 206
MTPFDHALEL TLGLEGGYSN HLMDRGGETM CGITEAVARR HGWEGEMRDL PIEMVRHIYK  60
VDYWDPLMGD YLGEHNPELA EELFDTAVNC GVGFASKILQ KSINVLNRNR TEDIAEDGQI  120
GPQTLKALRD LARRDYDYLL ECCKILQGNH YISLAHRDPT QRIFIRGWLT RV          172

SEQ ID NO: 207          moltype = DNA  length = 450
FEATURE                 Location/Qualifiers
source                  1..450
                        mol_type = other DNA
                        organism = Pseudomonas putida
SEQUENCE: 207
atgacataca acgctggaac gaaaccccgc gctgagacgg actacctggt agttcactgt  60
agcgccacgc gaccatccca agacatcggg gctgctgaca tcaaccgctg gcatcgcgcc  120
aaaggttggc ggtgcatcgg ctatcacttt gtcatccgcc gcaatggcgt ggtggaggag  180
ggccgcgagc tggatcaaat cggcgcccac gtagagggcc ataacatcaa ctccgtaggc  240
atttgcatgg ccggtggagt caccgaggcg gacatcaacg tccccgaaaa caacttcacg  300
cccgagcagt ttgcaagtct caagcacctg ctgggcgagc tgaaagagaa ataccccagc  360
gcgacaatcc aaggccaccg ggacttcccg aaagtagcca aggcttgccc gagcttcgac  420
gttaaaccgt gggtagcggc caacttataa                                   450

SEQ ID NO: 208          moltype = AA  length = 149
FEATURE                 Location/Qualifiers
source                  1..149
                        mol_type = protein
                        organism = Pseudomonas putida
SEQUENCE: 208
MTYNAGTKPR AETDYLVVHC SATRPSQDIG AADINRWHRA KGWRCIGYHF VIRRNGVVEE  60
GRELDQIGAH VEGHNINSVG ICMAGGVTEA DINVPENNFT PEQFASLKHL LGELKEKYPS  120
ATIQGHRDFP KVAKACPSFD VKPWVAANL                                    149

SEQ ID NO: 209          moltype = DNA  length = 636
FEATURE                 Location/Qualifiers
source                  1..636
                        mol_type = other DNA
                        organism = Micavibrio aeruginosavorus
SEQUENCE: 209
atgtttagac catcttatat tttgcccggt gtggcggcgg tgatgctgtt ggcatcgacg  60
gcggcgcatg cggccggata tgaatggaaa cgcgttgatt accaatacct gcaaagcgtt  120
tccgaaaaag agcgcggcat gttgcgtatt tataaagatt acgaagaacg cgagccgtgc  180
caaaattacc gcgagcttcc gcccgaggta aaatacgtgg attgtaaatt gtatcaccgc  240
gtagcaatcc cagatccacc acccccaccc gctccgccac cggctcccga gcctccgaaa  300
gttgtgtcca gctatgaaat cttcttccca ctggacagca cggctctgga tctgcaggcc  360
aatgccatgg ttgataaagc cgctgccgac attgcgctgt atcaacccag caccgtgatt  420
gtggccgggt ataccgacac gtccggcgcg gcggattata atgaccagtt gtctgccaac  480
cgggccatgg cggtgtctgc cgcgttgagc cagcgtggca tcccgaacac ggcgatggac  540
ctggaggctc acggtcagaa tgacctgaaa gtgccgacag cggacgatgt tcacgagccg  600
caaaaccgcc gcacggtcat tcatttcatg aaatag                             636
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SEQ ID NO: 210 moltype = AA length = 211
FEATURE Location/Qualifiers
source 1..211
mol_type = protein
organism = Micavibrio aeruginosavorus
SEQUENCE: 210
MFRPSYILPG VAAVMLLAST AAHAAGYEWK RVDYQYLQSV SEKERGMLRI YKDYEEREPC 60
QNYRELPPEV KYVDCKLYHR VAIPDPPPPP APPPAPEPPK VVSSYEIFFP LDSTALDLQA 120
NAMVDKAAAD IALYQPSTVI VAGYTDTSGA ADYNDQLSAN RAMAVSAALS QRGIPNTAMD 180
LEAHGQNDLK VPTADDVHEP QNRRTVIHFM K 211

SEQ ID NO: 211 moltype = DNA length = 723
FEATURE Location/Qualifiers
misc_feature 1..723
note = SMAP29-KZ144(Artilysin) AMP fusion to N-terminus
source 1..723
mol_type = other DNA
organism = synthetic construct
SEQUENCE: 211
ggagaattca ccatgagggg acttcgaaga ctgggtagga agatagcaca tggtgtgaag 60
aagtatggcc caactgttct ccgaataatc agaatagctt ctgataaacg cgttgaaatt 120
accggaaacg tttccggttt tttcgagtcc ggtggccgtg gtgtaaaaac cgtttctacc 180
ggcaaaggtg acaacggcgg tgtgagctac ggcaagcatc agctggcgtc gaataacggc 240
tctatggctc tgttccttga atctccgttc ggtgctccgt accgtgcgca attcgcagga 300
ctgaaaccgg gaaccgctgc gtttacttcc gtgtacaaca aaatcgcaaa tgaaacgccg 360
accgcgtttg aacgggacca gttccaatac atcgcggctt cgcactacga tccacaagcg 420
gccaagctga aagccgaagg cattaacgtc gatgaccgac atgtcgcggt gcgtgaatgc 480
gtgttcagcg tagccgtgca atatggtcga aatacttcga tcattatcaa agcactcggc 540
agtaatttcc ggggcagcga caaagacttc atcgaaaagg tgcaggacta tcgcggtgcc 600
acggttaaca cctactttaa atccagtagc cagcaaactc gcgacagcgt gaaaaaccgc 660
tcgcagcaag aaaagcaaat gctgctgaaa ctcctgaata gttaataagc ttggctgttt 720
tgg 723

SEQ ID NO: 212 moltype = AA length = 230
FEATURE Location/Qualifiers
REGION 1..230
note = SMAP29-GN13, (Artilysin) AMP fusion to N-terminus
source 1..230
mol_type = protein
organism = synthetic construct
SEQUENCE: 212
MRGLRRLGRK IAHGVKKYGP TVLRIIRIAS DKRVEITGNV SGFFESGGRG VKTVSTGKGD 60
NGGVSYGKHQ LASNNGSMAL FLESPFGAPY RAQFAGLKPG TAAFTSVYNK IANETPTAFE 120
RDQFQYIAAS HYDPQAAKLK AEGINVDDRH VAVRECVFSV AVQYGRNTSI IIKALGSNFR 180
GSDKDFIEKV QDYRGATVNT YFKSSSQQTR DSVKNRSQQE KQMLLKLLNS 230

SEQ ID NO: 213 moltype = DNA length = 1005
FEATURE Location/Qualifiers
source 1..1005
mol_type = other DNA
organism = Staphylococcus sciuri
SEQUENCE: 213
ggagaattca ccatggaaaa tatacaaaaa ggtatcaccg tagacatcgc aagaaaatca 60
tattccttag aaactttaaa aaccatcgtt aaacatatac atgatcacaa tggtcaatac 120
cttcaattac atttttcaga tgatgaaaat tacgcaattg aatcagaata ttttgatcgt 180
aaaagttttt ctaatccata ttatttaaca aaaacagaag tgaaatcact tattgagtat 240
agtaatgatt taaatgtaat ggtcattcca gatatggatt ttccctctca ttccaaagct 300
tttttatctt tgattaaaca aaatgataaa tcattatatc aagaaataat cagtgattat 360
agtgataaca ctttagattt tttctcaaat cgtaaagcag tagatgttac aaatagacaa 420
attgatgaaa taacagagtt gtttaaacaa cctcaatttg cagaacaaca acgaattgta 480
ctcggtgggg atgaagtagc aggtggaggt gcgcatcaaa atagctttat agaatatatg 540
aatcaaatag gtgactatgc atttcaacaa ggatatgagc cacagatgtg gaatgatatg 600
gtcacgcatg aaggggtgaa gtctttaaat aaccattatt caatattata ttggaagcaa 660
aatgaagaca ataaatctaa tttaactgta gaagattttg ataaatatta ttttgatgta 720
tataactata attattattc gttatatttc ttgccttcaa aacagtttag ccaggacgat 780
attaatgaac aggctgaata tataggttgg gcatatgcat ataacaaatt ttattataat 840
aagaatcctt atagtgaagt gaatagtcaa aatgttaaag gatctgcatt atcattttgg 900
ggtgaacatg caactgatat gacacaagaa gaattaatca atcaagaagt gcctttgatt 960
aaagtatatt ttaatcttaa gaagtgataa gcctggctgt tctgg 1005

SEQ ID NO: 214 moltype = AA length = 324
FEATURE Location/Qualifiers
source 1..324
mol_type = protein
organism = Staphylococcus sciuri
SEQUENCE: 214

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MENIQKGITV DIARKSYSLE TLKTIVKHIH DHNGQYLQLH FSDDENYAIE SEYFDRKSFS  60
NPYYLTKTEV KSLIEYSNDL NVMVIPDMDF PSHSKAFLSL IKQNDKSLYQ EIISDYSDNT  120
LDFFSNRKAV DVTNRQIDEI TELFKQPQFA EQQRIVLGGD EVAGGGAHQN SFIEYMNQIG  180
DYAFQQGYEP QMWNDMVTHE GVKSLNNHYS ILYWKQNEDN KSNLTVEDFD KYYFDVYNYN  240
YYSLYFLPSK QFSQDDINEQ AEYIGWAYAY NKFYYNKNPY SEVNSQNVKG SALSFWGEHA  300
TDMTQEELIN QEVPLIKVYF NLKK                                          324

SEQ ID NO: 215          moltype = DNA  length = 834
FEATURE                 Location/Qualifiers
misc_feature            1..834
                        note = OBG_GN4_2 (Lyz+C-term)
source                  1..834
                        mol_type = other DNA
                        organism = synthetic construct
SEQUENCE: 215
ggagaattca ccatgaaaaa tagcgagaag aatgcatcga taattatgtc gatacagaga  60
acgctcgctt cactctcact ctatggaggc cgcatcgacg gcctctttgg agagaagtgt  120
cgtggggcta tcatcttgat gctgaataag gtctatccta atttcagcac caacaaactt  180
ccgagtaaca catatgaagc ggaatccgtg ttcacgtttc tccagactgc tttggctggt  240
gttggtcttt ataccattac tattgatggt aaatggggtg gtacttctca aggtgctatt  300
gacgccctcg tcaagtctta ccgtcaaatt accgaagcgg agcgagctgg gtcgacgttg  360
ccattaggtc ttgctactgt gatgtctaca tcccaacgag gcatcgacct catcaaatcc  420
ttcgagggcc tgcgcctgtc cgcttaccag gactcggtgg gtgtctggac cataggttac  480
ggcaccactc ggggcgtcac ccgctacatg acgatcaccg tcgagcaggc cgagcggatg  540
ctgtcgaacg acattcagcg cttcgagcca gagctagaca ggctggcgaa ggtgccactg  600
aaccagaacc agtgggatgc cctgatgagc ttcgtgtaca acctgggcgc ggccaatctg  660
gcgtcgtcca cgctgctcaa gctgctgaac aagggtgact accagggagc agcggaccag  720
ttcccgcgct gggtgaatgc gggcggtaag cgcttggatg gtctggttaa gcgtcgagca  780
gccgagcgtg cgctgttcct ggagccacta tcgtaataag cttggctgtt ttgg         834

SEQ ID NO: 216          moltype = AA  length = 267
FEATURE                 Location/Qualifiers
REGION                  1..267
                        note = OBG_GN4_2 (Lyz+C-term)
source                  1..267
                        mol_type = protein
                        organism = synthetic construct
SEQUENCE: 216
MKNSEKNASI IMSIQRTLAS LSLYGGRIDG LFGEKCRGAI ILMLNKVYPN FSTNKLPSNT  60
YEAESVFTFL QTALAGVGLY TITIDGKWGG TSQGAIDALV KSYRQITEAE RAGSTLPLGL  120
ATVMSTSQRG IDLIKSFEGL RLSAYQDSVG VWTIGYGTTR GVTRYMTITV EQAERMLSND  180
IQRFEPELDR LAKVPLNQNQ WDALMSFVYN LGAANLASST LLKLLNKGDY QGAADQFPRW  240
VNAGGKRLDG LVKRRAAERA LFLEPLS                                       267

SEQ ID NO: 217          moltype = DNA  length = 438
FEATURE                 Location/Qualifiers
source                  1..438
                        mol_type = other DNA
                        organism = Pseudomonas putida
SEQUENCE: 217
atgagcattt tcagtttcgt caaagaagca ggcgagaaac ttatcgacct gttgaccccg  60
ggtaatgcca atgccagcga gcagttgaag gagcatgtct ccaaggtagg cttgggcaat  120
ccgaacattc agacaactgt cgagggcagc aaggtgacgg tcaccggcga ggtggccagc  180
caggaagaga aggagaaaat cctgctggcg ctgggcaaca ttgccggtgt ggagtcggtg  240
gatgatcaga tcactgttac cgggcctctg gttgccgctg cccgttttgt cgtggtgaag  300
aagggcgaca ccctcagtgc catttccctg gctgtgtacg gcaacgccaa ccagtacaac  360
aagattttcg aagccaacaa gccgctgctc agccacccgg acaagatcta cccgggccag  420
accctgcgca tccctgaa                                                 438

SEQ ID NO: 218          moltype = AA  length = 146
FEATURE                 Location/Qualifiers
source                  1..146
                        mol_type = protein
                        organism = Pseudomonas putida
SEQUENCE: 218
MSIFSFVKEA GEKLIDLLTP GNANASEQLK EHVSKVGLGN PNIQTTVEGS KVTVTGEVAS  60
QEEKEKILLA LGNIAGVESV DDQITVTGPL VAAARFVVVK KGDTLSAISL AVYGNANQYN  120
KIFEANKPLL SHPDKIYPGQ TLRIPE                                        146

SEQ ID NO: 219          moltype = DNA  length = 891
FEATURE                 Location/Qualifiers
source                  1..891
                        mol_type = other DNA
                        organism = Pseudomonas protegens
SEQUENCE: 219
gtttaacttt aagaaggaga attcaccatg aacacactcc ggcacggcga tcgctcgcaa  60
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gcggtacgca gcctgcagaa gaacctcaac agccacgggg ccatcctggt ggtggacggc  120
gactacggcg acgccaccga agcggccgtg cgcgcctacc agctcaaggc cggcctggtg  180
gtggacggta tcgccggcga gaaaacccaa accagcctgg tcggtggcga ttgcgctctg  240
ctgctgaaga acgccgacct ggtcagcgcc gcccagcgcc tggatctgcc cctcgccagt  300
gtctacgcgg tcaatgaggt cgaatcgaac ggcaagggct tcttcgccaa cggcaagccg  360
gcgatcctgt ttgagcggca catcatgtac cgccaattga agacgccacg ctacccaggc  420
gacgacccgg cagaactcaa gcgccacgcc gacgagcttg cggcgcagta cccggccatc  480
atcaatccga acccgggtgg ttatgccggc ggccctgctg agcatcagcg cctggccacg  540
gcccgcctga tcgatgacac cgcggccctg gagtctgcct cctggggcgc cttccagatc  600
atgggctttc actggaagcg cctcggctat gccagcgtgc aggacttcgt gacggccatg  660
agcgcgagcg agccccgcca gtttgaggcc ttcgtccgct tcatcgagac cgatccggcc  720
ctccacaaag cgctgaaggc ccgcaagtgg tccgacttcg ccaggcagta caacgggccg  780
aactaccaac gcaacctgta cgacaccaag ctccagcgcg cctatgagcg acatagcgcc  840
tgcagctgcg gtcaggaggt accggcatga taaaagcttg gctgttttgg c           891

SEQ ID NO: 220         moltype = AA  length = 280
FEATURE                Location/Qualifiers
source                 1..280
                       mol_type = protein
                       organism = Pseudomonas protegens
SEQUENCE: 220
MNTLRHGDRS QAVRSLQKNL NSHGAILVVD GDYGDATEAA VRAYQLKAGL VVDGIAGEKT  60
QTSLVGGDCA LLLKNADLVS AAQRLDLPLA SVYAVNEVES NGKGFFANGK PAILFERHIM  120
YRQLKTPRYP GDDPAELKRH ADELAAQYPA IINPNPGGYA GGPAEHQRLA TARLIDDTAA  180
LESASWGAFQ IMGFHWKRLG YASVQDFVTA MSASEPRQFE AFVRFIETDP ALHKALKARK  240
WSDFARQYNG PNYQRNLYDT KLQRAYERHS ACSCGQEVPA                        280

SEQ ID NO: 221         moltype = DNA  length = 897
FEATURE                Location/Qualifiers
misc_feature           1..897
                       note = SMAP29-KZ144, (Artilysin) AMP fusion to N-terminus
source                 1..897
                       mol_type = other DNA
                       organism = synthetic construct
SEQUENCE: 221
ggagaattca ccatgagggg acttcgaaga ctgggtagga agatagcaca tggtgtgaag  60
aagtatggcc caactgttct ccgaataatc agaatagcta aagtattacg caaaggcgat  120
aggggtgatg aggtaagcca actccagaca ctcttaaatt taagcggcta tgatgttgga  180
aagccagatg gtatttttgg aaataacacc tttaatcagg tagttaaatt tcaaaaagat  240
aatagcctag atagtgatgg tattgtaggt aagaatactt gggctgaatt attcagtaaa  300
tattctccac ctattcctta taaaactatc cctatgccaa ctgcaaataa atcacgtgca  360
gctgcaactc cagttatgaa tgcagtagaa aatgctactg gcgttcgtag ccagttgcta  420
ctaacatttg cttctattga atcagcattc gattacgaaa taaaagctaa gacttcatca  480
gctactggtt ggttccaatt ccttactgga acatggaaaa caatgattga aaattatggc  540
atgaagtatg gcgtacttac tgatccaact ggggcattac gtaaagatcc acgtataagt  600
gctttaatgg gtgccgaact aattaaagag aatatgaata ttcttcgtcc tgtccttaaa  660
cgtgaaccaa ctgatactga tctttattta gctcacttct ttgggcctgg tgcagcccgt  720
cgtttcctga ccactggcca gaatgaatta gctgctaccc atttcccaaa agaagctcag  780
gcaaacccat ctatttttta taacaaagat gggtcaccta aaaccattca agaagtttat  840
aacttaatgg atggtaaagt tgcagcacat agaaaataat aagcttggct gttttgg     897

SEQ ID NO: 222         moltype = AA  length = 288
FEATURE                Location/Qualifiers
REGION                 1..288
                       note = SMAP29-KZ144, (Artilysin) AMP fusion to N-terminus
source                 1..288
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 222
MRGLRRLGRK IAHGVKKYGP TVLRIIRIAK VLRKGDRGDE VSQLQTLLNL SGYDVGKPDG  60
IFGNNTFNQV VKFQKDNSLD SDGIVGKNTW AELFSKYSPP IPYKTIPMPT ANKSRAAATP  120
VMNAVENATG VRSQLLLTFA SIESAFDYEI KAKTSSATGW FQFLTGTWKT MIENYGMKYG  180
VLTDPTGALR KDPRISALMG AELIKENMNI LRPVLKREPT DTDLYLAHFF GPGAARRFLT  240
TGQNELAATH FPKEAQANPS IFYNKDGSPK TIQEVYNLMD GKVAAHRK               288

SEQ ID NO: 223         moltype = DNA  length = 945
FEATURE                Location/Qualifiers
misc_feature           1..945
                       note = SMAP29-KZ144 (1440) C Term His, HisTagged Art175
                        (SMAP29-KZ144)
source                 1..945
                       mol_type = other DNA
                       organism = synthetic construct
SEQUENCE: 223
gtttaacttt aagaaggaga attcaccatg cgtggtctgc gtcgtctggg tcgtaaaatc  60
gctcacggtg ttaaaaaata cggtccgacc gttctgcgta tcatccgtat cgctggtgga  120
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tccaaagtat tacgcaaagg cgataggggt gatgaggtaa gccaactcca gacactctta  180
aatttaagcg gctatgatgt tggaaagcca gatggtattt ttggaaataa caccttaat  240
caggtagtta aatttcaaaa agataatagc ctagatagtg atggtattgt aggtaagaat  300
acttgggctg aattattcag taaatattct ccacctattc cttataaaac tatccctatg  360
ccaactgcaa ataaatcacg tgcagctgca actccagtta tgaatgcagt agaaaatgct  420
actggcgttc gtagccagtt gctactaaca tttgcttcta ttgaatcagc attcgattac  480
gaaataaaag ctaagacttc atcagctact ggttggttcc aattccttac tggaacatgg  540
aaaacaatga ttgaaaatta tggcatgaag tatggcgtac ttactgatcc aactggggca  600
ttacgtaaag atccacgtat aagtgcttta atgggtgccg aactaattaa agagaatatg  660
aatattcttc gtcctgtcct taaacgtgaa ccaactgata ctgatcttta tttagctcac  720
ttctttgggc ctggtgcagc ccgtcgtttc ctgaccactg gccagaatga attagctgct  780
acccatttcc caaaagaagc tcaggcaaac ccatctattt tttataacaa agatgggtca  840
cctaaaacca ttcaagaagt ttataactta atggatggta aagttgcagc acatagaaaa  900
ctcgagcatc accatcatca ccactagtaa gcttggctgt tttgg                  945

SEQ ID NO: 224         moltype = AA  length = 299
FEATURE                Location/Qualifiers
REGION                 1..299
                       note = SMAP29-KZ144 (1440) C Term His, HisTagged Art175
                        (SMAP29-KZ144)
source                 1..299
                       mol_type = protein
                       organism = synthetic construct
SEQUENCE: 224
MRGLRRLGRK IAHGVKKYGP TVLRIIRIAG GSKVLRKGDR GDEVSQLQTL LNLSGYDVGK  60
PDGIFGNNTF NQVVKFQKDN SLDSDGIVGK NTWAELFSKY SPPIPYKTIP MPTANKSRAA  120
ATPVMNAVEN ATGVRSQLLL TFASIESAFD YEIKAKTSSA TGWFQFLTGT WKTMIENYGM  180
KYGVLTDPTG ALRKDPRISA LMGAELIKEN MNILRPVLKR EPTDTDLYLA HFFGPGAARR  240
FLTTGQNELA ATHFPKEAQA NPSIFYNKDG SPKTIQEVYN LMDGKVAAHR KLEHHHHHH   299

SEQ ID NO: 225         moltype = DNA  length = 1086
FEATURE                Location/Qualifiers
source                 1..1086
                       mol_type = other DNA
                       organism = Actinobacillus pleuropneumoniae
SEQUENCE: 225
ggagaattca ccatggactt acctaaaaaa gaaagcggtc tgacgttaga tatcgcacgt  60
cgtttctata ccgttgatac gataaaacaa tttatcgata cgattcatca ggcgggcggc  120
acttttctgc atttacattt ttccgatcac gagaattatg cattggaaag ttcttatttg  180
gaacaacgag aagaaaatgc gaccgagaaa aacggaacct atttcaatcc gaaaacaaat  240
aagccgtttc tcacttataa acagctcaat gaaattatct attatgccaa agaacgaaat  300
attgaaattg tgcctgaagt cgatagcccg aatcatatga cggcgatttt tgatctttta  360
acccttaagc acggaaagga atacgtaaaa gggctaaaat cgccttatat cgccgaggaa  420
atcgatatta ataaccccga agcggttgaa gttattaaaa ccttaatcgg tgaagtgatc  480
tatattttcg gacattcaag ccggcatttc catatcggcg gagatgaatt tagctatgcg  540
gtcgaaaata atcatgaatt tattcggtat gtgaatacct taaatgattt tatcaattcc  600
aaagggctaa ttacccgtgt ttggaatgac ggtttgatca aaaacaactt aagcgaactc  660
aataaaaaca ttgaaatcac ttactggagc tacgacggtg acgctcaagc caaagaagat  720
attcaatatc gacgtgaaat aagagccgat ttgcccgaac tgctggcaaa cggttttaag  780
gttttaaact ataattctta ttatttatac tttgtgccta aatccggttc taatattcac  840
aatgacggta aatatgcggc tgaagacgta ttaaataact ggacattagg taaatgggac  900
ggaaaaaaca gctcaaatca cgtacaaaat acgcagaata ttatcggttc ttctttgtcg  960
atttgggggg aacgttccag cgcattaaat gaacaaacta ttcagcaagc ctctaaaaat  1020
ttattaaaag cggtgatcca aaaaactaat gatccgaaat cgcattaata agcttggctg  1080
ttttgg                                                             1086

SEQ ID NO: 226         moltype = AA  length = 351
FEATURE                Location/Qualifiers
source                 1..351
                       mol_type = protein
                       organism = Actinobacillus pleuropneumoniae
SEQUENCE: 226
MDLPKKESGL TLDIARRFYT VDTIKQFIDT IHQAGGTFLH LHFSDHENYA LESSYLEQRE  60
ENATEKNGTY FNPKTNKPFL TYKQLNEIIY YAKERNIEIV PEVDSPNHMT AIFDLLTLKH  120
GKEYVKGLKS PYIAEEIDIN NPEAVEVIKT LIGEVIYIPG HSSRHFHIGG DEFSYAVENN  180
HEFIRYVNTL NDFINSKGLI TRVWNDGLIK NNLSELNKNI EITYWSYDGD AQAKEDIQYR  240
REIRADLPEL LANGFKVLNY NSYYLYFVPK SGSNIHNDGK YAAEDVLNNW TLGKWDGKNS  300
SNHVQNTQNI IGSSLSIWGE RSSALNEQTI QQASKNLLKA VIQKTNDPKS H           351

SEQ ID NO: 227         moltype = AA  length = 186
FEATURE                Location/Qualifiers
source                 1..186
                       mol_type = protein
                       organism = Delftia sp.
SEQUENCE: 227
MALTEQDFQS AADDLGVDVA SVKAVTKVES RGSGFLLSGV PKILFERHWM FKLLKRKLGR  60
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DPEINDVCNP KAGGYLGGQA EHERLDKAVK MDRDCALQSA SWGLFQIMGF HWEALGYASV  120
QAFVNAQYAS EGSQLNTFVR FIKTNPAIHK ALKSKDWAEF ARRYNGPDYK KNNYDVKLAE  180
AYQSFK                                                             186
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1.-**19**. (canceled)

20. A method of treating a bacterial infection caused by a Gram-negative bacteria, wherein the Gram-negative bacteria is an extensively antibiotic-resistant (XDR) bacteria, which method comprises:

administering to a subject diagnosed with, at risk for, or exhibiting symptoms of a bacterial infection, a pharmaceutical composition comprising a lysin-AMP polypeptide construct comprising:

(a) a first component comprising the polypeptide sequence of:

(i) SEQ ID NO: 118 (GN202); or

(ii) a polypeptide having lytic activity and having at least 80% sequence identity with the polypeptide sequence of SEQ ID NO: 118 (GN202); or

(iii) an active fragment of SEQ ID NO: 118 (GN202); and

(b) a second component comprising the polypeptide sequence of at least one antimicrobial peptide (AMP), wherein the at least one AMP comprises the polypeptide sequence of SEQ ID NO: 114 (FIRL).

21. The method according to claim **20**, wherein the lysin-AMP polypeptide construct comprises the polypeptide sequence of SEQ ID NO: 44 (GN370).

22. The method according to claim **20**, wherein the bacterial infection is a topical bacterial infection.

23. The method according to claim **20**, wherein the Gram-negative bacteria is *Pseudomonas aeruginosa.*

24. The method according to claim **20**, wherein the Gram-negative bacteria is selected from the group consisting of *Klebsiella pneumoniae, Acinetobacter baumannii, Enterobacter cloacae Escherichia coli, Stentrophomonas maltophilia, Achromobacter* spp., and *Pandorea apista.*

25. The method according to claim **20**, further comprising administering an antibiotic to the subject.

26. The method according to claim **25**, wherein the antibiotic is selected from one or more of ceftazidime, cefepime, cefoperazone, ceftobiprole, ciprofloxacin, levofloxacin, aminoglycosides, imipenem, meropenem, doripenem, gentamicin, tobramycin, amikacin, piperacillin, ticarcillin, penicillin, rifampicin, polymyxin B, and colistin.

27. The method of claim **20**, wherein the bacterial infection caused by a Gram-negative bacteria is a bacterial infection of an organ or tissue in which pulmonary surfactant is present.

28. The method of claim **20**, wherein the bacterial infection comprises pneumonia.

29. A method of preventing, disrupting or eradicating a Gram-negative bacterial biofilm, wherein the Gram-negative bacteria is an extensively antibiotic-resistant (XDR) bacteria, the method comprising:

administering a lysin-AMP polypeptide construct comprising:

(a) a first component comprising the polypeptide sequence of:

(i) SEQ ID NO: 118 (GN202); or

(ii) a polypeptide having lytic activity and having at least 80% sequence identity with the polypeptide sequence of SEQ ID NO: 118 (GN202); or

(iii) an active fragment of SEQ ID NO: 118 (GN202); and

(b) a second component comprising the polypeptide sequence of at least one antimicrobial peptide (AMP), wherein the at least one AMP comprises the polypeptide sequence of SEQ ID NO: 114 (FIRL) in an amount effective to kill Gram-negative bacteria in a biofilm to a subject in need thereof.

30. The method according to claim **29**, wherein the lysin-AMP construct comprises the polypeptide sequence of SEQ ID NO: 44 (GN370).

* * * * *