



## (51) International Patent Classification:

A61K 38/16 (2006.01) C07K 14/005 (2006.01)

A61K 38/46 (2006.01) C12N 15/62 (2006.01)

A61P 31/04 (2006.01)

62/860,836

13 June 2019 (13.06.2019)

US

## (21) International Application Number:

PCT/US2019/047916

## (22) International Filing Date:

23 August 2019 (23.08.2019)

## (25) Filing Language:

English

## (26) Publication Language:

English

## (30) Priority Data:

62/721,969 23 August 2018 (23.08.2018) US

62/722,793 24 August 2018 (24.08.2018) US

PCT/US2019/024912

29 March 2019 (29.03.2019) US

62/849,320 17 May 2019 (17.05.2019) US

(71) Applicant: CONTRAFECT CORPORATION [US/US]; 28 Wells Avenue, Yonkers, NY 10701 (US).

(72) Inventors: SCHUCH, Raymond; 116 Lake Drive, Mountain Lakes, NJ 07046 (US). INDIANI, Chiari; 421 Fair Street, Carmel, NY 10512 (US).

(74) Agent: PARKER, Linda T.; MH2 Technology Law Group, 1951 Kidwell Drive, Suite 310, Tysons Corner, VA 22180 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,

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

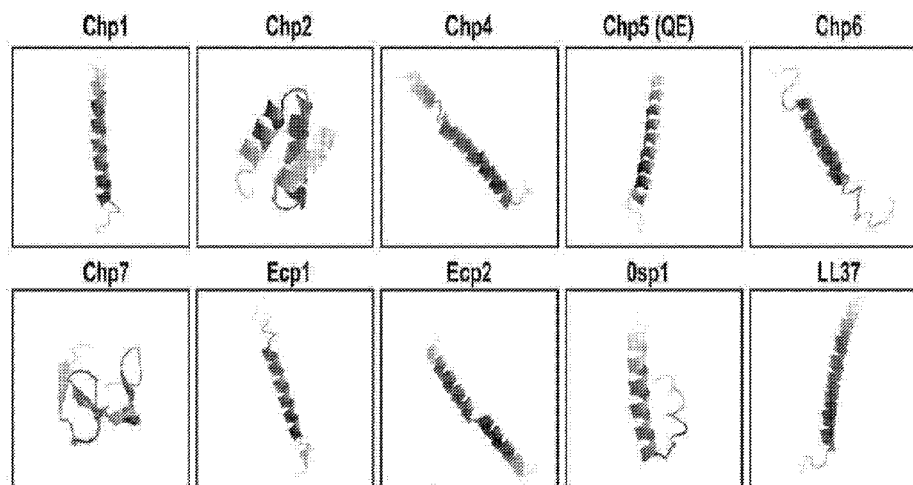


FIG. 1

(57) Abstract: The present disclosure is directed to lysin-AMP polypeptide constructs, isolated lysin polypeptides, and pharmaceutical compositions comprising the isolated polypeptides and/or lysin-AMP polypeptide constructs. Methods of using the lysin-AMP polypeptide constructs, isolated lysin polypeptides and pharmaceutical compositions are also herein provided, including methods of treating a bacterial infection of an organ or tissue in which pulmonary surfactant is present or Gram-negative bacterial infections that are associated with a biofilm. In addition, isolated polynucleotides encoding the lysin-AMP polypeptide constructs and isolated lysin polypeptides are disclosed herein.



OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

- (84) Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published:**

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
- *with information concerning one or more priority claims considered void (Rule 26bis.2(d))*
- *with sequence listing part of description (Rule 5.2(a))*

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

### **CROSS-REFERENCE TO RELATED APPLICATIONS**

[1] This application claims the benefit of, and relies on the filing date of PCT Application No. PCT/US2019/024912, filed on 29 March 2019, which claims the benefit of priority of U.S. provisional Application No. 62/722,793, filed 24 August 2018, U.S. Provisional Application No. 62/650,235, filed on 29 March 2018, and U.S. Provisional Application No. 62/721,969, filed on 23 August 2018, and also relies on the filing date of U.S. Provisional Application No. 62/849,320 filed on 17 May 2019 and U.S. Provisional Application No. 62/860,836 filed 13 June 2019, each of which is herein incorporated by reference in its entirety.

### **SEQUENCE LISTING**

[2] 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 August 22, 2019, is named 0341\_0021-00-304\_ST25.txt and is 249,856 bytes in size.

### **FIELD OF THE DISCLOSURE**

[3] 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**

[4] 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 surface and water supplies where it poses a host of threats to vulnerable patients.

[5] 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.

[6] 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 strains of *P. aeruginosa* that frequently require treatment with drugs of last resort, such as colistin.

[7] Moreover, reduced effectiveness of certain antibiotics is observed in combating 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, 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 Apr; 54(4):1404-1413.

[8] 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.

[9] 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.

[10] 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).

[11] 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  $\alpha$ -helical domains with polycationic, amphipathic, and hydrophobic features, are capable of translocating across the OM. However, artilysins typically exhibit low *in vivo* activity.

[12] 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

[13] 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.

**[14]** 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) a lysin selected from the group consisting of 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: 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.

**[15]** 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.

**[16]** 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 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: 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), 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.

**[17]** 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.

**[18]** 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,

wherein the isolated lysin comprises at least one of: (i) 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: 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

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 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: 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), ALCE1 (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.

**[19]** In 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.

**[20]** 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.

**[21]** 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,

wherein the isolated lysin comprises at least one of: (i) 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: 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

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 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: 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.

**[22]** 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,

wherein the isolated lysin comprises at least one of: (i) 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: 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

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 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: 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, 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.

### BRIEF DESCRIPTION OF THE DRAWINGS

[23] **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.

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

[25] **FIG. 2B** 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.

[26] **FIG. 3** is a series of photomicrographs showing microscopic analysis (x2000 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.

[27] **FIGS. 4A-4E** 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. 4A**), GN351 (**FIG. 4B**), GN370 (**FIG. 4C**), GN428 (**FIG. 4D**) and Ciprofloxacin (**FIG. 4E**).

## DETAILED DESCRIPTION

### Definitions

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

[29] “**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.

[30] “**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.

[31] “**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-log<sub>10</sub> (99.9%) or better reduction among an initial population of bacteria over an 18-24 hour period.

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

[33] “**Antibacterial**” refers to both bacteriostatic and bactericidal agents.

[34] “**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.

[35] “**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.

[36] “**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.

[37] **“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.

[38] **“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.

[39] **“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.

**[40] “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.

**[41] “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.

**[42] “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.

**[43] “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.

**[44] “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.

**[45] “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).

**[46] “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.

**[47] “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.

**[48] “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.

[49] “**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.

[50] “**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.

[51] 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 (GFP), 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.

**[52] “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.

**[53]** 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.

**[54]** 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).

**[55]** “**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.

**[56]** “**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.

[57] **“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.

[58] **“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.

[59] **“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.

[60] **“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.

[61] **“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 O-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**

### **Lysins, variant lysins, active fragments thereof or derivatives**

**[62]** 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, 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.

**[63]** 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  $\alpha$ -helical domains that facilitate binding to the anionic outer membrane of a Gram-negative bacteria to effect translocation into the sub-adjacent peptidoglycan.

**[64]** 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.

**[65]** 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.

**[66]** 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. T4 phage lysozyme is commercially available, e.g. from Sigma-Aldrich, Inc. GN126 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.

**[67]** 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.

[68] 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 Microbiol.* 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.

[69] 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. Microbiol.* 37: 1771-1776, which is also herein incorporated by reference in its entirety).

[70] 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  $1 \times 10^5$  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 ( $\Sigma$ FICs) are calculated for each drug and the minimum  $\Sigma$ FIC value ( $\Sigma$ FICmin) is used to determine the effect of the lysin/antibiotic combination.

[71] 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  $\leq 2$  for antibiotic sensitive bacteria, a MIC value of 4 for intermediately sensitive bacteria and a MIC value of  $\geq 8$  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.

[72] 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.

[73] 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).

**[74]** 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.

**[75]** Additional examples of suitable lysins of the present disclosure, particularly those for use with the present lysin-AMP polypeptide constructs, include the GN76 lysin obtained from *Acinetobacter* phage vB\_AbaP\_CEB1 (NCBI Reference Sequence ALC76575.1, SEQ ID NO: 203 GenBank: ALC76575.1), the GN4 lysin obtained from *Pseudomonas* phage PAJU2 (NCBI Reference Sequence YP\_002284361.1, SEQ ID NO: 74), the GN14 lysin obtained from *Pseudomonas* phage Lull (NCBI Reference Sequence YP\_006382555.1, SEQ ID NO: 124) and the GN37 lysin obtained from *Micavibrio aeruginosavorus* (NCBI Reference Sequence WP\_014102102.1, SEQ ID NO: 84). Each of the foregoing lysins is also disclosed in WO 2017/049233, which is herein incorporated by reference in its entirety.

**[76]** 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 and/or active fragment thereof described herein.

[77] 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.

[78] 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 December 12, 2017 and U.S. Provisional Application No. 62/721,969, which was filed on 23 August 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.

[79] 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 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: 203, 74, 78, 124, 84, 22, 96, 26, 56, 118, 58, 60, 64, 66, 28, 68, 173 and 175.

**[80]** 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.

**[81]** 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.

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

**[83]** In some embodiments, the  $\alpha$ -helix domain is located at the C terminus of a lysin. In other embodiments, the  $\alpha$ -helix domain is located at the N-terminus of a lysin. More typically, the  $\alpha$ -helix domain is located at the C terminus. The  $\alpha$ -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  $\alpha$ -helix domain, which is located at the N terminus, contains 15 amino acids (residues 66 to 80 of SEQ ID NO: 124). The GN37  $\alpha$ -helix domain, which is located at the C terminus, contains 14 amino acids (residues 113 to 126 of SEQ

ID NO: 84). The GN4  $\alpha$ -helix domain, which is also located at the C terminus, contains 25 amino acids (residues 116 to 140 of SEQ ID NO: 74).

**[84]** 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, 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).

**[85]** 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. Patent No. 5,604,109, which is incorporated herein in its entirety by reference.

**[86]** For example, one of skill in the art can reasonably make and test substitutions or replacements to, *e.g.*, the  $\alpha$ -helix domain or regions outside of the  $\alpha$ -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.

**[87]** 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.

**[88]** 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 anti-bacterial 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.

**[89]** 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 *P. aeruginosa* and optionally at least one 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. 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  $\alpha$ -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.

**[90]** 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) and GN121 (SEQ ID NO: 175) or an active fragment thereof, wherein the lysin or active fragment thereof 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. 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, 173 or 175. In certain embodiments, the at least one amino acid substitution is a conservative amino acid substitution.

**[91]** 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 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. 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.

**[92]** 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 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. 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.

#### *Anti-Microbial Peptides*

[93] 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,  $\beta$ -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.

[94] 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 in the presence and/or absence of human serum. 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.

[95] 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. 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 are known in the art and include those methods described above for the present lysins, derivatives and active fragments thereof.

[96] In some embodiments, the present AMPs are variant AMPs 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 any of the AMPs described herein, wherein the variant AMP thereof retains an AMP activity.

[97] In some embodiments, the present AMPs comprise a helical domain, such as an  $\alpha$ -helical domain. In some embodiments, the  $\alpha$ -helical domain spans most of the molecule. See, for example, Chp1 and Chp4 of FIG. 1. In other embodiments, the  $\alpha$ -helix domain is either interrupted (e.g., Chp2) or truncated (e.g., Chp6 and Osp1). The  $\alpha$ -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.

[98] 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  $\alpha$ -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.

[99] 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  $\phi$ X174 (Family Microviridae, genus *Microvirints*), 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 $\sim$  (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 Leviviridae, 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.

**[100]** In contrast to amurins, the amurin peptides of the present disclosure are small cationic peptides with predicted  $\alpha$ -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 Chlamydia microviruses 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.”

**[101]** 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 March, 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).

**[102]** 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 Spi2 (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).

**[103]** 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).

**[104]** 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  $\alpha$ -helical domain. Typically, the variant amurin peptides retain the  $\alpha$ -helical domain. The retention of the  $\alpha$ -helical domain in any variant amurin peptide is typically accurately identified using

various software programs, such as Jpred4 ([compio.dundee.ac.uk/jpred](http://compio.dundee.ac.uk/jpred)), Helical Wheel ([hael.net/helical.htm](http://hael.net/helical.htm)), HeliQuest ([zhanglab.ccmb.med.umich.edu/I-TASSER/](http://zhanglab.ccmb.med.umich.edu/I-TASSER/)) and PEP-FOLD 3 ([bioserv.rpbs.univ-paris-diderot.fr/services/PEP-FOLD3](http://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.

**[105]** 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  $\alpha$ -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.

**[106]** 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.

**[107]** 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.

[108] 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.

[109] 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).

### **Structure stabilizing components**

[110] 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.

[111] 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). GGGSGGGSGGGGS (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).

**[112]** 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 (**RPPGGGSGGGSGGGGS** residues 126 to 141 of SEQ ID NO: 12), at the N terminus of the BBA\_K1486037 linker (**PPGGGSGGGSGGGGS**, 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 (GGGSGGGSGGG**SPP**, residues 135-149 of SEQ ID NO: 20).

**[113]** In other embodiments, the peptides MIDR (SEQ ID NO: 112) and/or NP<sup>TH</sup> (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 NP<sup>TH</sup> (SEQ ID NO: 116) such as depicted at residues 1-12 of SEQ ID NO: 46 (**MIDRFIRLNP<sup>TH</sup>**) and residues 1-26 of SEQ ID NO: 44.

### Examples of Lysin-AMP Polypeptide Constructs

**[114]** In some embodiments, the lysin-AMP construct comprises: (a) a first component comprising (i) at least one lysin selected from the group consisting of 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

lysine 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 with the polypeptide sequence of any of SEQ ID NOs: 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 lysine, 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), ALCE1 (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.

**[115]** Typically, any of the AMP variants sharing at least 80% identity or more with the disclosed AMPs 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.

**[116]** 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).

**[117]** 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 AGAGAGAGAGAGAGAGAS (SEQ ID NO: 122).

**[118]** 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) 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 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.

**[119]** 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.

**[120]** 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.

**[121]** 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.

**[122]** 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.

**[123]** 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.

**[124]** 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.

**[125]** 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.

**[126]** 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.

**[127]** 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 TI15 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.

**[128]** 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.

**[129]** 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.

**[130]** 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.

**[131]** 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.

**[132]** 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.

**[133]** 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.

**[134]** 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.

**[135]** 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.

**[136]** 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 C-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.

**[137]** 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.

**[138]** 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. The purification tag for GN486 (SEQ ID NO: 66) is italicized and bolded. Single point mutations are bolded.

**Table 1**

| <b>GN #</b> | <b>Polypeptide Sequence</b>                                                                                                                                                                                                         |
|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GN168       | <u>MRLKMARRRYRLPRRRSRRLFSRTALRMHPRNRLRRIMRGGIRFTAGGTAGGRTSQRGIDLIKSFEGLRLSAYQDSVGVWTIGYGTTRGVTRYMTITVEQAERMLSNDIQRFEPELDR</u> LAKVPLNQNW DALMSFVYNLGAANLASSTLLDLLNKGDYQGAADQFPHWVNAGGKRLDGLVKRRAAERALFLEPLS ( <b>SEQ ID NO: 2</b> ) |
| GN176       | <u>MSENVTPKFKRWQLYFRGRMW</u> <u>TAGGTAGGRTSQRGIDLIKSFEGLRLSAYQDSVGVWTIGYGTTRGVTRYMTITVEQAERMLSNDIQRFEPELDR</u> LAKVPLNQNW DALMSFVYNLGAANLASSTLLDLLNKGDYQGAADQFPHWVNAGGKRLDGLVKRRAAERALFLEPLS ( <b>SEQ ID NO: 4</b> )                |

| GN #  | Polypeptide Sequence                                                                                                                                                                                                                                                                                          |
|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GN178 | MPPIFSKLAGKKIKNLLISGLKGGSGSGSGSGSPRTSQRGIDLIKSFEGLRLS<br>AYQDSVGVWTIGYGTTRGVTRYMTITVEQAERMLSNDIQRFEPELDRLA<br>KVPLNQNQWDALMSFVYNLGAANLASSTLLDLLNKGDYQGAADQFPH<br>WVNAGGKRLDGLVKRRRAERALEPLS (SEQ ID NO: 6)                                                                                                    |
| GN217 | MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL<br>VAAGASKTMNSRHLTGHAVDLAAYVNGIHWDWPLYDAIAVAVKAAAK<br>ELGVAIVWGGDWTTFKDGPHFELDRSKYR (SEQ ID NO: 8)                                                                                                                                                         |
| GN218 | <u>MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL</u><br><u>VAAGASKTMNSRHLTGHAVDLAAYVNGIRWDWPLYDAIAVAVKAAAK</u><br><u>ELGVAIVWGGDWTTFKDGPHFELDRSKYGGGSGGGGSGGGSRKKIGKV</u><br><u>LKWI (SEQ ID NO: 10)</u>                                                                                                 |
| GN223 | <u>MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL</u><br><u>VAAGASKTMNSRHLTGHAVDLAAYVNGIRWDWPLYDAIAVAVKAAAK</u><br><u>ELGVAIVWGGDWTTFKDGPHFELDRSKYRPPGGGSGGGGSGGGSSKKAS</u><br><u>RKSFTEGAVKVHKKNPTRVPMRGGIRL (SEQ ID NO: 12)</u>                                                                         |
| GN239 | <u>MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL</u><br><u>VAAGASKTMNSRHLTGHAVDLAAYVNGIRWDWPLYDAIAVAVKAAAK</u><br><u>ELGVAIVWGGDWTTFKDGPHFELDRSKYGGGSGGGGSGGGSRKKTRKRL</u><br><u>KKIGKVLKWI (SEQ ID NO: 14)</u>                                                                                          |
| GN243 | <u>MTYTLSKRSLDNLKGVHPDLVAVVHRAIQLTPVDFAVIEGLRSVSRQKEL</u><br><u>VAAGASKTMNSRHLTGHAVDLAAYVNGIRWDWPLYDAIAVAVKAAAK</u><br><u>ELGVAIVWGGDWTTFKDGPHFELDRSKYRKKTRKRLKKIGKVLKWIPP</u><br><u>GGSGGGGSGGGSTRKRLKKIGKVLKWI (SEQ ID NO: 16)</u>                                                                          |
| GN280 | <u>MKLSEKRALFTQLLAQLILWAGTQDRVSVALDQVKRTQAEADANAKSG</u><br><u>AGIRNSLHLLGLAGDLILYKDGKYMCKSEDYKFLGDYWKSLHPLCRWG</u><br><u>GDFKSRPDGNHFSLEHEGVQRKKTRKRLKKIGKVLKWI</u><br><u>PPTAGGTAGGTRKRLKKIGKVLKWI (SEQ ID NO: 18)</u>                                                                                       |
| GN281 | <u>MKLSEKRALFTQLLAQLILWAGTQDRVSVALDQVKRTQAEADANAKSG</u><br><u>AGIRNSLHLLGLAGDLILYKDGKYMCKSEDYKFLGDYWKSLHPLCRWG</u><br><u>GDFKSRPDGNHFSLEHEGVQRKKTRKRLKKIGKVLKWI</u><br><u>GGGSGGGGSGG GSPTRKRLKKIGKVLKWI (SEQ ID NO: 20)</u>                                                                                  |
| GN316 | MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRVAVQAGAGL<br>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV<br>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK<br>AGGYTGGAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE<br>EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWADEFARRYNGPAY<br>AQNQYDTKLAAAYKSFS (SEQ ID NO: 22) |
| GN329 | MITDREYQQAEMLGVDVPAIKAVTKVEAPVGGFQPTGEPTILYERHQM<br>YRQLQAKGLPTEGHPPDLVNKVAGGYGKYSEQHAKLARAVKIDRDSALE<br>SCSWGMFQIMGYHWKLMGYPTLQAFVNAMYASEGAQMDAFCRFIKAQP<br>TTHAALKAHDWAKFARLYNGPGYAKNKYDVKLEKAYAEASG (SEQ ID<br>NO: 26)                                                                                     |

| GN #  | Polypeptide Sequence                                                                                                                                                                                                                                                                                                                                                                                              |
|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GN333 | MALTEQDFQSAADDLGVDVASVKAVTKVESRSGSGLLSGVPKILFERHW<br>MFKLLKRKLGRDPEINDVCNPKAGGYLGGQAEHERLDKAVKMDRDCAL<br>QSASWGLFQIMGFHWEALGYASVQAFVNAQYASEGSQNLNFTFVRFIKTNP<br>AIHKALKSKDWADEFARRYNGPDYKKNNDYDVKLA EAYQSFK (SEQ ID<br>NO: 28)                                                                                                                                                                                    |
| GN349 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDELTGERAQLMAFVKFIKADANLWKALKDKNWADEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSESTAGGTAGGARRYRLSRRRSRRLFSRTALRMHR</u><br><u>RNRLRRIMRGGIRF (SEQ ID NO: 30)</u>  |
| GN351 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDELTGERAQLMAFVKFIKADANLWKALKDKNWADEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSESTAGGTAGGARSRRRMSKRSSRRSFRKYAKSHK</u><br><u>KNFKARSMRGGIRL (SEQ ID NO: 32 )</u> |
| GN352 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDELTGERAQLMAFVKFIKADANLWKALKDKNWADEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSESTAGGTAGGKRRKMTRKGSKRLFTATADKTKSI</u><br><u>NTAPPPMRGGIRL (SEQ ID NO: 34)</u>   |
| GN353 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDELTGERAQLMAFVKFIKADANLWKALKDKNWADEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSESTAGGTAGGRKRMSKRVDKRVFRRTAASAKKIN</u><br><u>IDPKIYRGGIRL (SEQ ID NO: 36)</u>    |
| GN357 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRAVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDELTGERAQLMAFVKFIKADANLWKALKDKNWADEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSESTAGGTAGGRRLRLWLRLLR (SEQ ID NO: 38)</u>                                        |

| GN #  | Polypeptide Sequence                                                                                                                                                                                                                                                                                                                                                               |
|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GN359 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSFE</u> <u>STAGGTAGGTRKRLKKIGKVLKWI</u> (SEQ ID NO: 40) |
| GN369 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSFS</u> <u>SRKKTRKRLKKIGKVLKWI</u> (SEQ ID NO: 42)      |
| GN370 | <u>MIDREIRLNPTHGPRRPRRPGRRAPVRTSQRGIDLIKSFEGRLRLSAYQDSVG</u><br><u>VWTIGYGTTRGVTRYMTITVEQAERMLSNDIQRFEPELDRLAKVPLNQNQ</u><br><u>WDALMSFVYNLGAANLASSTLLDLLNKGDYQGAADQFPHWVNAGGKR</u><br><u>LDGLVKRRAAERALEPLS</u> (SEQ ID NO: 44)                                                                                                                                                   |
| GN371 | <u>MIDREIRLNPTHRTSQRGIDLIKSFEGRLRLSAYQDSVGVWTIGYGTTRGVTR</u><br><u>YMTITVEQAERMLSNDIQRFEPELDRLAKVPLNQNQWDALMSFVYNLGA</u><br><u>ANLASSTLLDLLNKGDYQGAADQFPHWVNAGGKRLDGLVKRRAAERALE</u><br><u>FLEPLS</u> (SEQ ID NO: 46)                                                                                                                                                              |
| GN394 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDFLTGERAQLMAFVDFIKADANLWKALKDKNWAEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSFS</u> (SEQ ID NO: 48)                                 |
| GN396 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDFLTGERAQLMAFVKFIKADANLWDALKDKNWAEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSFS</u> (SEQ ID NO: 50)                                 |
| GN408 | <u>MAILKIGSKGLEVKNLQTSLNKIGFNLVADGIFGKATDNAVRVQAGAGL</u><br><u>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAAHEL</u> <u>SVDLASIKAVNQV</u><br><u>ESRGTGFTKSGKIKTLFERHIMYKKLNAKFGQAKANALAQLYPTLVNAK</u><br><u>AGGYTGGDAELERLHGAIKDCAYESASYGLFQIMGFNCVICGYDNAE</u><br><u>EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKNWAEFARRYNGPAY</u><br><u>AQNQYDTKLAAAYKSFS</u> (SEQ ID NO: 52)                         |

| GN #  | Polypeptide Sequence                                                                                                                                                                                                                                                                                                                                                                   |
|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GN418 | MAILKIGSKGLEVKNLQTSLN <b>D</b> IGFNLVADGIFGKATDNVRAVQAGAGL<br>VVDGIAGPKTMYAIRNAGESHQDHLTEADLIDAARELSVDLASIKAVNQV<br>ESRGTGFTKSGKIKTLFERHIMYKKLN <b>A</b> KFGQAKANAL <b>A</b> QLYPTLVNAK<br>AGGYTGGDAELERLHGAIAIDKDCAYESASYGLFQIMGFNCVICGYDNAE<br>EMFNDFLTGERAQLMAFVKFIKADANLWKALKDKN <b>W</b> AEFARRYNGPAY<br>AQNQYDTKLAAAYKSFS (SEQ ID NO: 54 )                                       |
| GN424 | MNTLRFNSRGAEVGV <b>L</b> QQRLVRAGYPIDVTHLYDEATEQAVKALQAAA<br>GIVVDGIAGPNTYAVLSAGQRDRKHLTEADIARAADKLG <b>V</b> SPACVRAVN<br>EVESRGS <b>G</b> FLADGRPVILFERHVMYNRLVAAKRAVDAASAAQ <b>R</b> FPNVVS<br>AKPGGYQGGAAEYVRLDTAARIDAAIAYESASWGAFQVMGYHWERLG <b>Y</b><br>SSIDEFVAR <b>M</b> ETSEGEQLDAFVRFVAADSSLRTALKNRKWAAFAKGYNG<br>PDYARNLYDAKLAQAYERYAGTKAAA (SEQ ID NO: 56 )                |
| GN425 | MTLRLDDVGLDVLHLQKRLNELGANPRLLPDGQFGEVTERAVRA <b>F</b> QQRA<br>GLVVDGVAGPKTMAALS <b>G</b> HSTSRL <b>L</b> GQRDLQRAADRLGVPLASVMALN<br>AVESRGEGFAANGRPVILFERHVMHERLQV <b>N</b> GLSEAEADALAARHPGLV<br>SRRPGGYVGDTAEHQRLANARLLHDTAALESASWG <b>L</b> FQVMGYHWQAL<br>GYDTTQDFTERMARHEAEHLEAFVRFIEADPALHKALKGRKWAEFARRY<br>NGPAYARNLYDVKLARAFEQFSDALQAAA (SEQ ID NO: 58 )                      |
| GN428 | MAILKLGNRGSEVKALQQSLNKIGFSLTADGIFGKATENAVKSVQAGAGL<br>VIDGIAGPKTFYAIRNAGDAHQEHLTEADLVDAARELGVELAS <b>M</b> KAVNQ<br>VESRGTGFTKTGKIKTLFERHIMYKKVTAKFGQARANALYQLYPTLVNPN<br>SGGYIGGDAELERLQGAIALDEDCAYESASYGLFQIMGFNCQICGY <b>S</b> NAK<br>EMFTDFLTGERAHL <b>L</b> AFVKFIKADANMWKALK <b>N</b> KNWAEFARRYNGPAY<br>AKNQYDTKLAAAYKSFC (SEQ ID NO: 60)                                       |
| GN93  | <u>MKFFKFFKFFK</u> AGAGAGAGAGAGAGAGASNNELPWVAEARKYIGLREDTS<br>KTSHNP <b>K</b> LLAMLD <b>R</b> MGEFSNESRAWWHDD <b>E</b> TPWCGLFVG <b>Y</b> CLGVAGR<br>YVVREWYRARAW <b>E</b> APQLTKLDRPAYGALVTFTRSGGGHVGFIVGKDAR<br>GNLMVLGGNQSN <b>A</b> VSIAPFAVSRVTGYFWPSFWRNKTAVKSVPFEERY <b>S</b><br>LPLLKSNGELSTNEA (SEQ ID NO: 62 )                                                               |
| GN431 | MAILKLGNRGTEVKALQDSL <b>N</b> KIGFTLVADGIFGKATENAVKTVQAGAG<br>LVIDGIVGPKTSYAIRNAGEAHQDHLTEADLIEAANQLGVDLASV <b>K</b> AVNQ<br>VESRGTGFTKSGKIKTLFERHIMYKK <b>L</b> MAKFGQARANAMGQMYPTLVSP<br>VAGGYTGGDAELDR <b>L</b> HAAINIDEDCAYESASYGLFQIMGFNCQVC <b>G</b> YAN<br>AKEMFNDFLTGERAHLMAFVKFIKADAK <b>L</b> WQALKDKN <b>W</b> AEFARRYNGP<br>AYTKNQYDTKLAAAYNSFN (SEQ ID NO: 64 )           |
| GN486 | <b>M</b> G <b>S</b> <b>H</b> <b>H</b> <b>H</b> <b>H</b> <b>H</b> <b>H</b> <b>H</b> <b>G</b> GPRRPRRPGRRAPV <b>R</b> TSQRGID <b>L</b> IKSF <b>E</b> GLRLSAYQDSV<br>GVWTIGYGTTRGVTRYMTITVEQAER <b>M</b> LSNDIQRFE <b>P</b> ELDR <b>L</b> AKVPL <b>N</b> QN<br>QWDALMSFVYNLGAANLAS <b>T</b> LLKLLNKGDYQGAADQFPRWVNAGG <b>K</b><br>RLDGLVKRRAAER <b>A</b> L <b>F</b> LEPLS (SEQ ID NO:66 ) |
| GN485 | MPGLSGFIRNADTPV <b>T</b> SLGSAGHVHVPE <b>G</b> PLIRINPDCL <b>L</b> GT <b>P</b> FKFFKFFK <b>F</b><br>FKFFKFFKFFKFFK <b>N</b> ECV <b>L</b> L (SEQ ID NO: 68)                                                                                                                                                                                                                             |

[139] 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.

[140] 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.

[141] 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,  $(CH_2CH_2-O)_n$ , 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

[142] 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.

**[143]** 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.

**[144]** 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 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 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 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.

**[145]** 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.

**[146]** 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.

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

(a) a first nucleic acid molecule encoding a first component comprising: (i) a lysin selected from the group consisting of 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: 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;

(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.

**[148]** 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).

**[149]** 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.

**[150]** 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 AGAGAGAGAGAGAGAGAS (SEQ ID NO: 122).

**[151]** 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.

**[152]** 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.

**[153]** 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.

**[154]** 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.

**[155]** 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.

**[156]** 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.

**[157]** 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.

**[158]** 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.

**[159]** 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.

**[160]** 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.

**[161]** 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.

**[162]** 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.

**[163]** 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.

**[164]** 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.

**[165]** 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.

**[166]** 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.

**[167]** 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.

**[168]** 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.

**[169]** 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.

**[170]** 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.

**[171]** 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.

**[172]** 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.

**[173]** 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.

**[174]** 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.

**[175]** 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.

**[176]** 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.

**[177]** 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.

**[178]** 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.

**[179]** 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.

**[180]** 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.

**[181]** 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.

**[182]** 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.

**[183]** 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.

**[184]** 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.

**[185]** 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.

**[186]** 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.

**[187]** 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.

**[188]** 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**

**[189]** 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 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.

**[190]** 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.

**[191]** 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.

**[192]** 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.

**[193]** 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 colEI, pCRI, pBR322, pMB9 and their derivatives, plasmids such as RP4, pBAD24 and pBAD-TOPO; phage DNAs, *e.g.*, the numerous 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.

**[194]** 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, 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.

**[195]** 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, 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*, *Bacillus*, *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.).

**[196]** 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).

**[197]** 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, 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.

**[198]** 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.

**[199]** 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 be employed for lysin polypeptide purification.

**[200]** 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, Life Technologies, Clontech, etc.

**[201]** 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**

**[202]** In another aspect, the present disclosure is directed to a pharmaceutical composition comprising an effective amount of lysin-AMP polypeptides, 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.

**[203]** 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.

**[204]** 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.

**[205]** 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.

**[206]** 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.

**[207]** 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.

**[208]** 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.

**[209]** 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.

**[210]** 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.

**[211]** 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.

**[212]** 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.

**[213]** 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.

**[214]** 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.

**[215]** 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.

**[216]** 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.

**[217]** 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.

**[218]** 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.

**[219]** 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*.

**[220]** 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**

[221] 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. 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.

[222] 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.

[223] 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.

**[224]** 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.

**[225]** 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

**[226]** In another aspect, the present disclosure is directed to a method of treating a bacterial infection caused by *P. aeruginosa* and optionally one or more additional species of Gram-negative

bacteria 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.

[227] 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) and nosocomial respiratory tract infections; sexually transmitted diseases, such as gonococcal cervicitis and gonococcal urethritis; urinary tract infections; acute otitis media; sepsis including neonatal septicemia and catheter-related sepsis; and osteomyelitis. Infections caused by drug-resistant bacteria and multidrug-resistant bacteria are also contemplated.

[228] 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 devices; 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 calcaneus 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. Musculoskeletal system infections.

[229] The one or more additional species of Gram-negative bacteria of the present methods may include any of the additional species of Gram-negative bacteria as described herein. Typically, the additional species of Gram-negative bacteria are selected from one or more of *Acinetobacter baumannii*, *Acinetobacter haemolyticus*, *Actinobacillus actinomycetemcomitans*, *Aeromonas hydrophila*, *Bacteroides* spp., such as, *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*,

*Bacteroides distasonis*, *Bacteroides ovatus*, *Bacteroides vulgatus*, *Bartonella Quintana*, *Bordetella pertussis*, *Brucella* spp., such as, *Brucella melitensis*, *Burkholderia* spp, such as, *Burkholderia cepacia*, *Burkholderia pseudomallei*, and *Burkholderia mallei*, *Fusobacterium*, *Prevotella corporis*, *Prevotella intermedia*, *Prevotella endodontalis*, *Porphyromonas asaccharolytica*, *Campylobacter jejuni*, *Campylobacter fetus*, *Campylobacter coli*, *Chlamydia* spp., such as *Chlamydia pneumoniae* and *Chlamydia trachomatis*, *Citrobacter freundii*, *Citrobacter koseri*, *Coxiella burnetii*, *Edwarsiella* spp., such as, *Edwarsiella tarda*, *Eikenella corrodens*, *Enterobacter* spp., such as, *Enterobacter cloacae*, *Enterobacter aerogenes*, and *Enterobacter agglomerans*, *Escherichia coli*, *Francisella tularensis*, *Haemophilus influenzae*, *Haemophilus ducreyi*, *Helicobacter pylori*, *Kingella kingae*, *Klebsiella* spp., such as, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Klebsiella rhinoscleromatis*, and *Klebsiella ozaenae*, *Legionella pneumophila*, *Moraxella* spp., such as, *Moraxella catarrhalis*, *Morganella* spp., such as, *Morganella morganii*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *P. aeruginosa*, *Pasteurella multocida*, *Plesiomonas shigelloides*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus penneri*, *Proteus myxofaciens*, *Providencia* spp., such as, *Providencia stuartii*, *Providencia rettgeri*, *Providencia alcalifaciens*, *Pseudomonas fluorescens*, *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*, *Yersinia pseudotuberculosis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Rickettsia prowazekii*, *Coxiella burnetii*, *Ehrlichia chaffeensis* and/or *Bartonella henselae*.

[230] More typically, the at least one other species of Gram-negative bacteria 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*, *Haemophilus 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*, *Stenotrophomonas maltophilia*, *Vibrio cholerae*, and/or *Chlamydia pneumoniae*.

[231] 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 baumannii*, *Klebsiella pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *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.

[232] 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 tularensis*.

[233] 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.

|                                |                                                  |
|--------------------------------|--------------------------------------------------|
| <i>Salmonella typhimurium</i>  | Gastrointestinal (GI) infections- salmonellosis  |
| <i>Shigella</i> spp.           | shigellosis                                      |
| <i>Escherichia coli</i>        | Urinary tract infections (UTIs)                  |
| <i>Acinetobacter baumannii</i> | Wound infections                                 |
| <i>Pseudomonas aeruginosa</i>  | bloodstream infections and pneumonia             |
| <i>Klebsiella pneumoniae</i>   | UTIs, and bloodstream infections                 |
| <i>Neisseria gonorrhoeae</i>   | Sexually transmitted disease (STD)-<br>gonorrhea |
| <i>Neisseria meningitidis</i>  | Meningitis                                       |

|                                                                                                                                                         |                                                                                |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
|                                                                                                                                                         |                                                                                |
| <i>Serratia</i> spp.                                                                                                                                    | Catheter contaminations, UTIs, and pneumonia                                   |
| <i>Proteus mirabilis</i>                                                                                                                                | UTIs                                                                           |
| <i>Morganella</i> spp.                                                                                                                                  | UTIs                                                                           |
| <i>Providencia</i> spp.                                                                                                                                 | UTIs                                                                           |
| <i>Edwardsiella</i> spp                                                                                                                                 | UTIs                                                                           |
| <i>Salmonella typhi</i>                                                                                                                                 | GI infections - typhoid fever                                                  |
| <i>Yersinia pestis</i>                                                                                                                                  | Bubonic and pneumonic plague                                                   |
| <i>Yersinia enterocolitica</i>                                                                                                                          | GI infections                                                                  |
| <i>Yersinia pseudotuberculosis</i>                                                                                                                      | GI infections                                                                  |
| <i>Haemophilus influenza</i>                                                                                                                            | Meningitis                                                                     |
| <i>Bartonella Quintana</i>                                                                                                                              | Trench fever                                                                   |
| <i>Brucella</i> spp.                                                                                                                                    | Brucellosis                                                                    |
| <i>Bordetella pertussis</i>                                                                                                                             | Respiratory - Whooping cough                                                   |
| <i>Burkholderia</i> spp.                                                                                                                                | Respiratory                                                                    |
| <i>Moraxella</i> spp.                                                                                                                                   | Respiratory                                                                    |
| <i>Francisella tularensis</i>                                                                                                                           | Tularemia                                                                      |
| <i>Legionella pneumophila</i>                                                                                                                           | Respiratory - Legionnaires' disease                                            |
| <i>Coxiella burneti</i>                                                                                                                                 | Q fever                                                                        |
| <i>Bacteroides</i> spp.                                                                                                                                 | Abdominal infections                                                           |
| <i>Enterobacter</i> spp.                                                                                                                                | UTIs and respiratory                                                           |
| <i>Chlamydia</i> spp.                                                                                                                                   | STDs, respiratory, and ocular                                                  |
| <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> ,<br><i>Acinetobacter</i> spp., <i>Proteus mirabilis</i> and/or<br><i>Pseudomonas aeruginosa</i> | Infections of implants, catheters, prosthetic joints and other medical devices |

[234] In some embodiments, the lysin-AMP polypeptides, 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).

[235] 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, 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.

[236] The lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure can be co-administered with standard 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<br>Piperacillin-tazobactam |

|                  |                                         |
|------------------|-----------------------------------------|
| Cephalosporins   | Ceftazidime<br>Cefepime<br>Cefoperazone |
| Monobactams      | Aztreonam                               |
| Fluoroquinolones | Ciprofloxacin<br>Levofloxacin           |
| Carbapenems      | Imipenem<br>Meropenem<br>Doripenem      |
| Aminoglycosides  | Gentamicin<br>Tobramycin<br>Amikacin    |
| Polymixins       | Colistin<br>Polymixin B                 |
| Macrolides       | Azithromycin                            |
| Rifamycin        | Rifampicin                              |
| Fosfomycin       | Fosfomycin                              |

**[237]** 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.

**[238]** Combining lysin-AMP polypeptides, lysin polypeptides, variants, active fragments thereof or derivatives of the present disclosure with antibiotics provides an efficacious antibacterial regimen. 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.

**[239]** 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, 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.

**[240]** The lysin-AMP polypeptides, 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).

**[241]** 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, 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.

[242] 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 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.

[243] Examples of medical devices that can be protected using the lysin-AMP polypeptides, 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 intrainestinal 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.

[244] The lysin-AMP polypeptides, 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.

[245] For example, in some embodiments, the present lysin-AMP polypeptides, 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.

**[246]** 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, 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.

**[247]** 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, 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.

**[248]** 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.

**[249]** 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.

**[250]** 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.

**[251]** 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.

**[252]** 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 lysins and lysin-AMP polypeptide constructs in medium supplemented with human serum.**

#### **Materials and Methods**

[253] 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<sub>2</sub>HPO<sub>4</sub>, Sigma-Aldrich; 1 mM MgSO<sub>4</sub>, Sigma-Aldrich), CAA supplemented with 150 mM NaCl, CAA supplemented with 2.5% human serum (Type AB, male, pooled; Sigma-Aldrich), CAA supplemented with 12.5% human serum, and CAA supplemented with 6.25% Survanta®. For both the CAA supplemented with 12.5% human serum and 6.25% Survanta®, a range of *P. aeruginosa* isolates were evaluated. 6.25% Survanta® corresponds to 1.5 mg/mL phospholipids.

#### *Determination of Minimal Inhibitory Concentrations (MIC)*

[254] 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 either CAA media (with and without NaCl), CAA supplemented with 2.5% human serum (Table 4), CAA supplemented with 12.5% human serum (Table A), or CAA supplemented with 6.25% Survanta® (Table B). MIC is the minimum concentration of peptide sufficient to suppress at least 80% of the bacterial growth compared to control.

## Results

[255] The results of these experiments are summarized in Tables 4, A and B below. Table 4 also provides the molecular weight and isoelectric point of the present 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.

[256] For example, the effects of the single point mutations on GN316 (SEQ ID NO: 22) can be seen. 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 in the 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.

[257] 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.

### **Example 2. Synergy between antibiotics and lysins or lysin-AMP polypeptide constructs.**

[258] Synergy between GN76 (SEQ ID NO: 203), GN121 (SEQ ID NO: 175), GN123 (SEQ ID NO: 173), GN351 (SEQ ID NO: 32), GN370 (SEQ ID NO: 44) and GN428 (SEQ ID NO: 60) and 12 different antibiotics were examined in checkerboard assays using CAA medium, supplemented with 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.

[259] As indicated in Table 5, 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 3. Resensitization of carbapenem-resistant clinical strains using antibiotics in combination with lysins.**

[260] 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  $\leq 2$  for carbapenem-sensitive isolates, a MIC value of 4 for intermediately sensitive carbapenem isolates and a MIC value of  $\geq 8$  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.

[261] As indicated in Tables 6-9 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.

**Example 4. Resensitization of carbapenem-resistant clinical strains using antibiotics in combination with additional lysins or lysin-AMP constructs.**

[262] 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.

[263] As indicated in Table 10 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.

[264] The findings in Examples 3 and 4 indicate that the lysins and lysin-AMP polypeptide constructs described herein 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.

[265] **Table A** – Activity of lysins or lysin-AMP polypeptide constructs in human serum

| <i>P. aeruginosa</i><br>Strain | Meropenem<br>MIC<br>(μg/mL) | CAA + 12.5% Human Serum MIC (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     |
| CFS1539 (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     |
| CFS 1109 (ATCC 17646)          | 0.5                         | 0.5                                 | 1     | 1     | 1     |

[266] **Table B** – Activity in pulmonary surfactant (Survanta®)

| <i>P. aeruginosa</i><br>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     |
| CFS1539 (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     |

[267] **Table 4.** Sensitivity of lysins or lysin-AMP polypeptide constructs in human serum

| MIC (mg/mL)           |          |      |                 |                     |
|-----------------------|----------|------|-----------------|---------------------|
| 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              |

|                       |          |      |      |        |
|-----------------------|----------|------|------|--------|
| NO: 42)               |          |      |      |        |
| 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  | ND   | ND     |
| 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. | n.d.   |

**[268] Table 5.** Synergy between antibiotics and lysins or lysin-AMP polypeptide constructs

| Antibiotic    | GN76<br>(SEQ ID<br>NO: 203)<br>(MIC) | GN121(S<br>EQ ID<br>NO: 175)<br>(MIC) | GN123(SEQ<br>ID NO: 173)<br>(MIC) | GN351<br>(SEQ ID<br>NO: 32)<br>(MIC) | GN370<br>(SEQ ID<br>NO: 44)<br>(MIC) | GN428<br>(SEQ ID<br>NO: 60)<br>(MIC) |
|---------------|--------------------------------------|---------------------------------------|-----------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| 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                                |
| Pipercillin   | 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                                |

**[269] Table 6.** Gram-negative bacterial resensitization using a combination of IMIPENEM and GN123 (SEQ ID NO: 173)

| Isolate                                                  | IMIPENEM MIC ( $\mu\text{g/mL}$ ) |             | GN123 ( $\mu\text{g/mL}$ ) |             | FICI  |
|----------------------------------------------------------|-----------------------------------|-------------|----------------------------|-------------|-------|
|                                                          | Alone                             | Combination | Alone                      | Combination |       |
| PA19                                                     | 32 (R)                            | 0.5 (S)     | 8                          | 0.125       | 0.03  |
| Analysis of additional CARBAPENEM <sup>R</sup> 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

**[270] Table 7.** Gram-negative bacterial resensitization using a combination of MEROPENEM and GN123 (SEQ ID NO: 173)

| Isolate | MEROPENEM MIC ( $\mu\text{g/mL}$ ) |             | GN123 ( $\mu\text{g/mL}$ ) |             | FICI  |
|---------|------------------------------------|-------------|----------------------------|-------------|-------|
|         | Alone                              | Combination | Alone                      | Combination |       |
| 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

**[271] Table 8.** Gram-negative bacterial resensitization using a combination of IMIPENEM and GN121 (SEQ ID NO: 175)

| Isolate | Imipenem MIC ( $\mu\text{g/mL}$ ) |             | GN121 ( $\mu\text{g/mL}$ ) |             | FICI  |
|---------|-----------------------------------|-------------|----------------------------|-------------|-------|
|         | Alone                             | Combination | Alone                      | Combination |       |
| 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

**[272] Table 9.** Gram-negative bacterial resensitization using a combination of MEROPENEM and GN121 (SEQ ID NO: 175)

| Isolate | Meropenem MIC ( $\mu\text{g/mL}$ ) |             | GN121 ( $\mu\text{g/mL}$ ) |             | FICI  |
|---------|------------------------------------|-------------|----------------------------|-------------|-------|
|         | Alone                              | Combination | Alone                      | Combination |       |
| 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

**[273] Table 10.** 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<br>vs. WC-452 | Antibiotic MIC |             | Lysin MIC |             | FICI  |
|----------------------------|----------------|-------------|-----------|-------------|-------|
|                            | Alone          | Combination | Alone     | Combination |       |
| 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 5. Gram-negative lysin bactericidal activity against *Pseudomonas aeruginosa* in human serum and pulmonary surfactant**

**[274]** 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 gram-negative lysin action was further evaluated by fluorescence and transmission electron microscopy (TEM), as discussed in Examples 6 and 7.

**[275] Materials and methods:** MICs were determined by broth microdilution in media supplemented with human serum and pulmonary surfactant (Survanta®; Myoderm Clinical Supplies). Synergy with antibiotics was examined in checkerboard assays and 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.

**[276] Results:** The activity of gram-negative 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<sub>4</sub>) 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 11 below, it was concluded that the gram-negative lysins GN121, GN351, GN428, and GN370 are active in human serum and pulmonary surfactant. Likewise, as shown in Table C below, the lysins and AMP-lysin

polypeptide constructs exhibited a potent antibiofilm effect using 12.5% human serum, with MBECs values  $\leq 1\mu\text{g/mL}$ , similar to those observed for MICs.

**[277] Table 11** – 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 ( $\mu\text{g/mL}$ ) | MIC in 0.78% Survanta® ( $\mu\text{g/mL}$ ) |
|-------|---------------------|-------------|--------------------------------------------------------|---------------------------------------------|
| 1525  | GN121               | 1           | 0.5                                                    | 2                                           |
| 1799  | GN351               | 1           | 0.0625                                                 | 4                                           |
| 1876  | GN428               | 4           | 0.125                                                  | 4                                           |
| 1818  | GN370               | 4           | 2                                                      | 2                                           |

**[278] Table C** – MBEC values for lysins and lysin-AMP polypeptide constructs

| Lysin or Lysin-AMP polypeptide construct | MBEC ( $\mu\text{g/mL}$ ) in CAA supplemented with 12.5% human serum |
|------------------------------------------|----------------------------------------------------------------------|
| GN121                                    | 0.25                                                                 |
| GN351                                    | 0.5                                                                  |
| GN428                                    | 1                                                                    |
| GN370                                    | 1                                                                    |

**[279]** The activity of gram-negative lysins in the presence of pulmonary surfactant (Survanta®) was measured over a range of concentrations of Survanta® in the MIC assay format. Fold changes in MIC in the presence of various concentrations of Survanta® (25%, 12.5%, 6.25%, 3.12%, 1.56%, 0.78%, and 0.39%) supplemented into the AST-format (25% SAA) is shown in Table 12. Fold changes are based on comparisons of MIC values to that determined in 25% CAA alone. Physiological concentrations of pulmonary surfactant range between 0.78% and 0.39%. *Pseudomonas aeruginosa* strain CFS-1292 (meropenem resistant) was used as the reporter strain.

It was concluded that the gram-negative lysins tested are active in the presence of physiological levels of pulmonary surfactant (Survanta®).

**[280] Table 12** – Fold increase (MIC) in the presence of Survanta®

| Gram-negative lysin | CAA MIC (µg/mL) | % Survanta® |      |      |      |      |      |      |
|---------------------|-----------------|-------------|------|------|------|------|------|------|
|                     |                 | 25          | 12.5 | 6.25 | 3.12 | 1.56 | 0.78 | 0.39 |
| GN121               | 2               | 4           | 2    | 2    | 2    | 1    | 1    | 1    |
| GN351               | 2               | 2           | 2    | 2    | 1    | 1    | 1    | 1    |
| GN428               | 4               | 4           | 2    | 1    | 1    | 1    | 1    | 1    |
| GN370               | 4               | 4           | 2    | 2    | 1    | 1    | 1    | 1    |

**[281]** The activity of gram-negative lysins 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<sub>2</sub>, 0.78 mM MgCl<sub>2</sub>, and a combination of 1.25 mM CaCl<sub>2</sub> and 0.78 mM MgCl<sub>2</sub>) supplemented into the AST medium (25% CAA). The results are shown below in Table 13. It is noted that 25% CAA typically has 0.25 nM MgSO<sub>4</sub>. *Pseudomonas aeruginosa* strain CFS-1292 (meropenem resistant) was used as the reporter strain. It was concluded that the gram-negative lysins tested are active in the presence of physiological levels of calcium and magnesium.

**[282] Table 13** – Fold Increase (MIC) in presence of cations

|                     |         | 25% CAA supplemented with: |                           |                                                         |
|---------------------|---------|----------------------------|---------------------------|---------------------------------------------------------|
| Gram-negative lysin | 25% CAA | 1.25 mM CaCl <sub>2</sub>  | 0.78 mM MgCl <sub>2</sub> | 1.25 mM CaCl <sub>2</sub> and 0.78 mM MgCl <sub>2</sub> |
| GN121               | 1       | 2                          | 2                         | 2                                                       |
| GN351               | 1       | 2                          | 1                         | 2                                                       |
| GN428               | 4       | 2                          | 4                         | 4                                                       |
| GN370               | 4       | 4                          | 2                         | 4                                                       |

**Example 6. Ability of gram-negative lysins to destabilize bacterial outer membrane**

[283] The ability of gram-negative lysins to destabilize the outer membrane of *P. aeruginosa* was evaluated through the use of an N-phenyl-1-naphthylamine (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 λ = 350 nm; emission λ = 420 nm) over two hours. The NPN incorporated into the membrane resulted in an increase in fluorescence. As shown in Figures 2A and 2B, 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 14.

[284] **Table 14** – Fluorescence over time for *P. aeruginosa* exposed to NPN and gram-negative lysins

| Time in minutes | %RFU   |       |       |       |       |
|-----------------|--------|-------|-------|-------|-------|
|                 | 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 7. Microscopy shows gram-negative lysin bactericidal activity in serum

[285] *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 Figure 3, which shows a series of photomicrographs showing microscopic analysis (x2000 magnification), there was an absence of dead bacteria in the untreated row and a reduction of live bacteria in the treated row.

**Example 8. Synergy of gram-negative lysins and meropenem in human serum**

**[286]** Standard checkerboard assays were performed to assess synergy of gram-negative 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 15, all of GN121, GN351, GN370, and GN428 exhibited synergy with meropenem for each of the three *P. aeruginosa* strains evaluated.

**[287] Table 15 – 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               |

| Strain                | Gram-negative lysin | FICI value (Run #1) | FICI value (Run #2) |
|-----------------------|---------------------|---------------------|---------------------|
| 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               |

**[288] Example 9. Low Propensity for Resistance to GN lysins**

**[289]** 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 5x10<sup>6</sup> 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.

**[290]** In the assay, GN121, GN351, GN370, and GN428 lysin MICs increased by up to 1-log<sub>2</sub> dilutions (2-fold) over 18 days, which was comparable to passage control (absence of treatment). FIGS. 4A-4D. In contrast, the Ciprofloxacin control increased 4-log<sub>2</sub> dilutions (16-fold) over 18 days (FIG. 4E). 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 February 26, 2019, and is herein incorporated by reference in its entirety.

We claim:

1. A lysin-AMP polypeptide construct comprising:

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

(i) a lysin selected from the group consisting of 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, GN76 (SEQ ID NO: 203), 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: 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 presence of pulmonary surfactant.

2. The lysin-AMP polypeptide construct according to claim 1, 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).

3. The lysin-AMP polypeptide construct according to claim 1 or 2, wherein the construct further comprises 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 substantially the same as in an unconjugated lysin and/or AMP.

4. The lysin-AMP polypeptide construct according to claim 3, wherein the at least one structure stabilizing component is a peptide.

5. The lysin-AMP polypeptide construct according to claim 4, wherein 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 AGAGAGAGAGAGAGAGAS (SEQ ID NO: 122).

6. The lysin-AMP polypeptide construct of any of claims 1-5, wherein the GN37 lysin (SEQ ID NO: 84) comprises a single pI-increasing mutation and wherein the GN316 (SEQ ID NO: 22) comprises a single point mutation, wherein the GN37 (SEQ ID NO: 84) with the single pI-increasing mutation is GN217 (SEQ ID NO: 8) and wherein the GN316 (SEQ ID NO: 22) with the single point mutation is selected from the group consisting of GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52), GN418 (SEQ ID NO: 54) and GN394 (SEQ ID NO: 48).

7. The lysin-AMP polypeptide construct according to any one of claims 1-5, wherein the lysin-AMP polypeptide construct comprises (i) a polypeptide sequence selected from the group consisting of GN168 (SEQ ID NO: 2), GN176 (SEQ ID NO: 4), GN178 (SEQ ID NO: 6) GN218 (SEQ ID NO: 10), GN223 (SEQ ID NO: 12), GN239 (SEQ ID NO: 14), GN243 (SEQ ID NO: 16), GN280 (SEQ ID NO: 18), GN281 (SEQ ID NO: 20), GN349 (SEQ ID NO: 30), GN351 (SEQ ID NO: 32), GN352 (SEQ ID NO: 34), GN353 (SEQ ID NO: 36), GN357 (SEQ ID NO: 38), GN359 (SEQ ID NO: 40), GN369 (SEQ ID NO: 42), GN370 (SEQ ID NO: 44), GN371 (SEQ ID NO: 46), GN428 (SEQ ID NO: 60), and GN93 (SEQ ID NO: 62), or (ii) a polypeptide having lysin activity and at least 80% identity with 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, 60 and 62.

8. The lysin-AMP polypeptide construct according to any one of claims 1-5, wherein the lysin-AMP polypeptide construct comprises (i) a polypeptide sequence selected from the group consisting of GN351 (SEQ ID NO: 32) and GN370 (SEQ ID NO: 36), or (ii) a polypeptide having lysin activity and at least 80% identity with at least one of SEQ ID NOS: 32 and 36.

9. 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 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 presence of pulmonary surfactant.

10. The isolated polypeptide of claim 9, wherein the lysin is selected from the group consisting of GN121 (SEQ ID NO: 175) and GN428 (SEQ ID NO: 60).

11. 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 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: 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;

(b) a second nucleic acid molecule encoding 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 presence of pulmonary surfactant.

12. The isolated polynucleotide of claim 11, wherein the nucleic acid molecule further comprises (c) a third nucleic acid molecule encoding a third component comprising at least one structure stabilizing component, wherein the at least one structure stabilizing component maintains at least a portion of the structure of the first and/or second component in the construct substantially the same as in an unconjugated lysin and/or AMP.

13. The isolated polynucleotide of claim 12, wherein the at least one structure stabilizing component comprises a peptide.

14. The isolated polynucleotide of claim 13, wherein 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 AGAGAGAGAGAGAGAS (SEQ ID NO: 122).

15. The isolated polynucleotide of any of claims 11-14, wherein the GN37 (SEQ ID NO: 84) comprises a single pI-increasing mutation and wherein the GN316 (SEQ ID NO: 22) comprises a single point mutation, wherein the GN37 (SEQ ID NO: 84) with the single pI-increasing mutation is GN217 (SEQ ID NO: 8) and wherein the GN316 (SEQ ID NO: 22) with the single point mutation is selected from the group consisting of GN396 (SEQ ID NO: 50), GN408 (SEQ ID NO: 52), GN418 (SEQ ID NO: 54) and GN394 (SEQ ID NO: 48).

16. The isolated polynucleotide of any of claims 11-14, wherein the nucleic acid molecule encoding the lysin-AMP polypeptide construct is

(i) selected from the group consisting of GN168 (SEQ ID NO: 2), GN176 (SEQ ID NO: 4), GN178 (SEQ ID NO: 6), GN218 (SEQ ID NO: 10), GN223 (SEQ ID NO: 12), GN239 (SEQ ID NO: 14), GN243 (SEQ ID NO: 16), GN280 (SEQ ID NO: 18), GN281 (SEQ ID NO: 20), GN349 (SEQ ID NO: 30), GN351 (SEQ ID NO: 32), GN352 (SEQ ID NO: 34), GN353 (SEQ ID NO: 36), GN357 (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) and GN93 lysin (SEQ ID NO: 62); or

(ii) a nucleic acid molecule encoding a polypeptide having lysin activity and having at least 80% 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.

17. 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 presence of pulmonary surfactant.

18. The isolated polynucleotide of any one of claims 11-17, wherein the isolated polynucleotide comprises DNA.
19. The isolated polynucleotide of any one of claims 11-17, wherein the isolated polynucleotide comprises cDNA.
20. A recombinant vector comprising the isolated polynucleotide sequence according to any one of claims 11-18.
21. The recombinant vector of any of claim 20, wherein the isolated polynucleotide sequence is operatively linked to a heterologous promoter.
22. The recombinant vector of any one of claims 20-21, wherein the recombinant vector is a recombinant expression vector.
23. An isolated host cell comprising the recombinant vector of any one of claims 20-22.
24. A pharmaceutical composition comprising an isolated lysin and/or a lysin-antimicrobial peptide (AMP) polypeptide construct and a pharmaceutically acceptable carrier,  
wherein the isolated lysin comprises at least one of:  
(i) 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: 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

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 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: 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 pharmaceutical composition inhibits *P. aeruginosa* bacterial growth, reduces a *P. aeruginosa* bacterial population and/or kills *P. aeruginosa* in the presence of pulmonary surfactant.

25. The pharmaceutical composition of claim 24, wherein the lysin-AMP polypeptide construct further comprises 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 substantially the same as in the unconjugated lysin and/or AMP.

26. The pharmaceutical composition of claim 25, wherein the at least one structure stabilizing component is a peptide.

27. The pharmaceutical composition of claim 26, wherein 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 AGAGAGAGAGAGAGAGAS (SEQ ID NO: 122).

28. The pharmaceutical composition of any of claims 24-27, wherein the lysin is selected from the group consisting 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), Lysin PaP2\_gp17 (SEQ ID NO: 96) and an active fragment thereof.

29. The pharmaceutical composition of claim 28, wherein the lysin or active fragment thereof comprises at least one amino acid substitution relative to SEQ ID NOS: 22, 26, 28, 56, 58, 60, 64, 68 or 96.

30. The pharmaceutical composition of any one of claims 24-29, wherein the lysin-AMP polypeptide construct comprises a polypeptide sequence selected from at least one of GN168 (SEQ ID NO: 2), GN176 (SEQ ID NO: 4), GN178 (SEQ ID NO: 6) GN218 (SEQ ID NO: 10), GN223 (SEQ ID NO: 12), GN239 (SEQ ID NO: 14), GN243 (SEQ ID NO: 16), GN280 (SEQ ID NO: 18), GN281 (SEQ ID NO: 20), GN349 (SEQ ID NO: 30), GN351 (SEQ ID NO: 32), GN352 (SEQ ID NO: 34), GN353 (SEQ ID NO: 36), GN357 (SEQ ID NO: 38), GN359 (SEQ ID NO: 40), GN369 (SEQ ID NO: 42), GN370 (SEQ ID NO: 44), GN371 (SEQ ID NO: 46), GN428 (SEQ ID NO: 60), GN93 (SEQ ID NO: 62), or a polypeptide sequence having lysin activity and at least 80% identity to 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, 60 and 62.

31. The pharmaceutical composition of any one of claims 24-29, wherein the isolated lysin comprises a polypeptide sequence selected from at least one of GN121 (SEQ ID NO: 175) and GN428 (SEQ ID NO: 60), or a polypeptide sequence having lysin activity and at least 80% identity to at least one of SEQ ID NOS: 175 and 60.

32. The pharmaceutical composition of any one of claims 24-31, wherein the pharmaceutical composition is formulated as a solution, a suspension, an emulsion, an inhalable powder, an aerosol, or a spray.

33. The pharmaceutical composition of any one of claims 24-32, wherein the pharmaceutical composition further comprises an antibiotic suitable for the treatment of Gram-negative bacteria.

34. 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 according to any one of claims 24-33.

35. The method of claim 34, wherein the bacterial infection is a topical or systemic pathogenic bacterial infection.

36. 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 according to any one of claims 24-35, and

a second effective amount of an antibiotic suitable for the treatment of a Gram-negative bacterial infection.

37. 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, wherein the isolated lysin comprises at least one of:

- (i) 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: 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

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 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: 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 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 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 of pulmonary surfactant than administration of either the antibiotic or the lysin or lysin-AMP polypeptide construct individually.

38. 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,

wherein the isolated lysin comprises at least one of:

(i) 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: 175, 173, 8, 24, 22, 26, 28, 48, 50, 52, 54, 56, 58, 60, 64, 66, 68, or 96;

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 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: 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, 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 presence of pulmonary surfactant.

39. The method of any one of claims 34, 35 and 38, wherein the one or more additional species of Gram-negative bacteria is selected from the group consisting of *Klebsiella spp.*, *Enterobacter spp.*, *Escherichia coli*, *Citrobacter freundii*, *Salmonella typhimurium*, *Yersinia pestis*, and *Franciscella tularensis*.

40. The method of claim 36 or 37 or the pharmaceutical composition of claim 33, 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.

41. The lysin-AMP polypeptide construct, the isolated polypeptide, the isolated polynucleotide, the recombinant vector, the host cell, the pharmaceutical composition or the methods of any one

of the preceding claims, wherein the at least one activity further comprises inhibiting the growth, or reducing a population of at least one species of Gram-negative bacteria in addition to *P. aeruginosa*.

42. The lysin-AMP polypeptide construct, the isolated polypeptide, the isolated polynucleotide, the recombinant vector, the host cell, the pharmaceutical composition or the method of claim 38, wherein the at least one species of Gram-negative bacteria in addition to *P. aeruginosa* is selected from the group consisting of *Klebsiella spp.*, *Enterobacter spp.*, *Escherichia coli*, *Citrobacter freundii*, *Salmonella typhimurium*, *Yersinia pestis*, and *Francisella tularensis*.

43. The lysin-AMP polypeptide construct, the isolated polypeptide, the isolated polynucleotide, the recombinant vector, the host cell, the pharmaceutical composition or the methods of any one of the preceding claims, wherein the lysin-AMP polypeptide construct or the isolated polypeptide resensitizes *P. aeruginosa* to an antibiotic.

44. The lysin-AMP polypeptide construct, the isolated polypeptide, the isolated polynucleotide, the recombinant vector, the host cell, the pharmaceutical composition or the methods of claim 43, wherein the antibiotic is a carbapenem.

45. The lysin-AMP polypeptide construct, the isolated polypeptide, the isolated polynucleotide, the recombinant vector, the host cell, the pharmaceutical composition or the methods of any one of the preceding claims, wherein the antibiotic is meropenem.

46. The lysin-AMP polypeptide construct, the isolated polypeptide, the isolated polynucleotide, the recombinant vector, the host cell, the pharmaceutical composition or the methods of any one of the preceding claims, 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.

47. A method of preventing, disrupting or eradicating a Gram-negative bacterial biofilm comprising:

contacting a surface with a composition comprising the lysin-AMP polypeptide construct of any one of claims 1-8, the isolated polypeptide of any one of claims 9-10 or the pharmaceutical composition of any one of claims 24-32 effective to kill Gram-negative bacteria in a biofilm, wherein the biofilm is effectively prevented, disrupted or eradicated.

48. A method of preventing, disrupting or eradicating a Gram-negative bacterial biofilm comprising:

administering a composition comprising the lysin-AMP polypeptide construct of any one of claims 1-8, the isolated polypeptide of any one of claims 9-10 or the pharmaceutical composition of any one of claims 24-32 effective to kill Gram-negative bacteria in a biofilm to a subject in need thereof, wherein the biofilm on a surface is effectively prevented, disrupted or eradicated.

49. The method of claim 47 or 48 wherein the surface comprises a surface of a medical device.

50. The method of claim 49, wherein the medical device is a contact lens, drug pump, implant, catheter or prosthetic device.

51. The method of any one of claims 47-50, wherein the composition or pharmaceutical composition further comprises one or more antibiotic(s).

52. The method of any one of claims 47-50, wherein the surface is additionally contacted with one or more antibiotic(s).

53. The method of claim 51 or 52, wherein the one or more antibiotics is/are selected from a penicillin, a cephalosporin, a monobactam, a fluoroquinolone, a carbapemens, an aminoglycoside, a polymyxin, a macrolides or fosfomycin.

54. The method of any one of claims 47-53, wherein the surface is a biotic surface.

55. The method of any one of claims 47-54, wherein the surface is infected with a Gram-negative bacterial infection selected from osteomyelitis, bacterial endocarditis, tonsillitis 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 and an infection of a medical device.

56. The method of any one of claims 47-55, wherein biofilm formation is prevented.

57. The method of any one of claims 47-55, wherein the biofilm is disrupted or eradicated.

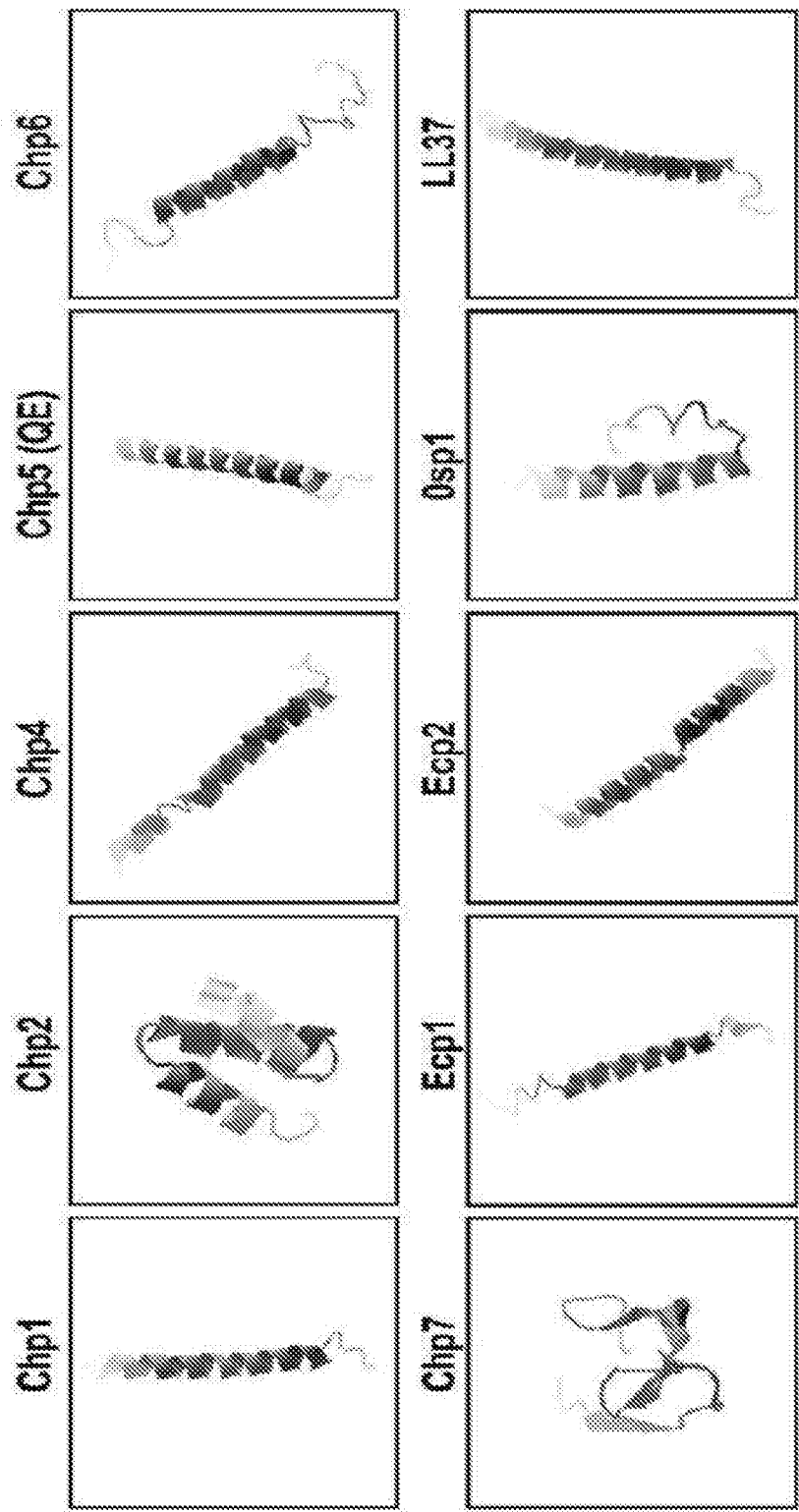


FIG. 1

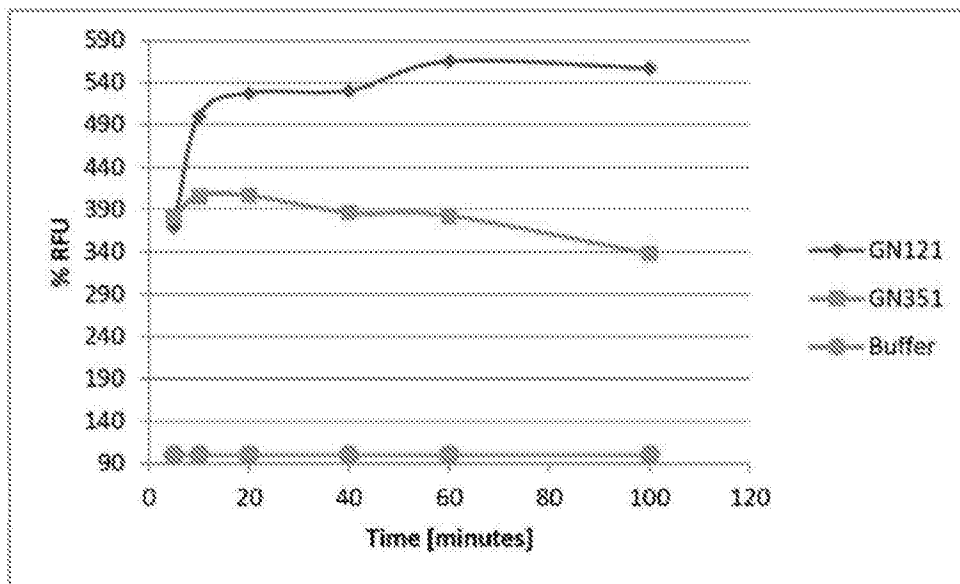


FIG. 2A

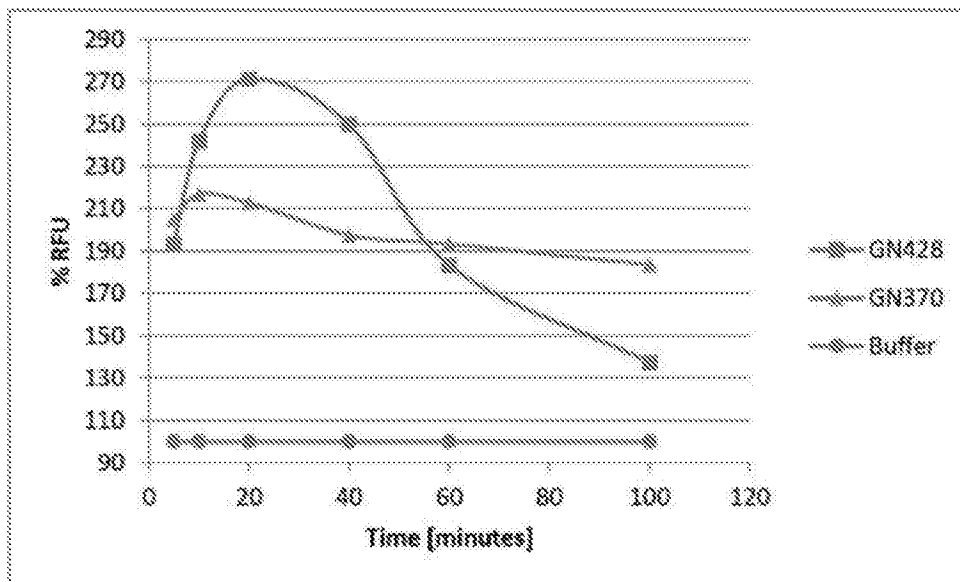


FIG. 2B

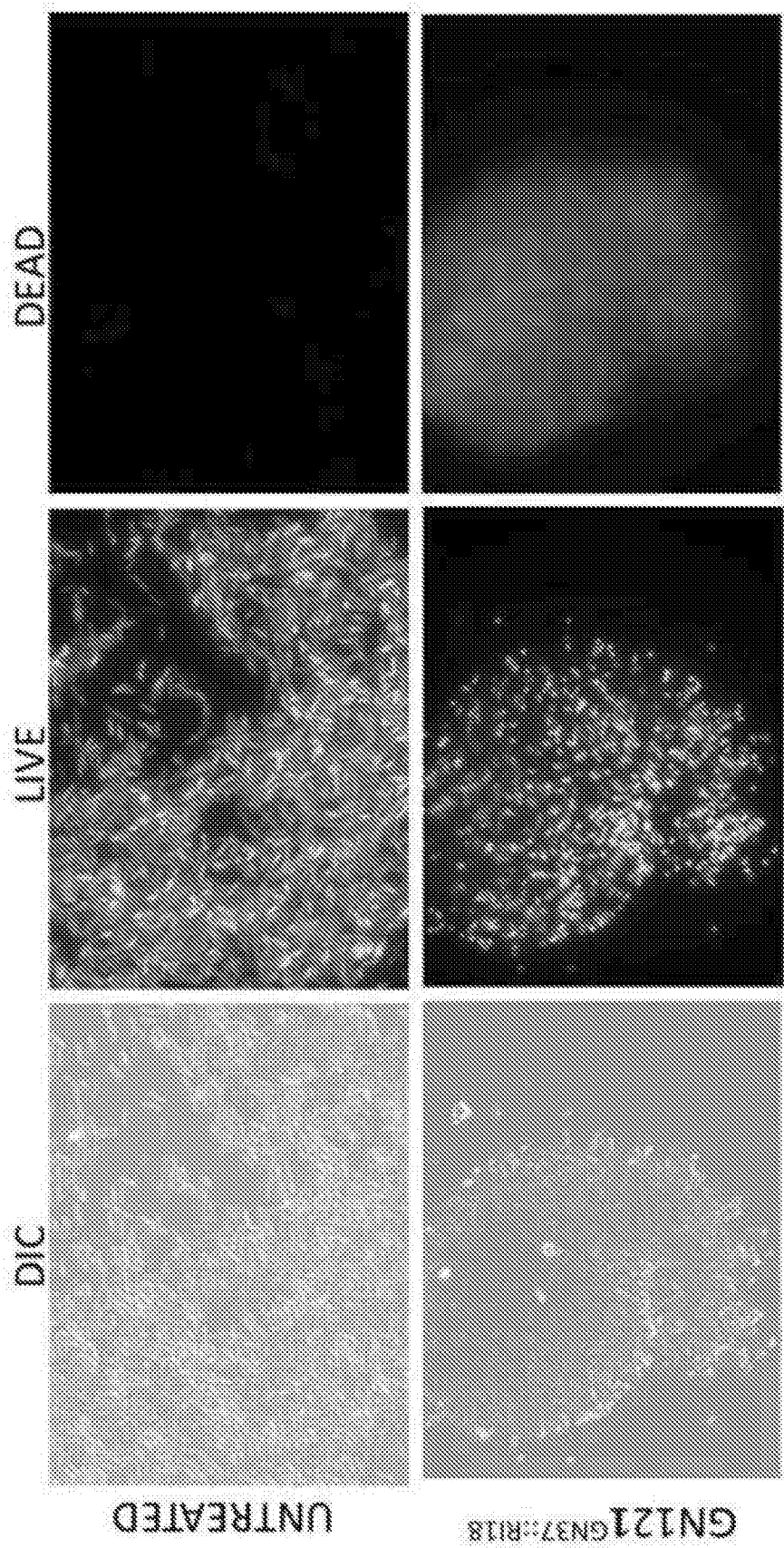


FIG. 3

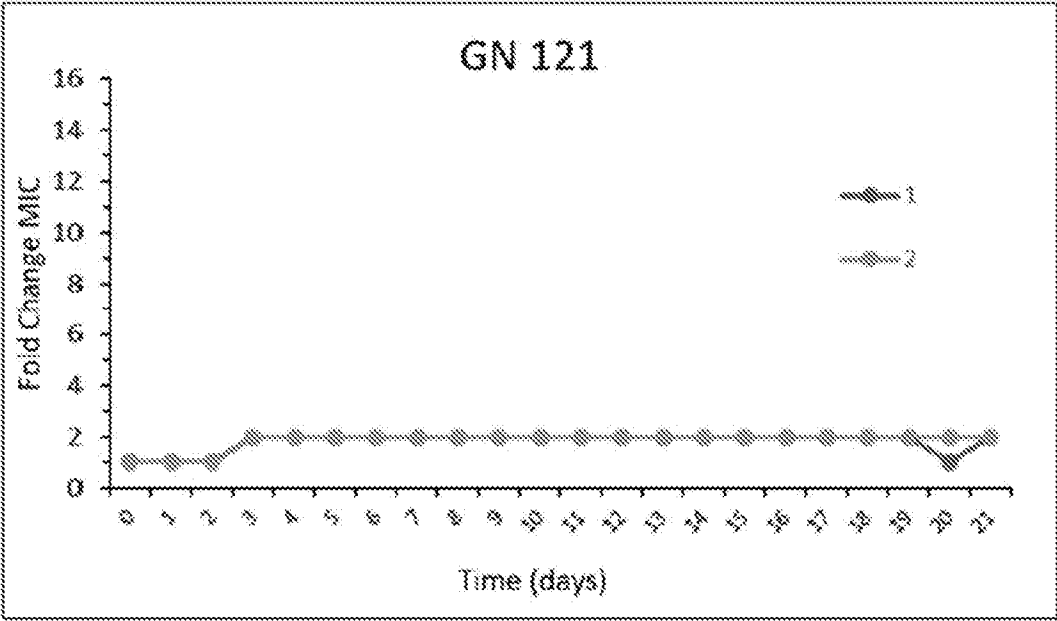


FIG. 4A

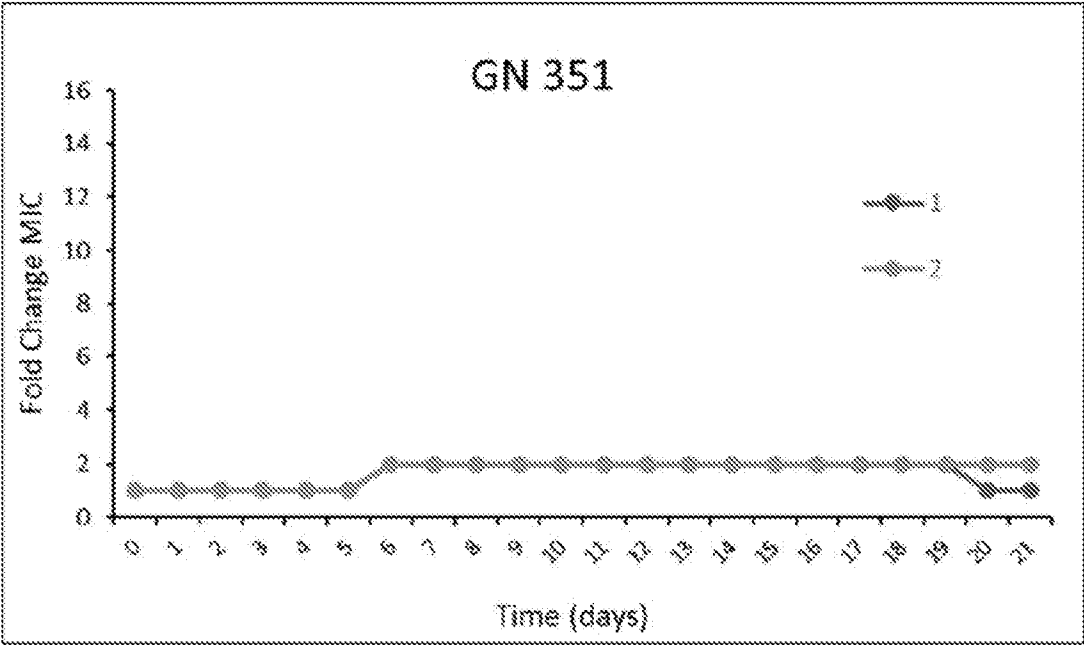


FIG. 4B

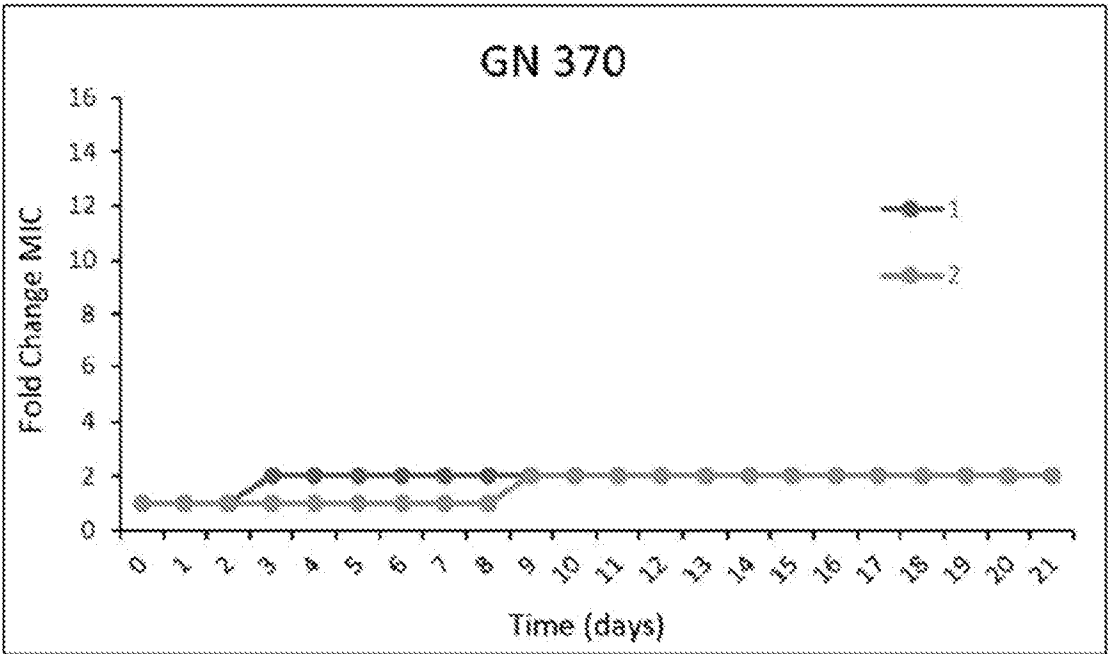


FIG. 4C

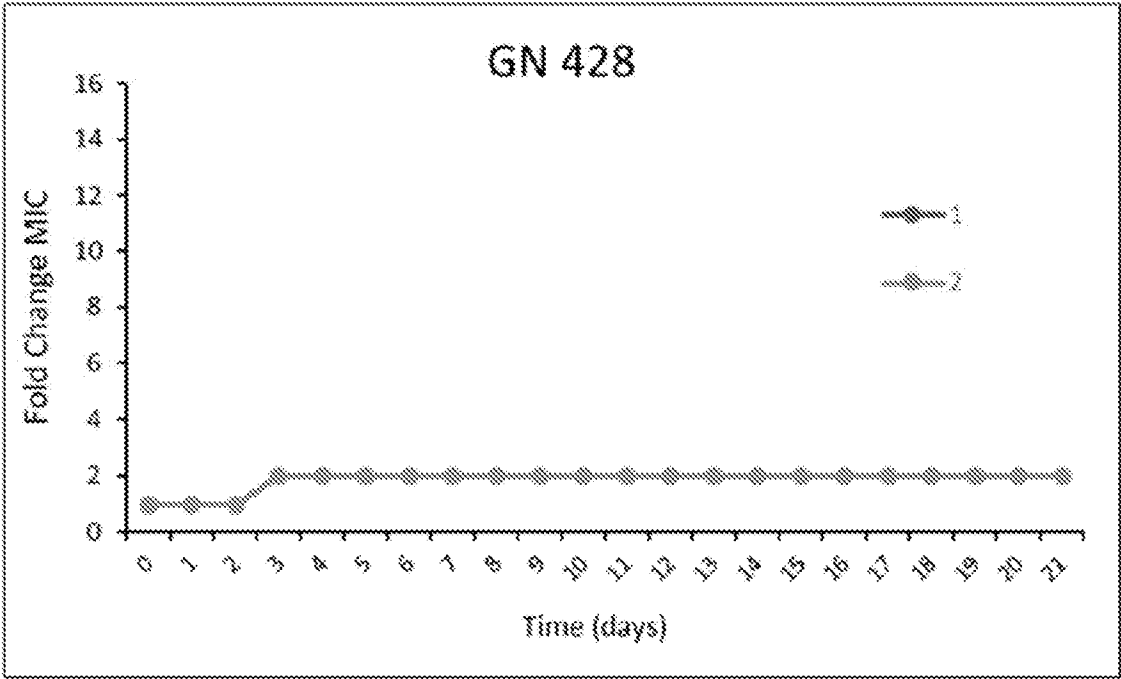


FIG. 4D

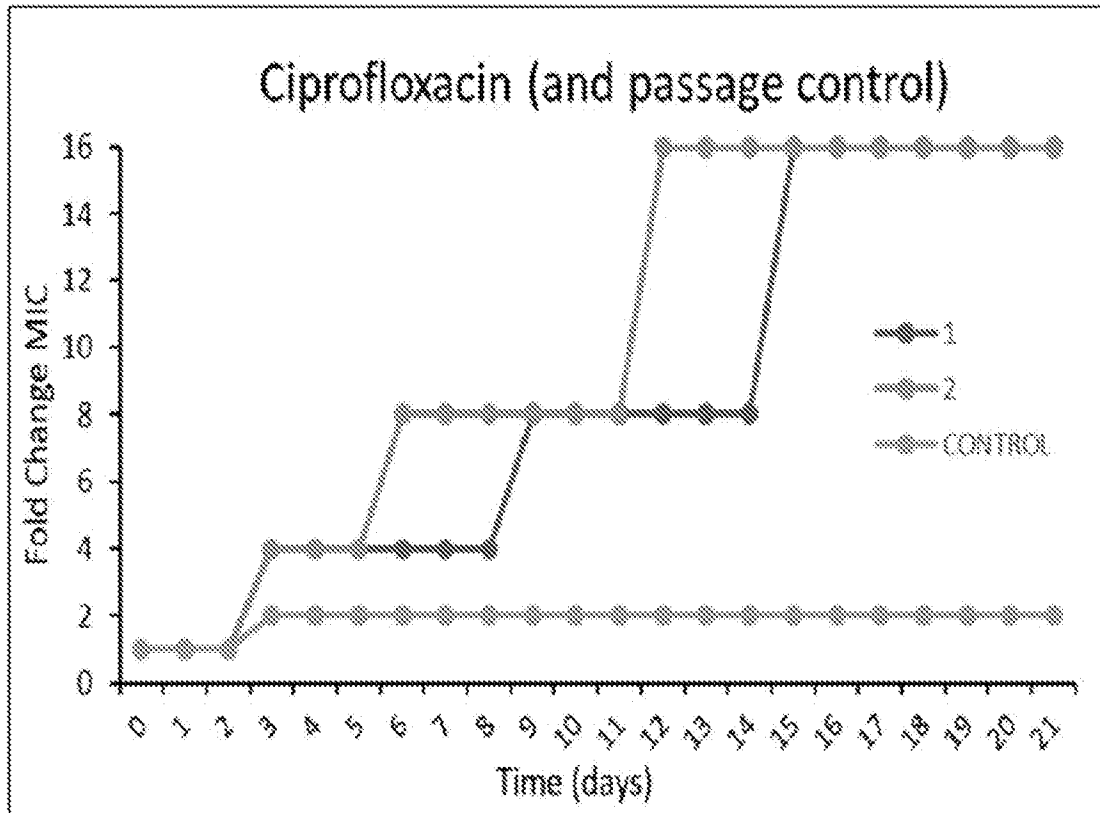


FIG. 4E

0341\_0021-00-304\_ST25 (1).txt  
SEQUENCE LISTING

<110> CONTRAFECT CORPORATION

<120> NUCLEIC ACIDS ENCODING LYSINS, LYSIN-ANTIMICROBIAL PEPTIDE (AMP)  
CONSTRUCTS, POLYPEPTIDES THEREOF AND USES THEREOF

<130> 0341.0021-00-304

<150> PCT/US19/024916  
<151> 2019-03-29

<150> 62/722,793  
<151> 2018-08-24

<150> 62/721,969  
<151> 2018-08-23

<150> 62/650,235  
<151> 2018-03-29

<150> 62860836  
<151> 2019-06-13

<150> 62849320  
<151> 2019-05-17

<160> 204

<170> PatentIn version 3.5

<210> 1  
<211> 636  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
<221> misc\_feature  
<222> (28)..(162)  
<223> GN168 lysin

<220>  
<221> CDS  
<222> (28)..(612)

<400> 1  
gtttaacttt aagaaggaga attcacc atg agg tta aaa atg gca cga aga aga  
Met Arg Leu Lys Met Ala Arg Arg Arg

54

|      |     |     |     |     |     |     |     |     |     |             |            |     |     |     |     |     |
|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------|------------|-----|-----|-----|-----|-----|
| tac  | aga | ctt | ccg | cga | cgt | aga | agt | cga | aga | ctt         | ttt        | tca | aga | act | gca | 102 |
| Tyr  | Arg | Leu | Pro | Arg | Arg | Arg | Ser | Arg | Arg | Leu         | Phe        | Ser | Arg | Thr | Ala |     |
| 10   |     |     |     |     | 15  |     |     |     |     | 20          |            |     |     |     | 25  |     |
| ttg  | agg | atg | cat | cca | aga | aat | agg | ctt | cga | aga         | att        | atg | cgt | ggc | ggc | 150 |
| Leu  | Arg | Met | His | Pro | Arg | Asn | Arg | Leu | Arg | Arg         | Ile        | Met | Arg | Gly | Gly |     |
|      |     |     |     | 30  |     |     |     |     | 35  |             |            |     |     | 40  |     |     |
| att  | agg | ttc | acc | gcg | ggc | ggc | acc | gcg | ggc | ggc         | cgt        | aca | tcc | caa | cga | 198 |
| Ile  | Arg | Phe | Thr | Ala | Gly | Gly | Thr | Ala | Gly | Gly         | Arg        | Thr | Ser | Gln | Arg |     |
|      |     |     | 45  |     |     |     |     | 50  |     |             |            |     | 55  |     |     |     |
| ggc  | atc | gac | ctc | atc | aaa | tcc | ttc | gag | ggc | ctg         | cgc        | ctg | tcc | gct | tac | 246 |
| Gly  | Ile | Asp | Leu | Ile | Lys | Ser | Phe | Glu | Gly | Leu         | Arg        | Leu | Ser | Ala | Tyr |     |
|      |     | 60  |     |     |     |     | 65  |     |     |             |            | 70  |     |     |     |     |
| cag  | gac | tcg | gtg | ggt | gtc | tgg | acc | ata | ggt | tac         | ggc        | acc | act | cgg | ggc | 294 |
| Gln  | Asp | Ser | Val | Gly | Val | Trp | Thr | Ile | Gly | Tyr         | Gly        | Thr | Thr | Arg | Gly |     |
|      | 75  |     |     |     |     | 80  |     |     |     |             | 85         |     |     |     |     |     |
| gtc  | acc | cgc | tac | atg | acg | atc | acc | gtc | gag | cag         | gcc        | gag | cgg | atg | ctg | 342 |
| Val  | Thr | Arg | Tyr | Met | Thr | Ile | Thr | Val | Glu | Gln         | Ala        | Glu | Arg | Met | Leu |     |
| 90   |     |     |     |     | 95  |     |     |     | 100 |             |            |     |     |     | 105 |     |
| tcg  | aac | gac | att | cag | cgc | ttc | gag | cca | gag | cta         | gac        | agg | ctg | gcg | aag | 390 |
| Ser  | Asn | Asp | Ile | Gln | Arg | Phe | Glu | Pro | Glu | Leu         | Asp        | Arg | Leu | Ala | Lys |     |
|      |     |     |     | 110 |     |     |     |     | 115 |             |            |     |     | 120 |     |     |
| gtg  | cca | ctg | aac | cag | aac | cag | tgg | gat | gcc | ctg         | atg        | agc | ttc | gtg | tac | 438 |
| Val  | Pro | Leu | Asn | Gln | Asn | Gln | Trp | Asp | Ala | Leu         | Met        | Ser | Phe | Val | Tyr |     |
|      |     |     | 125 |     |     |     |     | 130 |     |             |            |     | 135 |     |     |     |
| aac  | ctg | ggc | gcg | gcc | aat | ctg | gcg | tcg | tcc | acg         | ctg        | ctc | gac | ctg | ctg | 486 |
| Asn  | Leu | Gly | Ala | Ala | Asn | Leu | Ala | Ser | Ser | Thr         | Leu        | Leu | Asp | Leu | Leu |     |
|      |     | 140 |     |     |     |     | 145 |     |     |             | 150        |     |     |     |     |     |
| aac  | aag | ggt | gac | tac | cag | gga | gca | gcg | gac | cag         | ttc        | ccg | cat | tgg | gtg | 534 |
| Asn  | Lys | Gly | Asp | Tyr | Gln | Gly | Ala | Ala | Asp | Gln         | Phe        | Pro | His | Trp | Val |     |
|      | 155 |     |     |     |     | 160 |     |     |     | 165         |            |     |     |     |     |     |
| aat  | gcg | ggc | ggt | aag | cgc | ttg | gat | ggt | ctg | gtt         | aag        | cgt | cga | gca | gcc | 582 |
| Asn  | Ala | Gly | Gly | Lys | Arg | Leu | Asp | Gly | Leu | Val         | Lys        | Arg | Arg | Ala | Ala |     |
| 170  |     |     |     |     | 175 |     |     |     | 180 |             |            |     |     |     | 185 |     |
| gag  | cgt | gcg | ctg | ttc | ctg | gag | cca | cta | tcg | tgataaaaagc | ttggctgttt |     |     |     |     | 632 |
| Glu  | Arg | Ala | Leu | Phe | Leu | Glu | Pro | Leu | Ser |             |            |     |     |     |     |     |
|      |     |     |     | 190 |     |     |     |     | 195 |             |            |     |     |     |     |     |
| tggc |     |     |     |     |     |     |     |     |     |             |            |     |     |     |     | 636 |

<210> 2  
 <211> 195  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

<400> 2

Met Arg Leu Lys Met Ala Arg Arg Arg Tyr Arg Leu Pro Arg Arg Arg  
 1 5 10 15

Ser Arg Arg Leu Phe Ser Arg Thr Ala Leu Arg Met His Pro Arg Asn  
 20 25 30

Arg Leu Arg Arg Ile Met Arg Gly Gly Ile Arg Phe Thr Ala Gly Gly  
 35 40 45

Thr Ala Gly Gly Arg Thr Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser  
 50 55 60

Phe Glu Gly Leu Arg Leu Ser Ala Tyr Gln Asp Ser Val Gly Val Trp  
 65 70 75 80

Thr Ile Gly Tyr Gly Thr Thr Arg Gly Val Thr Arg Tyr Met Thr Ile  
 85 90 95

Thr Val Glu Gln Ala Glu Arg Met Leu Ser Asn Asp Ile Gln Arg Phe  
 100 105 110

Glu Pro Glu Leu Asp Arg Leu Ala Lys Val Pro Leu Asn Gln Asn Gln  
 115 120 125

Trp Asp Ala Leu Met Ser Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu  
 130 135 140

Ala Ser Ser Thr Leu Leu Asp Leu Leu Asn Lys Gly Asp Tyr Gln Gly  
 145 150 155 160

Ala Ala Asp Gln Phe Pro His Trp Val Asn Ala Gly Gly Lys Arg Leu

165

170

175

Asp Gly Leu Val Lys Arg Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu  
                   180                                  185                                  190

Pro Leu Ser  
                   195

<210> 3  
 <211> 567  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
 <221> CDS  
 <222> (28)..(543)

<220>  
 <221> misc\_feature  
 <222> (29)..(543)  
 <223> GN 176 lysin

<400> 3  
 gtttaacttt aagaaggaga attcacc atg agc ttt aac gtg acc ccg aaa ttt 54  
                                   Met Ser Phe Asn Val Thr Pro Lys Phe  
                                   1                                  5

aaa cgc tgg cag ctg tat ttt cgc ggc cgc atg tgg acc gcg ggc ggc 102  
 Lys Arg Trp Gln Leu Tyr Phe Arg Gly Arg Met Trp Thr Ala Gly Gly  
 10                                  15                                  20                                  25

acc gcg ggc ggc cgt aca tcc caa cga ggc atc gac ctc atc aaa tcc 150  
 Thr Ala Gly Gly Arg Thr Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser  
                                   30                                  35                                  40

ttc gag ggc ctg cgc ctg tcc gct tac cag gac tcg gtg ggt gtc tgg 198  
 Phe Glu Gly Leu Arg Leu Ser Ala Tyr Gln Asp Ser Val Gly Val Trp  
                                   45                                  50                                  55

acc ata ggt tac ggc acc act cgg ggc gtc acc gcg tac atg acg atc 246  
 Thr Ile Gly Tyr Gly Thr Thr Arg Gly Val Thr Arg Tyr Met Thr Ile  
                                   60                                  65                                  70

acc gtc gag cag gcc gag cgg atg ctg tcg aac gac att cag cgc ttc 294  
 Thr Val Glu Gln Ala Glu Arg Met Leu Ser Asn Asp Ile Gln Arg Phe

75

80

85

gag cca gag cta gac agg ctg gcg aag gtg cca ctg aac cag aac cag 342  
 Glu Pro Glu Leu Asp Arg Leu Ala Lys Val Pro Leu Asn Gln Asn Gln  
 90 95 100 105

tgg gat gcc ctg atg agc ttc gtg tac aac ctg ggc gcg gcc aat ctg 390  
 Trp Asp Ala Leu Met Ser Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu  
 110 115 120

gcg tcg tcc acg ctg ctc gac ctg ctg aac aag ggt gac tac cag gga 438  
 Ala Ser Ser Thr Leu Leu Asp Leu Leu Asn Lys Gly Asp Tyr Gln Gly  
 125 130 135

gca gcg gac cag ttc ccg cat tgg gtg aat gcg ggc ggt aag cgc ttg 486  
 Ala Ala Asp Gln Phe Pro His Trp Val Asn Ala Gly Gly Lys Arg Leu  
 140 145 150

gat ggt ctg gtt aag cgt cga gca gcc gag cgt gcg ctg ttc ctg gag 534  
 Asp Gly Leu Val Lys Arg Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu  
 155 160 165

cca cta tcg tgataaaagc ttggctgttt tggc 567  
 Pro Leu Ser  
 170

&lt;210&gt; 4

&lt;211&gt; 172

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Construct

&lt;400&gt; 4

Met Ser Phe Asn Val Thr Pro Lys Phe Lys Arg Trp Gln Leu Tyr Phe  
 1 5 10 15

Arg Gly Arg Met Trp Thr Ala Gly Gly Thr Ala Gly Gly Arg Thr Ser  
 20 25 30

Gln Arg Gly Ile Asp Leu Ile Lys Ser Phe Glu Gly Leu Arg Leu Ser  
 35 40 45

Ala Tyr Gln Asp Ser Val Gly Val Trp Thr Ile Gly Tyr Gly Thr Thr  
 50 55 60

Arg Gly Val Thr Arg Tyr Met Thr Ile Thr Val Glu Gln Ala Glu Arg  
65 70 75 80

Met Leu Ser Asn Asp Ile Gln Arg Phe Glu Pro Glu Leu Asp Arg Leu  
85 90 95

Ala Lys Val Pro Leu Asn Gln Asn Gln Trp Asp Ala Leu Met Ser Phe  
100 105 110

Val Tyr Asn Leu Gly Ala Ala Asn Leu Ala Ser Ser Thr Leu Leu Asp  
115 120 125

Leu Leu Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro His  
130 135 140

Trp Val Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Arg  
145 150 155 160

Ala Ala Glu Arg Ala Leu Phe Leu Glu Pro Leu Ser  
165 170

<210> 5  
<211> 582  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
<221> misc\_feature  
<222> (28)..(558)  
<223> GN178 lysin

<220>  
<221> CDS  
<222> (28)..(558)

<400> 5  
gtttaacttt aagaaggaga attcacc atg cca cca att ttt agc aaa ctg gcg  
Met Pro Pro Ile Phe Ser Lys Leu Ala  
1 5

0341\_0021-00-304\_ST25 (1).txt

|                                                                                                                                                     |     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| ggc aaa aaa att aaa aac ctg ctg att agc ggc ctg aaa ggc ggt agc<br>Gly Lys Lys Ile Lys Asn Leu Leu Ile Ser Gly Leu Lys Gly Gly Ser<br>10 15 20 25   | 102 |
| ggc agc ggt agc ggt agc ggc agc ccg cgt aca tcc caa cga ggc atc<br>Gly Ser Gly Ser Gly Ser Gly Ser Pro Arg Thr Ser Gln Arg Gly Ile<br>30 35 40      | 150 |
| gac ctc atc aaa tcc ttc gag ggc ctg cgc ctg tcc gct tac cag gac<br>Asp Leu Ile Lys Ser Phe Glu Gly Leu Arg Leu Ser Ala Tyr Gln Asp<br>45 50 55      | 198 |
| tcg gtg ggt gtc tgg acc ata ggt tac ggc acc act cgg ggc gtc acc<br>Ser Val Gly Val Trp Thr Ile Gly Tyr Gly Thr Thr Arg Gly Val Thr<br>60 65 70      | 246 |
| cgc tac atg acg atc acc gtc gag cag gcc gag cgg atg ctg tcg aac<br>Arg Tyr Met Thr Ile Thr Val Glu Gln Ala Glu Arg Met Leu Ser Asn<br>75 80 85      | 294 |
| gac att cag cgc ttc gag cca gag cta gac agg ctg gcg aag gtg cca<br>Asp Ile Gln Arg Phe Glu Pro Glu Leu Asp Arg Leu Ala Lys Val Pro<br>90 95 100 105 | 342 |
| ctg aac cag aac cag tgg gat gcc ctg atg agc ttc gtg tac aac ctg<br>Leu Asn Gln Asn Gln Trp Asp Ala Leu Met Ser Phe Val Tyr Asn Leu<br>110 115 120   | 390 |
| ggc gcg gcc aat ctg gcg tcg tcc acg ctg ctc gac ctg ctg aac aag<br>Gly Ala Ala Asn Leu Ala Ser Ser Thr Leu Leu Asp Leu Leu Asn Lys<br>125 130 135   | 438 |
| ggt gac tac cag gga gca gcg gac cag ttc ccg cat tgg gtg aat gcg<br>Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro His Trp Val Asn Ala<br>140 145 150   | 486 |
| ggc ggt aag cgc ttg gat ggt ctg gtt aag cgt cga gca gcc gag cgt<br>Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Ang Ala Ala Glu Arg<br>155 160 165   | 534 |
| gcg ctg ttc ctg gag cca cta tcg tgataaaagc ttggctgttt tggc<br>Ala Leu Phe Leu Glu Pro Leu Ser<br>170 175                                            | 582 |

<210> 6  
<211> 177  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Synthetic Construct

&lt;400&gt; 6

Met Pro Pro Ile Phe Ser Lys Leu Ala Gly Lys Lys Ile Lys Asn Leu  
 1 5 10 15

Leu Ile Ser Gly Leu Lys Gly Gly Ser Gly Ser Gly Ser Gly Ser Gly  
 20 25 30

Ser Pro Arg Thr Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser Phe Glu  
 35 40 45

Gly Leu Arg Leu Ser Ala Tyr Gln Asp Ser Val Gly Val Trp Thr Ile  
 50 55 60

Gly Tyr Gly Thr Thr Arg Gly Val Thr Arg Tyr Met Thr Ile Thr Val  
 65 70 75 80

Glu Gln Ala Glu Arg Met Leu Ser Asn Asp Ile Gln Arg Phe Glu Pro  
 85 90 95

Glu Leu Asp Arg Leu Ala Lys Val Pro Leu Asn Gln Asn Gln Trp Asp  
 100 105 110

Ala Leu Met Ser Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu Ala Ser  
 115 120 125

Ser Thr Leu Leu Asp Leu Leu Asn Lys Gly Asp Tyr Gln Gly Ala Ala  
 130 135 140

Asp Gln Phe Pro His Trp Val Asn Ala Gly Gly Lys Arg Leu Asp Gly  
 145 150 155 160

Leu Val Lys Arg Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu Pro Leu  
 165 170 175

Ser

&lt;210&gt; 7

<211> 429  
 <212> DNA  
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (28)..(405)

<223> GN217 lysin

<220>

<221> CDS

<222> (28)..(405)

<400> 7

|                                                                   |    |
|-------------------------------------------------------------------|----|
| gtttaacttt aagaaggaga attcacc atg acc tac acc ctg tct aaa cgt tct | 54 |
| Met Thr Tyr Thr Leu Ser Lys Arg Ser                               |    |
| 1 5                                                               |    |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| ctg gac aac ctg aaa ggt gtt cac ccg gac ctg gtt gct gtt gtt cac | 102 |
| Leu Asp Asn Leu Lys Gly Val His Pro Asp Leu Val Ala Val Val His |     |
| 10 15 20 25                                                     |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| cgt gct atc cag ctg acc ccg gtt gac ttc gct gtt atc gaa ggt ctg | 150 |
| Arg Ala Ile Gln Leu Thr Pro Val Asp Phe Ala Val Ile Glu Gly Leu |     |
| 30 35 40                                                        |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| cgt tct gtt tct cgt cag aaa gaa ctg gtt gct gct ggt gct tct aaa | 198 |
| Arg Ser Val Ser Arg Gln Lys Glu Leu Val Ala Ala Gly Ala Ser Lys |     |
| 45 50 55                                                        |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| acc atg aac tct cgt cac ctg acc ggt cac gct gtt gac ctg gct gct | 246 |
| Thr Met Asn Ser Arg His Leu Thr Gly His Ala Val Asp Leu Ala Ala |     |
| 60 65 70                                                        |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| tac gtt aac ggt atc cat tgg gac tgg ccg ctg tac gac gct atc gct | 294 |
| Tyr Val Asn Gly Ile His Trp Asp Trp Pro Leu Tyr Asp Ala Ile Ala |     |
| 75 80 85                                                        |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| gtt gct gtt aaa gct gct gct aaa gaa ctg ggt gtt gct atc gtt tgg | 342 |
| Val Ala Val Lys Ala Ala Ala Lys Glu Leu Gly Val Ala Ile Val Trp |     |
| 90 95 100 105                                                   |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| ggt ggt gac tgg acc acc ttc aaa gac ggt ccg cac ttc gaa ctg gac | 390 |
| Gly Gly Asp Trp Thr Thr Phe Lys Asp Gly Pro His Phe Glu Leu Asp |     |
| 110 115 120                                                     |     |

|                                                |     |
|------------------------------------------------|-----|
| cgt tct aaa tac cgt taataaaagc ttggctgttt tggc | 429 |
| Arg Ser Lys Tyr Arg                            |     |

125

<210> 8  
 <211> 126  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

<400> 8

Met Thr Tyr Thr Leu Ser Lys Arg Ser Leu Asp Asn Leu Lys Gly Val  
 1 5 10 15

His Pro Asp Leu Val Ala Val Val His Arg Ala Ile Gln Leu Thr Pro  
 20 25 30

Val Asp Phe Ala Val Ile Glu Gly Leu Arg Ser Val Ser Arg Gln Lys  
 35 40 45

Glu Leu Val Ala Ala Gly Ala Ser Lys Thr Met Asn Ser Arg His Leu  
 50 55 60

Thr Gly His Ala Val Asp Leu Ala Ala Tyr Val Asn Gly Ile His Trp  
 65 70 75 80

Asp Trp Pro Leu Tyr Asp Ala Ile Ala Val Ala Val Lys Ala Ala Ala  
 85 90 95

Lys Glu Leu Gly Val Ala Ile Val Trp Gly Gly Asp Trp Thr Thr Phe  
 100 105 110

Lys Asp Gly Pro His Phe Glu Leu Asp Arg Ser Lys Tyr Arg  
 115 120 125

<210> 9  
 <211> 501  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic polynucleotide

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; GN218 lysin

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (28)..(477)

&lt;400&gt; 9

gtttaacttt aagaaggaga attcacc atg acc tac acc ctg tct aaa cgt tct 54  
 Met Thr Tyr Thr Leu Ser Lys Arg Ser

1

5

ctg gac aac ctg aaa ggt gtt cac ccg gac ctg gtt gct gtt gtt cac 102  
 Leu Asp Asn Leu Lys Gly Val His Pro Asp Leu Val Ala Val Val His  
 10 15 20 25

cgt gct atc cag ctg acc ccg gtt gac ttc gct gtt atc gaa ggt ctg 150  
 Arg Ala Ile Gln Leu Thr Pro Val Asp Phe Ala Val Ile Glu Gly Leu  
 30 35 40

cgt tct gtt tct cgt cag aaa gaa ctg gtt gct gct ggt gct tct aaa 198  
 Arg Ser Val Ser Arg Gln Lys Glu Leu Val Ala Ala Gly Ala Ser Lys  
 45 50 55

acc atg aac tct cgt cac ctg acc ggt cac gct gtt gac ctg gct gct 246  
 Thr Met Asn Ser Arg His Leu Thr Gly His Ala Val Asp Leu Ala Ala  
 60 65 70

tac gtt aac ggt atc cgt tgg gac tgg ccg ctg tac gac gct atc gct 294  
 Tyr Val Asn Gly Ile Arg Trp Asp Trp Pro Leu Tyr Asp Ala Ile Ala  
 75 80 85

gtt gct gtt aaa gct gct gct aaa gaa ctg ggt gtt gct atc gtt tgg 342  
 Val Ala Val Lys Ala Ala Lys Glu Leu Gly Val Ala Ile Val Trp  
 90 95 100 105

ggt ggt gac tgg acc acc ttc aaa gac ggt ccg cac ttc gaa ctg gac 390  
 Gly Gly Asp Trp Thr Thr Phe Lys Asp Gly Pro His Phe Glu Leu Asp  
 110 115 120

cgt tct aaa tac ggc ggt ggc tct gga ggt ggt ggg tcc ggc ggt ggc 438  
 Arg Ser Lys Tyr Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly  
 125 130 135

tct cgc ctg aaa aaa att ggc aaa gtg ctg aaa tgg att taataaaagc 487  
 Ser Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
 140 145 150

ttggctgttt tggc 501

<210> 10  
 <211> 150  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

<400> 10

Met Thr Tyr Thr Leu Ser Lys Arg Ser Leu Asp Asn Leu Lys Gly Val  
 1 5 10 15

His Pro Asp Leu Val Ala Val Val His Arg Ala Ile Gln Leu Thr Pro  
 20 25 30

Val Asp Phe Ala Val Ile Glu Gly Leu Arg Ser Val Ser Arg Gln Lys  
 35 40 45

Glu Leu Val Ala Ala Gly Ala Ser Lys Thr Met Asn Ser Arg His Leu  
 50 55 60

Thr Gly His Ala Val Asp Leu Ala Ala Tyr Val Asn Gly Ile Arg Trp  
 65 70 75 80

Asp Trp Pro Leu Tyr Asp Ala Ile Ala Val Ala Val Lys Ala Ala Ala  
 85 90 95

Lys Glu Leu Gly Val Ala Ile Val Trp Gly Gly Asp Trp Thr Thr Phe  
 100 105 110

Lys Asp Gly Pro His Phe Glu Leu Asp Arg Ser Lys Tyr Gly Gly Gly  
 115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Arg Leu Lys Lys Ile Gly  
 130 135 140

Lys Val Leu Lys Trp Ile  
 145 150

<210> 11

<211> 573

<212> DNA

### <213> Artificial Sequence

 $\langle 220 \rangle$ 

<223> Description of Artificial Sequence: Synthetic polynucleotide

 $\langle 220 \rangle$ 

<221> misc feature

<222> (28)..(549)

<223> GN223 lysin

 $\langle 220 \rangle$ 

<221> CDS

<222> (28)..(549)

<400> 11

gtttaacttt aagaaggaga attcacc atg acc tac acc ctg tct aaa cgt tct 54  
Met Thr Tyr Thr Leu Ser Lys Arg Ser  
1 5

ctg gac aac ctg aaa ggt gtt cac ccg gac ctg gtt gct gtt gtt cac 102  
Leu Asp Asn Leu Lys Gly Val His Pro Asp Leu Val Ala Val Val His  
10 15 20 25

cgt gct atc cag ctg acc ccg gtt gac ttc gct gtt atc gaa ggt ctg 150  
Arg Ala Ile Gln Leu Thr Pro Val Asp Phe Ala Val Ile Glu Gly Leu  
30 35 40

cgt tct gtt tct cgt cag aaa gaa ctg gtt gct gct ggt gct tct aaa 198  
Arg Ser Val Ser Arg Gln Lys Glu Leu Val Ala Ala Gly Ala Ser Lys  
45 50 55

acc atg aac tct cgt cac ctg acc ggt cac gct gtt gac ctg gct gct 246  
Thr Met Asn Ser Arg His Leu Thr Gly His Ala Val Asp Leu Ala Ala  
60 65 70

tac gtt aac ggt atc cgt tgg gac tgg ccg ctg tac gac gct atc gct 294  
Tyr Val Asn Gly Ile Arg Trp Asp Trp Pro Leu Tyr Asp Ala Ile Ala  
75 80 85

ggt gct gtt aaa gct gct gct aaa gaa ctg ggt gtt gct atc gtt tgg 342  
Val Ala Val Lys Ala Ala Ala Lys Glu Leu Gly Val Ala Ile Val Trp  
90 95 100 105

ggt ggt gac tgg acc acc ttc aaa gac ggt ccg cac ttc gaa ctg gac 390  
Gly Gly Asp Trp Thr Thr Phe Lys Asp Gly Pro His Phe Glu Leu Asp  
110 115 120

cgt tct aaa tac cgt cca cca ggc ggt ggc tct gga ggt ggt ggg tcc 438

0341\_0021-00-304\_ST25 (1).txt

Arg Ser Lys Tyr Arg Pro Pro Gly Gly Gly Ser Gly Gly Gly Gly Ser  
125 130 135

ggc ggt ggc tct tcg aag aag gcg tcg agg aag agt ttt act aag ggt 486  
Gly Gly Gly Ser Ser Lys Lys Ala Ser Arg Lys Ser Phe Thr Lys Gly  
140 145 150

gcc gtt aag gtt cat aag aaa aat gtt cct act cgt gtt cct atg cgt 534  
Ala Val Lys Val His Lys Lys Asn Val Pro Thr Arg Val Pro Met Arg  
155 160 165

ggc ggt att agg ctt taataaaagc ttggctgttt tggc 573  
Gly Gly Ile Arg Leu  
170

<210> 12  
<211> 174  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Synthetic Construct

<400> 12

Met Thr Tyr Thr Leu Ser Lys Arg Ser Leu Asp Asn Leu Lys Gly Val  
1 5 10 15

His Pro Asp Leu Val Ala Val Val His Arg Ala Ile Gln Leu Thr Pro  
20 25 30

Val Asp Phe Ala Val Ile Glu Gly Leu Arg Ser Val Ser Arg Gln Lys  
35 40 45

Glu Leu Val Ala Ala Gly Ala Ser Lys Thr Met Asn Ser Arg His Leu  
50 55 60

Thr Gly His Ala Val Asp Leu Ala Ala Tyr Val Asn Gly Ile Arg Trp  
65 70 75 80

Asp Trp Pro Leu Tyr Asp Ala Ile Ala Val Ala Val Lys Ala Ala Ala  
85 90 95

Lys Glu Leu Gly Val Ala Ile Val Trp Gly Gly Asp Trp Thr Thr Phe  
100 105 110

Lys Asp Gly Pro His Phe Glu Leu Asp Arg Ser Lys Tyr Arg Pro Pro  
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Ser Lys Lys  
 130 135 140

Ala Ser Arg Lys Ser Phe Thr Lys Gly Ala Val Lys Val His Lys Lys  
 145 150 155 160

Asn Val Pro Thr Arg Val Pro Met Arg Gly Gly Ile Arg Leu  
 165 170

<210> 13  
 <211> 519  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
 <221> misc\_feature  
 <222> (28)..(495)  
 <223> GN239 lysin

<220>  
 <221> CDS  
 <222> (28)..(495)

<400> 13  
 gtttaacttt aagaaggaga attcacc atg acc tac acc ctg tct aaa cgt tct 54  
 Met Thr Tyr Thr Leu Ser Lys Arg Ser  
 1 5

ctg gac aac ctg aaa ggt gtt cac ccg gac ctg gtt gct gtt gtt cac 102  
 Leu Asp Asn Leu Lys Gly Val His Pro Asp Leu Val Ala Val Val His  
 10 15 20 25

cgt gct atc cag ctg acc ccg gtt gac ttc gct gtt atc gaa ggt ctg 150  
 Arg Ala Ile Gln Leu Thr Pro Val Asp Phe Ala Val Ile Glu Gly Leu  
 30 35 40

cgt tct gtt tct cgt cag aaa gaa ctg gtt gct gct ggt gct tct aaa 198  
 Arg Ser Val Ser Arg Gln Lys Glu Leu Val Ala Ala Gly Ala Ser Lys  
 45 50 55

0341\_0021-00-304\_ST25 (1).txt

acc atg aac tct cgt cac ctg acc ggt cac gct gtt gac ctg gct gct 246  
Thr Met Asn Ser Arg His Leu Thr Gly His Ala Val Asp Leu Ala Ala  
60 65 70

tac gtt aac ggt atc cgt tgg gac tgg ccg ctg tac gac gct atc gct 294  
Tyr Val Asn Gly Ile Arg Trp Asp Trp Pro Leu Tyr Asp Ala Ile Ala  
75 80 85

gtt gct gtt aaa gct gct gct aaa gaa ctg ggt gtt gct atc gtt tgg 342  
Val Ala Val Lys Ala Ala Ala Lys Glu Leu Gly Val Ala Ile Val Trp  
90 95 100 105

ggt ggt gac tgg acc acc ttc aaa gac ggt ccg cac ttc gaa ctg gac 390  
Gly Gly Asp Trp Thr Thr Phe Lys Asp Gly Pro His Phe Glu Leu Asp  
110 115 120

cgt tct aaa tac ggc ggt ggc tct gga ggt ggt ggg tcc ggc ggt ggc 438  
Arg Ser Lys Tyr Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly  
125 130 135

tct cgt aaa aaa acc cgt aaa cgt ctg aaa aaa atc ggt aaa gtt ctg 486  
Ser Arg Lys Lys Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val Leu  
140 145 150

aaa tgg atc taataaaagc ttggctgttt tggc 519  
Lys Trp Ile  
155

<210> 14  
<211> 156  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Synthetic Construct

<400> 14

Met Thr Tyr Thr Leu Ser Lys Arg Ser Leu Asp Asn Leu Lys Gly Val  
1 5 10 15

His Pro Asp Leu Val Ala Val Val His Arg Ala Ile Gln Leu Thr Pro  
20 25 30

Val Asp Phe Ala Val Ile Glu Gly Leu Arg Ser Val Ser Arg Gln Lys  
35 40 45

0341\_0021-00-304\_ST25 (1).txt

Glu Leu Val Ala Ala Gly Ala Ser Lys Thr Met Asn Ser Arg His Leu  
50 55 60

Thr Gly His Ala Val Asp Leu Ala Ala Tyr Val Asn Gly Ile Arg Trp  
65 70 75 80

Asp Trp Pro Leu Tyr Asp Ala Ile Ala Val Ala Val Lys Ala Ala Ala  
85 90 95

Lys Glu Leu Gly Val Ala Ile Val Trp Gly Gly Asp Trp Thr Thr Phe  
100 105 110

Lys Asp Gly Pro His Phe Glu Leu Asp Arg Ser Lys Tyr Gly Gly Gly  
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Arg Lys Lys Thr Arg Lys  
130 135 140

Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
145 150 155

<210> 15  
<211> 570  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
<221> misc\_feature  
<222> (28)..(546)  
<223> GN243 lysin

<220>  
<221> CDS  
<222> (28)..(546)

<400> 15  
gtttaacttt aagaaggaga attcacc atg acc tac acc ctg tct aaa cgt tct 54  
Met Thr Tyr Thr Leu Ser Lys Arg Ser  
1 5

ctg gac aac ctg aaa ggt gtt cac ccg gac ctg gtt gct gtt gtt cac 102

0341\_0021-00-304\_ST25 (1).txt

|     |     |     |     |            |            |      |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|------------|------------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Asp | Asn | Leu | Lys        | Gly        | Val  | His | Pro | Asp | Leu | Val | Ala | Val | Val | His |     |
| 10  |     |     |     |            | 15         |      |     |     |     | 20  |     |     |     |     | 25  |     |
| cgt | gct | atc | cag | ctg        | acc        | ccg  | gtt | gac | ttc | gct | gtt | atc | gaa | ggc | ctg | 150 |
| Arg | Ala | Ile | Gln | Leu        | Thr        | Pro  | Val | Asp | Phe | Ala | Val | Ile | Glu | Gly | Leu |     |
|     |     |     | 30  |            |            |      |     | 35  |     |     |     |     | 40  |     |     |     |
| cgt | tct | gtt | tct | cgt        | cag        | aaa  | gaa | ctg | gtt | gct | gct | ggc | gct | tct | aaa | 198 |
| Arg | Ser | Val | Ser | Arg        | Gln        | Lys  | Glu | Leu | Val | Ala | Ala | Gly | Ala | Ser | Lys |     |
|     |     |     | 45  |            |            |      | 50  |     |     |     |     | 55  |     |     |     |     |
| acc | atg | aac | tct | cgt        | cac        | ctg  | acc | ggc | cac | gct | gtt | gac | ctg | gct | gct | 246 |
| Thr | Met | Asn | Ser | Arg        | His        | Leu  | Thr | Gly | His | Ala | Val | Asp | Leu | Ala | Ala |     |
|     |     | 60  |     |            |            | 65   |     |     |     |     |     | 70  |     |     |     |     |
| tac | gtt | aac | ggc | atc        | cgt        | tgg  | gac | tgg | ccg | ctg | tac | gac | gct | atc | gct | 294 |
| Tyr | Val | Asn | Gly | Ile        | Arg        | Trp  | Asp | Trp | Pro | Leu | Tyr | Asp | Ala | Ile | Ala |     |
|     | 75  |     |     |            | 80         |      |     |     |     | 85  |     |     |     |     |     |     |
| gtt | gct | gtt | aaa | gct        | gct        | gct  | aaa | gaa | ctg | ggc | gtt | gct | atc | gtt | tgg | 342 |
| Val | Ala | Val | Lys | Ala        | Ala        | Ala  | Lys | Glu | Leu | Gly | Val | Ala | Ile | Val | Trp |     |
| 90  |     |     |     | 95         |            |      |     |     | 100 |     |     |     |     | 105 |     |     |
| ggc | ggc | gac | tgg | acc        | acc        | ttc  | aaa | gac | ggc | ccg | cac | ttc | gaa | ctg | gac | 390 |
| Gly | Gly | Asp | Trp | Thr        | Thr        | Phe  | Lys | Asp | Gly | Pro | His | Phe | Glu | Leu | Asp |     |
|     |     |     | 110 |            |            |      |     | 115 |     |     |     |     | 120 |     |     |     |
| cgt | tct | aaa | tac | cgt        | aaa        | aaa  | acc | cgt | aaa | cgt | ctg | aaa | aaa | atc | ggc | 438 |
| Arg | Ser | Lys | Tyr | Arg        | Lys        | Lys  | Thr | Arg | Lys | Arg | Leu | Lys | Lys | Ile | Gly |     |
|     |     |     | 125 |            |            |      |     | 130 |     |     |     |     | 135 |     |     |     |
| aaa | gtt | ctg | aaa | tgg        | atc        | cca  | cca | ggc | ggc | ggc | tct | gga | ggc | ggc | ggg | 486 |
| Lys | Val | Leu | Lys | Trp        | Ile        | Pro  | Pro | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Gly |     |
|     |     | 140 |     |            |            | 145  |     |     |     |     |     | 150 |     |     |     |     |
| tcc | ggc | ggc | ggc | tct        | acc        | cgc  | aaa | cgc | ctg | aaa | aaa | att | ggc | aaa | gtg | 534 |
| Ser | Gly | Gly | Gly | Ser        | Thr        | Arg  | Lys | Arg | Leu | Lys | Lys | Ile | Gly | Lys | Val |     |
|     | 155 |     |     |            |            | 160  |     |     |     | 165 |     |     |     |     |     |     |
| ctg | aaa | tgg | att | taataaaagc | ttggctgttt | tggc |     |     |     |     |     |     |     |     |     | 570 |
| Leu | Lys | Trp | Ile |            |            |      |     |     |     |     |     |     |     |     |     |     |
| 170 |     |     |     |            |            |      |     |     |     |     |     |     |     |     |     |     |

<210> 16  
 <211> 173  
 <212> PRT  
 <213> Artificial Sequence  
 <220>  
 <223> Synthetic Construct

&lt;400&gt; 16

Met Thr Tyr Thr Leu Ser Lys Arg Ser Leu Asp Asn Leu Lys Gly Val  
 1 5 10 15

His Pro Asp Leu Val Ala Val Val His Arg Ala Ile Gln Leu Thr Pro  
 20 25 30

Val Asp Phe Ala Val Ile Glu Gly Leu Arg Ser Val Ser Arg Gln Lys  
 35 40 45

Glu Leu Val Ala Ala Gly Ala Ser Lys Thr Met Asn Ser Arg His Leu  
 50 55 60

Thr Gly His Ala Val Asp Leu Ala Ala Tyr Val Asn Gly Ile Arg Trp  
 65 70 75 80

Asp Trp Pro Leu Tyr Asp Ala Ile Ala Val Ala Val Lys Ala Ala Ala  
 85 90 95

Lys Glu Leu Gly Val Ala Ile Val Trp Gly Gly Asp Trp Thr Thr Phe  
 100 105 110

Lys Asp Gly Pro His Phe Glu Leu Asp Arg Ser Lys Tyr Arg Lys Lys  
 115 120 125

Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile Pro  
 130 135 140

Pro Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Thr Arg  
 145 150 155 160

Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
 165 170

&lt;210&gt; 17

&lt;211&gt; 528

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (28)..(504)

<223> GN280 lysin

<220>

<221> CDS

<222> (28)..(504)

<400> 17

```
gtttaacttt aagaaggaga attcacc atg aaa ctc agc gaa aaa cga gca ctg      54
                Met Lys Leu Ser Glu Lys Arg Ala Leu
                  1                5
```

```
ttc acc cag ctg ctt gcc cag tta att ctt tgg gca gga act cag gat      102
Phe Thr Gln Leu Leu Ala Gln Leu Ile Leu Trp Ala Gly Thr Gln Asp
10                15                20                25
```

```
cga gtg tca gta gcc ttg gat caa gtg aaa agg aca cag gct gaa gct      150
Arg Val Ser Val Ala Leu Asp Gln Val Lys Arg Thr Gln Ala Glu Ala
                30                35                40
```

```
gat gcc aat gct aag tct gga gca ggc att agg aac tct ctc cat cta      198
Asp Ala Asn Ala Lys Ser Gly Ala Gly Ile Arg Asn Ser Leu His Leu
                45                50                55
```

```
ctg gga tta gcc ggt gat ctt atc ctc tac aag gat ggt aaa tac atg      246
Leu Gly Leu Ala Gly Asp Leu Ile Leu Tyr Lys Asp Gly Lys Tyr Met
        60                65                70
```

```
gat aag agc gag gat tat aag ttc ctg gga gat tac tgg aag agt ctc      294
Asp Lys Ser Glu Asp Tyr Lys Phe Leu Gly Asp Tyr Trp Lys Ser Leu
        75                80                85
```

```
cat cct ctt tgt cgg tgg ggc gga gat ttt aaa agc cgt cct gat ggt      342
His Pro Leu Cys Arg Trp Gly Gly Asp Phe Lys Ser Arg Pro Asp Gly
90                95                100                105
```

```
aat cat ttc tcc ttg gaa cac gaa gga gtg caa cgt aaa aaa acc cgt      390
Asn His Phe Ser Leu Glu His Glu Gly Val Gln Arg Lys Lys Thr Arg
                110                115                120
```

```
aaa cgt ctg aaa aaa atc ggt aaa gtt ctg aaa tgg atc cca cca acc      438
Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile Pro Pro Thr
                125                130                135
```

```
gcg ggc ggc acc gcg ggc ggc acc cgc aaa cgc ctg aaa aaa att ggc      486
Ala Gly Gly Thr Ala Gly Gly Thr Arg Lys Arg Leu Lys Lys Ile Gly
        140                145                150
```

aaa gtg ctg aaa tgg att taataaaagc ttggctgttt tggc  
 Lys Val Leu Lys Trp Ile  
 155

<210> 18  
 <211> 159  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

<400> 18

Met Lys Leu Ser Glu Lys Arg Ala Leu Phe Thr Gln Leu Leu Ala Gln  
 1 5 10 15

Leu Ile Leu Trp Ala Gly Thr Gln Asp Arg Val Ser Val Ala Leu Asp  
 20 25 30

Gln Val Lys Arg Thr Gln Ala Glu Ala Asp Ala Asn Ala Lys Ser Gly  
 35 40 45

Ala Gly Ile Arg Asn Ser Leu His Leu Leu Gly Leu Ala Gly Asp Leu  
 50 55 60

Ile Leu Tyr Lys Asp Gly Lys Tyr Met Asp Lys Ser Glu Asp Tyr Lys  
 65 70 75 80

Phe Leu Gly Asp Tyr Trp Lys Ser Leu His Pro Leu Cys Arg Trp Gly  
 85 90 95

Gly Asp Phe Lys Ser Arg Pro Asp Gly Asn His Phe Ser Leu Glu His  
 100 105 110

Glu Gly Val Gln Arg Lys Lys Thr Arg Lys Arg Leu Lys Lys Ile Gly  
 115 120 125

Lys Val Leu Lys Trp Ile Pro Pro Thr Ala Gly Gly Thr Ala Gly Gly  
 130 135 140

|            |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|------------|------------|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| <400>      | 19         |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| gtttaacttt | aagaaggaga | attcacc | atg | aaa | ctc | agc | gaa | aaa | cga | gca | ctg |     |     |     |     | 54  |
|            |            |         | Met | Lys | Leu | Ser | Glu | Lys | Arg | Ala | Leu |     |     |     |     |     |
|            |            |         | 1   |     |     |     | 5   |     |     |     |     |     |     |     |     |     |
|            |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| ttc        | acc        | cag     | ctg | ctt | gcc | cag | tta | att | ctt | tgg | gca | gga | act | cag | gat | 102 |
| Phe        | Thr        | Gln     | Leu | Leu | Ala | Gln | Leu | Ile | Leu | Trp | Ala | Gly | Thr | Gln | Asp |     |
| 10         |            |         |     |     | 15  |     |     |     |     | 20  |     |     |     |     | 25  |     |
|            |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| cga        | gtg        | tca     | gta | gcc | ttg | gat | caa | gtg | aaa | agg | aca | cag | gct | gaa | gct | 150 |
| Arg        | Val        | Ser     | Val | Ala | Leu | Asp | Gln | Val | Lys | Arg | Thr | Gln | Ala | Glu | Ala |     |
|            |            |         |     | 30  |     |     |     |     | 35  |     |     |     |     | 40  |     |     |
|            |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| gat        | gcc        | aat     | gct | aag | tct | gga | gca | ggc | att | agg | aac | tct | ctc | cat | cta | 198 |
| Asp        | Ala        | Asn     | Ala | Lys | Ser | Gly | Ala | Gly | Ile | Arg | Asn | Ser | Leu | His | Leu |     |
|            |            |         | 45  |     |     |     |     | 50  |     |     |     |     | 55  |     |     |     |
|            |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| ctg        | gga        | tta     | gcc | ggc | gat | ctt | atc | ctc | tac | aag | gat | ggc | aaa | tac | atg | 246 |
| Leu        | Gly        | Leu     | Ala | Gly | Asp | Leu | Ile | Leu | Tyr | Lys | Asp | Gly | Lys | Tyr | Met |     |
|            |            | 60      |     |     |     |     | 65  |     |     |     |     | 70  |     |     |     |     |
|            |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| gat        | aag        | agc     | gag | gat | tat | aag | ttc | ctg | gga | gat | tac | tgg | aag | agt | ctc | 294 |
| Asp        | Lys        | Ser     | Glu | Asp | Tyr | Lys | Phe | Leu | Gly | Asp | Tyr | Trp | Lys | Ser | Leu |     |
|            | 75         |         |     |     |     | 80  |     |     |     |     | 85  |     |     |     |     |     |
|            |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| cat        | cct        | ctt     | tgt | cgg | tgg | ggc | gga | gat | ttt | aaa | agc | cgt | cct | gat | ggc | 342 |
| His        | Pro        | Leu     | Cys | Arg | Trp | Gly | Gly | Asp | Phe | Lys | Ser | Arg | Pro | Asp | Gly |     |
| 90         |            |         |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |
|            |            |         |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| aat        | cat        | ttc     | tcc | ttg | gaa | cac | gaa | gga | gtg | caa | cgt | aaa | aaa | acc | cgt | 390 |
| Asn        | His        | Phe     | Ser | Leu | Glu | His | Glu | Gly | Val | Gln | Arg | Lys | Lys | Thr | Arg |     |

110

115

120

aaa cgt ctg aaa aaa atc ggt aaa gtt ctg aaa tgg atc ggc ggt ggc 438  
 Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile Gly Gly Gly  
                   125                                  130                                  135

tct gga ggt ggt ggg tcc ggc ggt ggc tct cca cca acc cgc aaa cgc 486  
 Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Pro Pro Thr Arg Lys Arg  
                   140                                  145                                  150

ctg aaa aaa att ggc aaa gtg ctg aaa tgg att taataaaaagc ttggctgttt 539  
 Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
                   155                                  160

tggc 543

<210> 20

<211> 164

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 20

Met Lys Leu Ser Glu Lys Arg Ala Leu Phe Thr Gln Leu Leu Ala Gln  
 1                  5                                  10                                  15

Leu Ile Leu Trp Ala Gly Thr Gln Asp Arg Val Ser Val Ala Leu Asp  
                   20                                  25                                  30

Gln Val Lys Arg Thr Gln Ala Glu Ala Asp Ala Asn Ala Lys Ser Gly  
                   35                                  40                                  45

Ala Gly Ile Arg Asn Ser Leu His Leu Leu Gly Leu Ala Gly Asp Leu  
                   50                                  55                                  60

Ile Leu Tyr Lys Asp Gly Lys Tyr Met Asp Lys Ser Glu Asp Tyr Lys  
 65                  70                                  75                                  80

Phe Leu Gly Asp Tyr Trp Lys Ser Leu His Pro Leu Cys Arg Trp Gly  
                   85                                  90                                  95

Gly Asp Phe Lys Ser Arg Pro Asp Gly Asn His Phe Ser Leu Glu His

100

105

110

Glu Gly Val Gln Arg Lys Lys Thr Arg Lys Arg Leu Lys Lys Ile Gly  
           115                                  120                                  125

Lys Val Leu Lys Trp Ile Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly  
           130                                  135                                  140

Gly Gly Ser Pro Pro Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val  
   145                                  150                                  155                                  160

Leu Lys Trp Ile

<210> 21  
 <211> 852  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
 <221> misc\_feature  
 <223> GN316 lysin

<400> 21  
 gaattcacca tgggatccca tcatcaccac catcatggtg ccattttaaa gattggcagc 60  
 aaaggtctgg aagttaagaa tcttcagacc agtctcaaca aaatcggggt 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 gccagcttt acccgacgtt ggtaacgcc 480  
 aaagccgggg gatacacagg tggggacgcg gagttggaac gactccatgg tgcaatagcg 540  
 atcgataaag attgcgccta cgagagcgct tcctacgggt tattccagat catgggggtc 600

```

aactgcgtta tttgtggata tgacaatgcc gaggagatgt tcaacgactt tctcactggg      660
gaacgtgctc agctcatggc atttgtcaag ttcatcaagg ctgacgcaa tctgtggaaa      720
gcattgaagg acaagaattg ggctgagttt gctcggcggtt acaatggccc ggcgtatgca      780
cagaaccagt acgacaccaa gctggctgca gcatacaaat cattcagtta gtaaaagctt      840
ggctgttttg gc                                                             852

```

```

<210> 22
<211> 264
<212> PRT
<213> Artificial Sequence

```

```

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

```

```

<220>
<221> MISC_FEATURE
<222> (1)..(264)
<223> GN316 lysin

```

```

<400> 22

```

```

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu
1           5           10           15

```

```

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile
          20           25           30

```

```

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala
          35           40           45

```

```

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile
50           55           60

```

```

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu
65           70           75           80

```

```

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala
          85           90           95

```

0341\_0021-00-304\_ST25 (1).txt

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
115 120 125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser  
260

<210> 23

<211> 879

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(879)

&lt;223&gt; modified GN316 lysin

&lt;400&gt; 23

```

gaattcacca tgggatccca tcatcaccac catcatgggtg ccggatccca tcatcaccac      60
catcatggta ttttaaagat tggcagcaaa ggtctggaag ttaagaatct tcagaccagt      120
ctcaacaaaa tcgggttcaa tctggttgcc gatggcatat ttggtaaagc gactgacaac      180
gccgtcaggg cagttcaggc aggtgccgga ctggctggtg atggatttgc tggccccaag      240
accatgtatg cgattcgcaa cgcaggggag tctcatcagg atcatctgac tgaggctgac      300
ttgattgacg ctgctcgtga attgtctgtt gaccttgcta gcatcaaggc agtcaaccaa      360
gtagaatcgc gcggtactgg cttaccaag tctggtaaga tcaagacatt gtttgaacgc      420
cacatcatgt acaaaaagct gaatgccaag ttcggtcagg caaaagccaa tgctctggcc      480
cagctttacc cgacgttggg taacgcaaaa gccgggggat acacagggtg ggacgcggag      540
ttggaacgac tccatgggtg aatagcgatc gataaagatt gcgcctacga gagcgcttcc      600
tacgggttat tccagatcat ggggttcaac tgcgttatatt 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

```

&lt;210&gt; 24

&lt;211&gt; 273

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Synthetic polypeptide

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (1)..(273)

&lt;223&gt; modified GN316 lysin

&lt;400&gt; 24

Met Gly Ser His His His His His His Gly Ala Ile Leu Lys Ile Gly  
1 5 10 15

Ser Lys Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile  
20 25 30

Gly Phe Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn  
35 40 45

Ala Val Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile  
50 55 60

Ala Gly Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His  
65 70 75 80

Gln Asp His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu  
85 90 95

Ser Val Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg  
100 105 110

Gly Thr Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg  
115 120 125

His Ile Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala  
130 135 140

Asn Ala Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly  
145 150 155 160

Gly Tyr Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile  
165 170 175

Ala Ile Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe  
180 185 190

Gln Ile Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu  
195 200 205

Glu Met Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala  
 210 215 220

Phe Val Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys  
 225 230 235 240

Asp Lys Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr  
 245 250 255

Ala Gln Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe  
 260 265 270

Ser

<210> 25  
 <211> 612  
 <212> DNA  
 <213> Pseudomonas phage KPP10

<220>  
 <221> misc\_feature  
 <222> (28)..(588)  
 <223> GN329

<220>  
 <221> CDS  
 <222> (28)..(588)

<400> 25  
 gtttaacttt aagaaggaga attcacc atg atc acc gac aga gag tat cag caa 54  
 Met Ile Thr Asp Arg Glu Tyr Gln Gln  
 1 5

gct gct gag atg ttg gga gta gat gtc cca gcg atc aag gca gtg acc 102  
 Ala Ala Glu Met Leu Gly Val Asp Val Pro Ala Ile Lys Ala Val Thr  
 10 15 20 25

aag gtg gag gcc ccg gta ggg ggc ttc cag cct aca gga gag cca acg 150  
 Lys Val Glu Ala Pro Val Gly Gly Phe Gln Pro Thr Gly Glu Pro Thr  
 30 35 40

atc ctc tac gag cgt cac cag atg tac cga cag ctc cag gcc aaa ggg 198  
 Ile Leu Tyr Glu Arg His Gln Met Tyr Arg Gln Leu Gln Ala Lys Gly

45

50

55

ctc cca acg gaa ggt cat ccc cca gac ctg gta aat aag gta gct ggt 246  
 Leu Pro Thr Glu Gly His Pro Pro Asp Leu Val Asn Lys Val Ala Gly  
           60                                65                                70

ggg tat gga aaa tac agc gag caa cac gct aaa ctg gcc cgt gcc gta 294  
 Gly Tyr Gly Lys Tyr Ser Glu Gln His Ala Lys Leu Ala Arg Ala Val  
           75                                80                                85

aag atc gac agg gac agc gcc ctg gag tcc tgc tcc tgg ggg atg ttc 342  
 Lys Ile Asp Arg Asp Ser Ala Leu Glu Ser Cys Ser Trp Gly Met Phe  
           90                                95                                100                                105

cag atc atg ggc tac cac tgg aag ctg atg ggg tac cct acc ctt caa 390  
 Gln Ile Met Gly Tyr His Trp Lys Leu Met Gly Tyr Pro Thr Leu Gln  
                                 110                                115                                120

gct ttc gta aac gcc atg tac gcc agc gaa gga gcc cag atg gac gcc 438  
 Ala Phe Val Asn Ala Met Tyr Ala Ser Glu Gly Ala Gln Met Asp Ala  
                                 125                                130                                135

ttc tgc cgg ttc atc aag gca caa ccc acc acg cat gct gcc ttg aaa 486  
 Phe Cys Arg Phe Ile Lys Ala Gln Pro Thr Thr His Ala Ala Leu Lys  
                                 140                                145                                150

gcc cat gat tgg gcc aag ttt gcc aga ctg tac aac ggt cca ggc tac 534  
 Ala His Asp Trp Ala Lys Phe Ala Arg Leu Tyr Asn Gly Pro Gly Tyr  
           155                                160                                165

gcc aag aac aag tat gac gtg aaa ttg gag aaa gca tat gct gaa gct 582  
 Ala Lys Asn Lys Tyr Asp Val Lys Leu Glu Lys Ala Tyr Ala Glu Ala  
           170                                175                                180                                185

agt ggc tgataaaagc ttggctgttt tggc 612  
 Ser Gly

&lt;210&gt; 26

&lt;211&gt; 187

&lt;212&gt; PRT

&lt;213&gt; Pseudomonas phage KPP10

&lt;400&gt; 26

Met Ile Thr Asp Arg Glu Tyr Gln Gln Ala Ala Glu Met Leu Gly Val  
 1                                5                                10                                15

Asp Val Pro Ala Ile Lys Ala Val Thr Lys Val Glu Ala Pro Val Gly  
           20                                25                                30

Gly Phe Gln Pro Thr Gly Glu Pro Thr Ile Leu Tyr Glu Arg His Gln  
35 40 45

Met Tyr Arg Gln Leu Gln Ala Lys Gly Leu Pro Thr Glu Gly His Pro  
50 55 60

Pro Asp Leu Val Asn Lys Val Ala Gly Gly Tyr Gly Lys Tyr Ser Glu  
65 70 75 80

Gln His Ala Lys Leu Ala Arg Ala Val Lys Ile Asp Arg Asp Ser Ala  
85 90 95

Leu Glu Ser Cys Ser Trp Gly Met Phe Gln Ile Met Gly Tyr His Trp  
100 105 110

Lys Leu Met Gly Tyr Pro Thr Leu Gln Ala Phe Val Asn Ala Met Tyr  
115 120 125

Ala Ser Glu Gly Ala Gln Met Asp Ala Phe Cys Arg Phe Ile Lys Ala  
130 135 140

Gln Pro Thr Thr His Ala Ala Leu Lys Ala His Asp Trp Ala Lys Phe  
145 150 155 160

Ala Arg Leu Tyr Asn Gly Pro Gly Tyr Ala Lys Asn Lys Tyr Asp Val  
165 170 175

Lys Leu Glu Lys Ala Tyr Ala Glu Ala Ser Gly  
180 185

<210> 27  
<211> 609  
<212> DNA  
<213> Delftia sp.

<220>  
<221> CDS  
<222> (28)..(585)

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (28)..(585)

&lt;223&gt; GN333 lysin

&lt;400&gt; 27

gtttaacttt aagaaggaga attcacc atg gct cta act gag caa gac ttc caa 54  
 Met Ala Leu Thr Glu Gln Asp Phe Gln  
 1 5

tcg gct gcc gat gat ctc gga gtc gat gtt gcc agt gta aag gcc gtc 102  
 Ser Ala Ala Asp Asp Leu Gly Val Asp Val Ala Ser Val Lys Ala Val  
 10 15 20 25

act aaa gta gag agt cgt ggg agc ggc ttt cta ctt tct ggc gtc cct 150  
 Thr Lys Val Glu Ser Arg Gly Ser Gly Phe Leu Leu Ser Gly Val Pro  
 30 35 40

aag att cta ttc gaa agg cac tgg atg ttc aag ctt ctc aaa agg aag 198  
 Lys Ile Leu Phe Glu Arg His Trp Met Phe Lys Leu Leu Lys Arg Lys  
 45 50 55

cta ggt cgt gac cct gaa ata aac gac gtt tgc aac cct aaa gct gga 246  
 Leu Gly Arg Asp Pro Glu Ile Asn Asp Val Cys Asn Pro Lys Ala Gly  
 60 65 70

gga tac ctc ggc gga caa gcg gag cac gaa cgt cta gat aaa gca gtc 294  
 Gly Tyr Leu Gly Gly Gln Ala Glu His Glu Arg Leu Asp Lys Ala Val  
 75 80 85

aag atg gat aga gac tgc gca ctt caa agt gcc tct tgg ggc cta ttc 342  
 Lys Met Asp Arg Asp Cys Ala Leu Gln Ser Ala Ser Trp Gly Leu Phe  
 90 95 100 105

cag att atg gga ttc cat tgg gag gca cta ggt tat gcg agt gtt cag 390  
 Gln Ile Met Gly Phe His Trp Glu Ala Leu Gly Tyr Ala Ser Val Gln  
 110 115 120

gca ttt gtc aat gcc cag tac gct agc gag gga tcg caa cta aac act 438  
 Ala Phe Val Asn Ala Gln Tyr Ala Ser Glu Gly Ser Gln Leu Asn Thr  
 125 130 135

ttt gtg cgc ttc atc aag acc aac ccg gca att cac aaa gct tta aag 486  
 Phe Val Arg Phe Ile Lys Thr Asn Pro Ala Ile His Lys Ala Leu Lys  
 140 145 150

tct aag gac tgg gca gaa ttc gca aga agg tat aac ggg ccg gat tac 534  
 Ser Lys Asp Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Asp Tyr  
 155 160 165

aag aaa aac aac tac gat gtt aag cta gca gaa gcc tat caa tcc ttc 582  
 Lys Lys Asn Asn Tyr Asp Val Lys Leu Ala Glu Ala Tyr Gln Ser Phe

170                      175                      180                      185

aag taataaaagc ttggctgttt tggc  
Lys

609

```
<210> 28
<211> 186
<212> PRT
<213> Delftia sp.
```

<400> 28

Met Ala Leu Thr Glu Gln Asp Phe Gln Ser Ala Ala Asp Asp Leu Gly  
1 5 10 15

Val Asp Val Ala Ser Val Lys Ala Val Thr Lys Val Glu Ser Arg Gly  
20 25 30

Ser Gly Phe Leu Leu Ser Gly Val Pro Lys Ile Leu Phe Glu Arg His  
35 40 45

Trp Met Phe Lys Leu Leu Lys Arg Lys Leu Gly Arg Asp Pro Glu Ile  
50 55 60

Asn Asp Val Cys Asn Pro Lys Ala Gly Gly Tyr Leu Gly Gly Gln Ala  
65 70 75 80

Glu His Glu Arg Leu Asp Lys Ala Val Lys Met Asp Arg Asp Cys Ala  
85 90 95

Leu Gln Ser Ala Ser Trp Gly Leu Phe Gln Ile Met Gly Phe His Trp  
100 105 110

Glu Ala Leu Gly Tyr Ala Ser Val Gln Ala Phe Val Asn Ala Gln Tyr  
115 120 125

Ala Ser Glu Gly Ser Gln Leu Asn Thr Phe Val Arg Phe Ile Lys Thr  
130 135 140

Asn Pro Ala Ile His Lys Ala Leu Lys Ser Lys Asp Trp Ala Glu Phe  
145 150 155 160

Ala Arg Arg Tyr Asn Gly Pro Asp Tyr Lys Lys Asn Asn Tyr Asp Val  
 165 170 175

Lys Leu Ala Glu Ala Tyr Gln Ser Phe Lys  
 180 185

<210> 29  
 <211> 984  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
 <221> misc\_feature  
 <222> (28)..(957)  
 <223> GN349 lysin

<220>  
 <221> CDS  
 <222> (28)..(957)

<400> 29  
 gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa 54  
 Met Ala Ile Leu Lys Ile Gly Ser Lys  
 1 5

ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc 102  
 Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe  
 10 15 20 25

aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc 150  
 Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val  
 30 35 40

agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc 198  
 Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly  
 45 50 55

ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat 246  
 Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp  
 60 65 70

cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt 294  
 His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val  
 75 80 85

## 0341\_0021-00-304\_ST25 (1).txt

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act | 342 |
| Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr |     |
| 90 95 100 105                                                   |     |
| ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc | 390 |
| Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile |     |
| 110 115 120                                                     |     |
| atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct | 438 |
| Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala |     |
| 125 130 135                                                     |     |
| ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac | 486 |
| Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr |     |
| 140 145 150                                                     |     |
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc | 534 |
| Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile |     |
| 155 160 165                                                     |     |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc | 582 |
| Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile |     |
| 170 175 180 185                                                 |     |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg | 630 |
| Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met |     |
| 190 195 200                                                     |     |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc | 678 |
| Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val |     |
| 205 210 215                                                     |     |
| aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag | 726 |
| Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys |     |
| 220 225 230                                                     |     |
| aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag | 774 |
| Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln |     |
| 235 240 245                                                     |     |
| aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt acc | 822 |
| Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser Thr |     |
| 250 255 260 265                                                 |     |
| gcg ggc ggc acc gcg ggc ggc gca cga aga tac aga ctt tcg cga cgc | 870 |
| Ala Gly Gly Thr Ala Gly Gly Ala Arg Arg Tyr Arg Leu Ser Arg Arg |     |
| 270 275 280                                                     |     |
| aga agt cga cga ctt ttt tca aga act gca tta aga atg cat cga aga | 918 |
| Arg Ser Arg Arg Leu Phe Ser Arg Thr Ala Leu Arg Met His Arg Arg |     |
| 285 290 295                                                     |     |

aat aga ctt cga aga att atg cgt ggc ggc att agg ttt tagtaataaa 967  
 Asn Arg Leu Arg Arg Ile Met Arg Gly Gly Ile Arg Phe  
           300                          305                          310

agcttggtg ttttggc 984

<210> 30  
 <211> 310  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

<400> 30

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
 1                          5                          10                          15

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
                           20                          25                          30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
                           35                          40                          45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
                           50                          55                          60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
 65                          70                          75                          80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
                           85                          90                          95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
                           100                          105                          110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
                           115                          120                          125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
                           130                          135                          140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser Thr Ala Gly Gly Thr Ala Gly Gly  
260 265 270

Ala Arg Arg Tyr Arg Leu Ser Arg Arg Arg Ser Arg Arg Leu Phe Ser  
275 280 285

Arg Thr Ala Leu Arg Met His Arg Arg Asn Arg Leu Arg Arg Ile Met  
290 295 300

Arg Gly Gly Ile Arg Phe  
305 310

<210> 31

<211> 984

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (28)..(957)

<223> GN351 lysin

<220>

<221> CDS

<222> (28)..(957)

<400> 31

```
gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa      54
                Met Ala Ile Leu Lys Ile Gly Ser Lys
                  1                      5
```

```
ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc      102
Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe
10                      15                      20                      25
```

```
aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc      150
Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val
                30                      35                      40
```

```
agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc      198
Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly
                45                      50                      55
```

```
ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat      246
Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp
                60                      65                      70
```

```
cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt      294
His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val
                75                      80                      85
```

```
gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act      342
Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr
90                      95                      100                      105
```

```
ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc      390
Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile
                110                      115                      120
```

```
atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct      438
Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala
                125                      130                      135
```

```
ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac      486
Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr
                140                      145                      150
```

0341\_0021-00-304\_ST25 (1).txt

|                                                                                                                                                       |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc<br>Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile<br>155 160 165     | 534 |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc<br>Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile<br>170 175 180 185 | 582 |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg<br>Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met<br>190 195 200     | 630 |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc<br>Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val<br>205 210 215     | 678 |
| aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag<br>Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys<br>220 225 230     | 726 |
| aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag<br>Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln<br>235 240 245     | 774 |
| aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt acc<br>Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser Thr<br>250 255 260 265 | 822 |
| gcg ggc ggc acc gcg ggc ggc gct cgt tcc cgt aga cgt atg tct aag<br>Ala Gly Gly Thr Ala Gly Gly Ala Arg Ser Arg Arg Arg Met Ser Lys<br>270 275 280     | 870 |
| cgt tct tcc cgc cgt tcg ttc cgc aag tat gcg aag tcg cat aag aag<br>Arg Ser Ser Arg Arg Ser Phe Arg Lys Tyr Ala Lys Ser His Lys Lys<br>285 290 295     | 918 |
| aac ttt aaa gcc cgc tca atg cgt ggc ggt atc cgt tta tgataataaa<br>Asn Phe Lys Ala Arg Ser Met Arg Gly Gly Ile Arg Leu<br>300 305 310                  | 967 |
| agcttggctg ttttggc                                                                                                                                    | 984 |

<210> 32  
 <211> 310  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Synthetic Construct

&lt;400&gt; 32

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
1 5 10 15

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
50 55 60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
65 70 75 80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
115 120 125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser Thr Ala Gly Gly Thr Ala Gly Gly  
260 265 270

Ala Arg Ser Arg Arg Arg Met Ser Lys Arg Ser Ser Arg Arg Ser Phe  
275 280 285

Arg Lys Tyr Ala Lys Ser His Lys Lys Asn Phe Lys Ala Arg Ser Met  
290 295 300

Arg Gly Gly Ile Arg Leu  
305 310

<210> 33  
<211> 981  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
<221> misc\_feature  
<223> GN352 lysin28

<220>  
<221> CDS  
<222> (28)..(954)

<400> 33  
gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa  
Met Ala Ile Leu Lys Ile Gly Ser Lys  
1 5

## 0341\_0021-00-304\_ST25 (1).txt

|                                                                                                                                                       |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc<br>Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe<br>10 15 20 25     | 102 |
| aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc<br>Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val<br>30 35 40        | 150 |
| agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc<br>Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly<br>45 50 55        | 198 |
| ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat<br>Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp<br>60 65 70        | 246 |
| cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt<br>His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val<br>75 80 85        | 294 |
| gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act<br>Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr<br>90 95 100 105   | 342 |
| ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc<br>Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile<br>110 115 120     | 390 |
| atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct<br>Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala<br>125 130 135     | 438 |
| ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac<br>Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr<br>140 145 150     | 486 |
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc<br>Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile<br>155 160 165     | 534 |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc<br>Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile<br>170 175 180 185 | 582 |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg<br>Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met<br>190 195 200     | 630 |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc<br>Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val<br>205 210 215     | 678 |

0341\_0021-00-304\_ST25 (1).txt

aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag 726  
Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys  
220 225 230

aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag 774  
Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln  
235 240 245

aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt acc 822  
Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser Thr  
250 255 260 265

gcg ggc ggc acc gcg ggc ggc aaa cgt aga aaa atg aca aga aaa ggt 870  
Ala Gly Gly Thr Ala Gly Gly Lys Arg Arg Lys Met Thr Arg Lys Gly  
270 275 280

tct aag cgt ctt ttt act gca act gct gat aaa act aaa tct atc aat 918  
Ser Lys Arg Leu Phe Thr Ala Thr Ala Asp Lys Thr Lys Ser Ile Asn  
285 290 295

act gcc ccg ccg cca atg cgt ggc ggt atc cgg ttg tagtaataaaa 964  
Thr Ala Pro Pro Pro Met Arg Gly Gly Ile Arg Leu  
300 305

agcttggtgctg ttttggc 981

<210> 34  
<211> 309  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Synthetic Construct

<400> 34

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
1 5 10 15

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
50 55 60

0341\_0021-00-304\_ST25 (1).txt

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
65 70 75 80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
115 120 125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser Thr Ala Gly Gly Thr Ala Gly Gly  
260 265 270

Lys Arg Arg Lys Met Thr Arg Lys Gly Ser Lys Arg Leu Phe Thr Ala  
275 280 285

Thr Ala Asp Lys Thr Lys Ser Ile Asn Thr Ala Pro Pro Pro Met Arg  
290 295 300

Gly Gly Ile Arg Leu  
305

<210> 35  
<211> 978  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
<221> misc\_feature  
<222> (28)..(951)  
<223> GN353 lysin

<220>  
<221> CDS  
<222> (28)..(951)

<400> 35  
gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa 54  
Met Ala Ile Leu Lys Ile Gly Ser Lys  
1 5

ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc 102  
Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe  
10 15 20 25

aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc 150  
Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val  
30 35 40

agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc 198  
Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly  
45 50 55

ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat 246  
Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp  
60 65 70

## 0341\_0021-00-304\_ST25 (1).txt

|                                                                                                                                                       |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt<br>His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val<br>75 80 85        | 294 |
| gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act<br>Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr<br>90 95 100 105   | 342 |
| ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc<br>Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile<br>110 115 120     | 390 |
| atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct<br>Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala<br>125 130 135     | 438 |
| ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac<br>Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr<br>140 145 150     | 486 |
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc<br>Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile<br>155 160 165     | 534 |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc<br>Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile<br>170 175 180 185 | 582 |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg<br>Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met<br>190 195 200     | 630 |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc<br>Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val<br>205 210 215     | 678 |
| aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag<br>Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys<br>220 225 230     | 726 |
| aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag<br>Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln<br>235 240 245     | 774 |
| aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt acc<br>Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser Thr<br>250 255 260 265 | 822 |
| gcg ggc ggc acc gcg ggc ggc aga aag cga atg tct aag cgt gtt gac<br>Ala Gly Gly Thr Ala Gly Gly Arg Lys Arg Met Ser Lys Arg Val Asp<br>270 275 280     | 870 |

0341\_0021-00-304\_ST25 (1).txt

aag aag gtg ttc cgt cgt act gcc gca tct gcc aag aag att aac att 918  
Lys Lys Val Phe Arg Arg Thr Ala Ala Ser Ala Lys Lys Ile Asn Ile  
285 290 295

gac ccc aag att tac cgt gga ggt att cgc cta tgataataaa agcttggctg 971  
Asp Pro Lys Ile Tyr Arg Gly Gly Ile Arg Leu  
300 305

ttttggc 978

<210> 36  
<211> 308  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Synthetic Construct

<400> 36

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
1 5 10 15

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
50 55 60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
65 70 75 80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
115 120 125

0341\_0021-00-304\_ST25 (1).txt

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser Thr Ala Gly Gly Thr Ala Gly Gly  
260 265 270

Arg Lys Arg Met Ser Lys Arg Val Asp Lys Lys Val Phe Arg Arg Thr  
275 280 285

Ala Ala Ser Ala Lys Lys Ile Asn Ile Asp Pro Lys Ile Tyr Arg Gly  
290 295 300

Gly Ile Arg Leu  
305

<210> 37  
<211> 903  
<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (28)..(879)

<220>

<221> misc\_feature

<222> (28)..(879)

<223> GN357 lysin

<220>

<221> CDS

<222> (28)..(879)

<400> 37

|            |            |         |                                     |    |
|------------|------------|---------|-------------------------------------|----|
| gtttaacttt | aagaaggaga | attcacc | atg gcc att tta aag att ggc agc aaa | 54 |
|            |            |         | Met Ala Ile Leu Lys Ile Gly Ser Lys |    |
|            |            |         | 1 5                                 |    |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc | 102 |
| Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe |     |
| 10 15 20 25                                                     |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc | 150 |
| Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val |     |
| 30 35 40                                                        |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc | 198 |
| Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly |     |
| 45 50 55                                                        |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat | 246 |
| Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp |     |
| 60 65 70                                                        |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt | 294 |
| His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val |     |
| 75 80 85                                                        |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act | 342 |
| Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr |     |
| 90 95 100 105                                                   |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc | 390 |
| Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile |     |
| 110 115 120                                                     |     |

0341\_0021-00-304\_ST25 (1).txt

|                                                                                                                                                       |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct<br>Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala<br>125 130 135     | 438 |
| ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac<br>Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr<br>140 145 150     | 486 |
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc<br>Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile<br>155 160 165     | 534 |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc<br>Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile<br>170 175 180 185 | 582 |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg<br>Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met<br>190 195 200     | 630 |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc<br>Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val<br>205 210 215     | 678 |
| aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag<br>Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys<br>220 225 230     | 726 |
| aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag<br>Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln<br>235 240 245     | 774 |
| aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt acc<br>Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser Thr<br>250 255 260 265 | 822 |
| gcg ggc ggc acc gcg ggc ggc cgc cgc ctg att cgc ctg tgg ctg cgc<br>Ala Gly Gly Thr Ala Gly Gly Arg Arg Leu Ile Arg Leu Trp Leu Arg<br>270 275 280     | 870 |
| ctg ctg cgc taataaaagc ttggctgttt tggc<br>Leu Leu Arg                                                                                                 | 903 |

<210> 38  
 <211> 284  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

&lt;400&gt; 38

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
 1 5 10 15

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
 20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
 35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
 50 55 60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
 65 70 75 80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
 85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
 100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
 115 120 125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
 130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
 145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
 165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
 180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly

195

200

205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
 210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
 225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
 245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser Thr Ala Gly Gly Thr Ala Gly Gly  
 260 265 270

Arg Arg Leu Ile Arg Leu Trp Leu Arg Leu Leu Arg  
 275 280

&lt;210&gt; 39

&lt;211&gt; 912

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Synthetic polynucleotide

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (28)..(888)

&lt;223&gt; GN359 lysin

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (28)..(888)

&lt;400&gt; 39

gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa 54  
 Met Ala Ile Leu Lys Ile Gly Ser Lys  
 1 5

ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc 102  
 Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe  
 10 15 20 25

aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc 150  
 Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val

| 30                                                              |     |  |  |  |  |  |  |  |  | 35 |  |  |  |  |  |  |  |  |  | 40 |  |  |  |  |  |  |  |  |  |  |
|-----------------------------------------------------------------|-----|--|--|--|--|--|--|--|--|----|--|--|--|--|--|--|--|--|--|----|--|--|--|--|--|--|--|--|--|--|
| agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc | 198 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 45 50 55                                                        |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat | 246 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 60 65 70                                                        |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt | 294 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 75 80 85                                                        |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act | 342 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 90 95 100 105                                                   |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc | 390 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 110 115 120                                                     |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct | 438 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 125 130 135                                                     |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac | 486 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 140 145 150                                                     |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc | 534 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 155 160 165                                                     |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc | 582 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 170 175 180 185                                                 |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg | 630 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 190 195 200                                                     |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc | 678 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 205 210 215                                                     |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag | 726 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| 220 225 230                                                     |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag | 774 |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |
| Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln |     |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |    |  |  |  |  |  |  |  |  |  |  |

235

240

245

aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt acc 822  
 Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser Thr  
 250 255 260 265

gcg ggc ggc acc gcg ggc ggc acc cgc aaa cgc ctg aaa aaa att ggc 870  
 Ala Gly Gly Thr Ala Gly Gly Thr Arg Lys Arg Leu Lys Lys Ile Gly  
 270 275 280

aaa gtg ctg aaa tgg att taataaaagc ttggctgttt tggc 912  
 Lys Val Leu Lys Trp Ile  
 285

&lt;210&gt; 40

&lt;211&gt; 287

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Construct

&lt;400&gt; 40

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
 1 5 10 15

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
 20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
 35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
 50 55 60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
 65 70 75 80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
 85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
 100 105 110

0341\_0021-00-304\_ST25 (1).txt

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
115 120 125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser Thr Ala Gly Gly Thr Ala Gly Gly  
260 265 270

Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
275 280 285

<210> 41

<211> 897

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (28)..(873)

&lt;223&gt; GN369 lysin

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (28)..(873)

&lt;400&gt; 41

gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa 54  
 Met Ala Ile Leu Lys Ile Gly Ser Lys  
 1 5

ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc 102  
 Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe  
 10 15 20 25

aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc 150  
 Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val  
 30 35 40

agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc 198  
 Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly  
 45 50 55

ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat 246  
 Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp  
 60 65 70

cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt 294  
 His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val  
 75 80 85

gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act 342  
 Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr  
 90 95 100 105

ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc 390  
 Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile  
 110 115 120

atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct 438  
 Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala  
 125 130 135

ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac 486  
 Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr  
 140 145 150

0341\_0021-00-304\_ST25 (1).txt

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc | 534 |
| Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile |     |
| 155 160 165                                                     |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc | 582 |
| Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile |     |
| 170 175 180 185                                                 |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg | 630 |
| Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met |     |
| 190 195 200                                                     |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc | 678 |
| Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val |     |
| 205 210 215                                                     |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag | 726 |
| Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys |     |
| 220 225 230                                                     |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag | 774 |
| Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln |     |
| 235 240 245                                                     |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt cgt | 822 |
| Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser Arg |     |
| 250 255 260 265                                                 |     |

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| aaa aaa acc cgt aaa cgt ctg aaa aaa atc ggt aaa gtt ctg aaa tgg | 870 |
| Lys Lys Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp |     |
| 270 275 280                                                     |     |

|                                |     |
|--------------------------------|-----|
| atc tagtaaaagc ttggctgttt tggc | 897 |
| Ile                            |     |

<210> 42  
 <211> 282  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

<400> 42

|                                                                 |
|-----------------------------------------------------------------|
| Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu |
| 1 5 10 15                                                       |

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile

20

25

30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
           35                          40                          45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
       50                          55                          60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
   65                          70                          75                          80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
                           85                          90                          95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
                           100                          105                          110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
           115                          120                          125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
       130                          135                          140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
   145                          150                          155                          160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
                           165                          170                          175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
                           180                          185                          190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
       195                          200                          205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
       210                          215                          220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg

Ala Ala Ala Tyr Lys Ser Phe Ser Arg Lys Lys Thr Arg Lys Arg Leu  
260 265 270

Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
275 280

|       |                     |
|-------|---------------------|
| <210> | 43                  |
| <211> | 558                 |
| <212> | DNA                 |
| <213> | Artificial Sequence |

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

```
<220>
<221> misc_feature
<222> (28)..(534)
<223> GN370 lysin
```

```
<220>  
<221> CDS  
<222> (28)..(534)
```

<400> 43  
gtttaacttt aagaaggaga attcacc atg atc gac cgt ttc att cgt ctg aat 54  
Met Ile Asp Arg Phe Ile Arg Leu Asn  
1 5

ccg acc cat ggt ccg cgt cgt ccg cgt cgt ccg ggt cgt cgt gct ccg 102  
Pro Thr His Gly Pro Arg Arg Pro Arg Arg Pro Gly Arg Arg Ala Pro  
10 15 20 25

gtt cgt aca tcc caa cga ggc atc gac ctc atc aaa tcc ttc gag ggc 150  
Val Arg Thr Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser Phe Glu Gly  
30 35 40

ctg cgc ctg tcc gct tac cag gac tcg gtg ggt gtc tgg acc ata ggt 198  
Leu Arg Leu Ser Ala Tyr Gln Asp Ser Val Gly Val Trp Thr Ile Gly  
45 50 55

tac ggc acc act cgg ggc gtc acc cgc tac atg acg atc acc gtc gag 246  
Tyr Gly Thr Thr Arg Gly Val Thr Arg Tyr Met Thr Ile Thr Val Glu

60

65

70

cag gcc gag cgg atg ctg tcg aac gac att cag cgc ttc gag cca gag 294  
 Gln Ala Glu Arg Met Leu Ser Asn Asp Ile Gln Arg Phe Glu Pro Glu  
 75 80 85

cta gac agg ctg gcg aag gtg cca ctg aac cag aac cag tgg gat gcc 342  
 Leu Asp Arg Leu Ala Lys Val Pro Leu Asn Gln Asn Gln Trp Asp Ala  
 90 95 100 105

ctg atg agc ttc gtg tac aac ctg ggc gcg gcc aat ctg gcg tcg tcc 390  
 Leu Met Ser Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu Ala Ser Ser  
 110 115 120

acg ctg ctc gac ctg ctg aac aag ggt gac tac cag gga gca gcg gac 438  
 Thr Leu Leu Asp Leu Leu Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp  
 125 130 135

cag ttc ccg cat tgg gtg aat gcg ggc ggt aag cgc ttg gat ggt ctg 486  
 Gln Phe Pro His Trp Val Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu  
 140 145 150

gtt aag cgt cga gca gcc gag cgt gcg ctg ttc ctg gag cca cta tcg 534  
 Val Lys Arg Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu Pro Leu Ser  
 155 160 165

tgataaaagc ttggctgttt tggc 558

<210> 44

<211> 169

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 44

Met Ile Asp Arg Phe Ile Arg Leu Asn Pro Thr His Gly Pro Arg Arg  
 1 5 10 15

Pro Arg Arg Pro Gly Arg Arg Ala Pro Val Arg Thr Ser Gln Arg Gly  
 20 25 30

Ile Asp Leu Ile Lys Ser Phe Glu Gly Leu Arg Leu Ser Ala Tyr Gln  
 35 40 45

Asp Ser Val Gly Val Trp Thr Ile Gly Tyr Gly Thr Thr Arg Gly Val

50

55

60

Thr Arg Tyr Met Thr Ile Thr Val Glu Gln Ala Glu Arg Met Leu Ser  
65 70 75 80

Asn Asp Ile Gln Arg Phe Glu Pro Glu Leu Asp Arg Leu Ala Lys Val  
85 90 95

Pro Leu Asn Gln Asn Gln Trp Asp Ala Leu Met Ser Phe Val Tyr Asn  
100 105 110

Leu Gly Ala Ala Asn Leu Ala Ser Ser Thr Leu Leu Asp Leu Leu Asn  
115 120 125

Lys Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro His Trp Val Asn  
130 135 140

Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Arg Ala Ala Glu  
145 150 155 160

Arg Ala Leu Phe Leu Glu Pro Leu Ser  
165

<210> 45

<211> 516

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (28)..(492)

<223> GN371lysin

<220>

<221> CDS

<222> (28)..(492)

<400> 45

gtttaacttt aagaaggaga attcacc atg atc gac cgt ttc att cgt ctg aat  
Met Ile Asp Arg Phe Ile Arg Leu Asn

54

## 0341\_0021-00-304\_ST25 (1).txt

1

5

ccg acc cat cgt aca tcc caa cga ggc atc gac ctc atc aaa tcc ttc 102  
 Pro Thr His Arg Thr Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser Phe  
 10 15 20 25

gag ggc ctg cgc ctg tcc gct tac cag gac tcg gtg ggt gtc tgg acc 150  
 Glu Gly Leu Arg Leu Ser Ala Tyr Gln Asp Ser Val Gly Val Trp Thr  
 30 35 40

ata ggt tac ggc acc act cgg ggc gtc acc cgc tac atg acg atc acc 198  
 Ile Gly Tyr Gly Thr Thr Arg Gly Val Thr Arg Tyr Met Thr Ile Thr  
 45 50 55

gtc gag cag gcc gag cgg atg ctg tcg aac gac att cag cgc ttc gag 246  
 Val Glu Gln Ala Glu Arg Met Leu Ser Asn Asp Ile Gln Arg Phe Glu  
 60 65 70

cca gag cta gac agg ctg gcg aag gtg cca ctg aac cag aac cag tgg 294  
 Pro Glu Leu Asp Arg Leu Ala Lys Val Pro Leu Asn Gln Asn Gln Trp  
 75 80 85

gat gcc ctg atg agc ttc gtg tac aac ctg ggc gcg gcc aat ctg gcg 342  
 Asp Ala Leu Met Ser Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu Ala  
 90 95 100 105

tcg tcc acg ctg ctc gac ctg ctg aac aag ggt gac tac cag gga gca 390  
 Ser Ser Thr Leu Leu Asp Leu Leu Asn Lys Gly Asp Tyr Gln Gly Ala  
 110 115 120

gcg gac cag ttc ccg cat tgg gtg aat gcg ggc ggt aag cgc ttg gat 438  
 Ala Asp Gln Phe Pro His Trp Val Asn Ala Gly Gly Lys Arg Leu Asp  
 125 130 135

ggt ctg gtt aag cgt cga gca gcc gag cgt gcg ctg ttc ctg gag cca 486  
 Gly Leu Val Lys Arg Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu Pro  
 140 145 150

cta tcg tgataaaagc ttggctgttt tggc 516  
 Leu Ser  
 155

&lt;210&gt; 46

&lt;211&gt; 155

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Construct

&lt;400&gt; 46

0341\_0021-00-304\_ST25 (1).txt

Met Ile Asp Arg Phe Ile Arg Leu Asn Pro Thr His Arg Thr Ser Gln  
1 5 10 15

Arg Gly Ile Asp Leu Ile Lys Ser Phe Glu Gly Leu Arg Leu Ser Ala  
20 25 30

Tyr Gln Asp Ser Val Gly Val Trp Thr Ile Gly Tyr Gly Thr Thr Arg  
35 40 45

Gly Val Thr Arg Tyr Met Thr Ile Thr Val Glu Gln Ala Glu Arg Met  
50 55 60

Leu Ser Asn Asp Ile Gln Arg Phe Glu Pro Glu Leu Asp Arg Leu Ala  
65 70 75 80

Lys Val Pro Leu Asn Gln Asn Gln Trp Asp Ala Leu Met Ser Phe Val  
85 90 95

Tyr Asn Leu Gly Ala Ala Asn Leu Ala Ser Ser Thr Leu Leu Asp Leu  
100 105 110

Leu Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro His Trp  
115 120 125

Val Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Arg Ala  
130 135 140

Ala Glu Arg Ala Leu Phe Leu Glu Pro Leu Ser  
145 150 155

<210> 47

<211> 846

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

&lt;222&gt; (28)..(819)

&lt;223&gt; GN394 lysin

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (28)..(819)

&lt;400&gt; 47

gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa 54

Met Ala Ile Leu Lys Ile Gly Ser Lys

1

5

ggc ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggc ttc 102

Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe

10

15

20

25

aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc 150

Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val

30

35

40

agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc 198

Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly

45

50

55

ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat 246

Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp

60

65

70

cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt 294

His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val

75

80

85

gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act 342

Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr

90

95

100

105

ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc 390

Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile

110

115

120

atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct 438

Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala

125

130

135

ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac 486

Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr

140

145

150

aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc 534

Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile

155

160

165

0341\_0021-00-304\_ST25 (1).txt

gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc 582  
Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile  
170 175 180 185

atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg 630  
Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met  
190 195 200

ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc 678  
Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val  
205 210 215

gac ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag 726  
Asp Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys  
220 225 230

aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag 774  
Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln  
235 240 245

aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt 819  
Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser  
250 255 260

tagtaataaaa agcttggctg ttttggc 846

<210> 48

<211> 264

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 48

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
1 5 10 15

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
50 55 60

0341\_0021-00-304\_ST25 (1).txt

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
65 70 75 80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
115 120 125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Asp Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser  
260

```
<210> 49
<211> 846
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polynucleotide
```

```
<220>
<221> misc_feature
<222> (28)..(819)
<223> GN396 lysin
```

```
<220>  
<221> CDS  
<222> (28)..(819)
```

```
<400> 49
gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa      54
          Met Ala Ile Leu Lys Ile Gly Ser Lys
          1               5
```

ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc 102  
 Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe  
 10 15 20 25

aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc 150  
Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val  
30 35 40

agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc 198  
Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly  
45 50 55

ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat 246  
Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp  
60 65 70

cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt 294  
His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val  
75 80 85

gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act 342  
Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr  
90 95 100 105

ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc 390  
Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile  
110 115 120

0341\_0021-00-304\_ST25 (1).txt

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct | 438 |
| Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala |     |
| 125 130 135                                                     |     |
| ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac | 486 |
| Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr |     |
| 140 145 150                                                     |     |
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc | 534 |
| Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile |     |
| 155 160 165                                                     |     |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc | 582 |
| Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile |     |
| 170 175 180 185                                                 |     |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg | 630 |
| Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met |     |
| 190 195 200                                                     |     |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc | 678 |
| Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val |     |
| 205 210 215                                                     |     |
| aag ttc atc aag gct gac gcc aat ctg tgg gac gca ttg aag gac aag | 726 |
| Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Asp Ala Leu Lys Asp Lys |     |
| 220 225 230                                                     |     |
| aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag | 774 |
| Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln |     |
| 235 240 245                                                     |     |
| aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt     | 819 |
| Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser     |     |
| 250 255 260                                                     |     |
| tagtaataaaa agcttggtg ttttggc                                   | 846 |

<210> 50

<211> 264

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 50

|                                                                 |
|-----------------------------------------------------------------|
| Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu |
| 1 5 10 15                                                       |

0341\_0021-00-304\_ST25 (1).txt

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
50 55 60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
65 70 75 80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
115 120 125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Asp Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser  
260

<210> 51

<211> 846

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (28)..(819)

<223> GN408 lysin

<220>

<221> CDS

<222> (28)..(819)

<400> 51

gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa 54  
Met Ala Ile Leu Lys Ile Gly Ser Lys  
1 5

ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac aaa atc ggg ttc 102  
Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Lys Ile Gly Phe  
10 15 20 25

aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc 150  
Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val  
30 35 40

agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc 198  
Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly  
45 50 55

ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat 246  
Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp  
60 65 70

## 0341\_0021-00-304\_ST25 (1).txt

|                                                                                                                                                       |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| cat ctg act gag gct gac ttg att gac gct gct cat gaa ttg tct gtt<br>His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala His Glu Leu Ser Val<br>75 80 85        | 294 |
| gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act<br>Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr<br>90 95 100 105   | 342 |
| ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc<br>Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile<br>110 115 120     | 390 |
| atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct<br>Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala<br>125 130 135     | 438 |
| ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac<br>Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr<br>140 145 150     | 486 |
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc<br>Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile<br>155 160 165     | 534 |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc<br>Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile<br>170 175 180 185 | 582 |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg<br>Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met<br>190 195 200     | 630 |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc<br>Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val<br>205 210 215     | 678 |
| aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag<br>Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys<br>220 225 230     | 726 |
| aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag<br>Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln<br>235 240 245     | 774 |
| aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt<br>Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser<br>250 255 260             | 819 |
| tagtaataaaa agcttggctg ttttggc                                                                                                                        | 846 |

&lt;210&gt; 52

<211> 264  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

<400> 52

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
 1 5 10 15

Gln Thr Ser Leu Asn Lys Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
 20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
 35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
 50 55 60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
 65 70 75 80

Ile Asp Ala Ala His Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
 85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
 100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
 115 120 125

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
 130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
 145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
 165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser  
260

<210> 53  
<211> 846  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
<221> misc\_feature  
<222> (28)..(819)  
<223> GN418 lysin

<220>  
<221> CDS  
<222> (28)..(819)

<400> 53  
gtttaacttt aagaaggaga attcacc atg gcc att tta aag att ggc agc aaa 54  
Met Ala Ile Leu Lys Ile Gly Ser Lys  
1 5

ggt ctg gaa gtt aag aat ctt cag acc agt ctc aac gac atc ggg ttc 102  
Gly Leu Glu Val Lys Asn Leu Gln Thr Ser Leu Asn Asp Ile Gly Phe  
10 15 20 25

## 0341\_0021-00-304\_ST25 (1).txt

|                                                                                                                                                       |     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| aat ctg gtt gcc gat ggc ata ttt ggt aaa gcg act gac aac gcc gtc<br>Asn Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Asp Asn Ala Val<br>30 35 40        | 150 |
| agg gca gtt cag gca ggt gcc gga ctg gtc gtt gat ggt att gct ggc<br>Arg Ala Val Gln Ala Gly Ala Gly Leu Val Val Asp Gly Ile Ala Gly<br>45 50 55        | 198 |
| ccc aag acc atg tat gcg att cgc aac gca ggg gag tct cat cag gat<br>Pro Lys Thr Met Tyr Ala Ile Arg Asn Ala Gly Glu Ser His Gln Asp<br>60 65 70        | 246 |
| cat ctg act gag gct gac ttg att gac gct gct cgt gaa ttg tct gtt<br>His Leu Thr Glu Ala Asp Leu Ile Asp Ala Ala Arg Glu Leu Ser Val<br>75 80 85        | 294 |
| gac ctt gct agc atc aag gca gtc aac caa gta gaa tcg cgc ggt act<br>Asp Leu Ala Ser Ile Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr<br>90 95 100 105   | 342 |
| ggc ttc acc aag tct ggt aag atc aag aca ttg ttt gaa cgc cac atc<br>Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile<br>110 115 120     | 390 |
| atg tac aaa aag ctg aat gcc aag ttc ggt cag gca aaa gcc aat gct<br>Met Tyr Lys Lys Leu Asn Ala Lys Phe Gly Gln Ala Lys Ala Asn Ala<br>125 130 135     | 438 |
| ctg gcc cag ctt tac ccg acg ttg gtt aac gcc aaa gcc ggg gga tac<br>Leu Ala Gln Leu Tyr Pro Thr Leu Val Asn Ala Lys Ala Gly Gly Tyr<br>140 145 150     | 486 |
| aca ggt ggg gac gcg gag ttg gaa cga ctc cat ggt gca ata gcg atc<br>Thr Gly Gly Asp Ala Glu Leu Glu Arg Leu His Gly Ala Ile Ala Ile<br>155 160 165     | 534 |
| gat aaa gat tgc gcc tac gag agc gct tcc tac ggg tta ttc cag atc<br>Asp Lys Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile<br>170 175 180 185 | 582 |
| atg ggg ttc aac tgc gtt att tgt gga tat gac aat gcc gag gag atg<br>Met Gly Phe Asn Cys Val Ile Cys Gly Tyr Asp Asn Ala Glu Glu Met<br>190 195 200     | 630 |
| ttc aac gac ttt ctc act ggt gaa cgt gct cag ctc atg gca ttt gtc<br>Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala Gln Leu Met Ala Phe Val<br>205 210 215     | 678 |
| aag ttc atc aag gct gac gcc aat ctg tgg aaa gca ttg aag gac aag<br>Lys Phe Ile Lys Ala Asp Ala Asn Leu Trp Lys Ala Leu Lys Asp Lys<br>220 225 230     | 726 |

0341\_0021-00-304\_ST25 (1).txt

aat tgg gct gag ttt gct cgg cgt tac aat ggc ccg gcg tat gca cag 774  
Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Gln  
235 240 245

aac cag tac gac acc aag ctg gct gca gca tac aaa tca ttc agt 819  
Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Ser  
250 255 260

tagtaataaaa agcttggtg ttttggc 846

<210> 54  
<211> 264  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Synthetic Construct

<400> 54

Met Ala Ile Leu Lys Ile Gly Ser Lys Gly Leu Glu Val Lys Asn Leu  
1 5 10 15

Gln Thr Ser Leu Asn Asp Ile Gly Phe Asn Leu Val Ala Asp Gly Ile  
20 25 30

Phe Gly Lys Ala Thr Asp Asn Ala Val Arg Ala Val Gln Ala Gly Ala  
35 40 45

Gly Leu Val Val Asp Gly Ile Ala Gly Pro Lys Thr Met Tyr Ala Ile  
50 55 60

Arg Asn Ala Gly Glu Ser His Gln Asp His Leu Thr Glu Ala Asp Leu  
65 70 75 80

Ile Asp Ala Ala Arg Glu Leu Ser Val Asp Leu Ala Ser Ile Lys Ala  
85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Ser Gly Lys  
100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Leu Asn Ala  
115 120 125

0341\_0021-00-304\_ST25 (1).txt

Lys Phe Gly Gln Ala Lys Ala Asn Ala Leu Ala Gln Leu Tyr Pro Thr  
130 135 140

Leu Val Asn Ala Lys Ala Gly Gly Tyr Thr Gly Gly Asp Ala Glu Leu  
145 150 155 160

Glu Arg Leu His Gly Ala Ile Ala Ile Asp Lys Asp Cys Ala Tyr Glu  
165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Val Ile  
180 185 190

Cys Gly Tyr Asp Asn Ala Glu Glu Met Phe Asn Asp Phe Leu Thr Gly  
195 200 205

Glu Arg Ala Gln Leu Met Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
210 215 220

Asn Leu Trp Lys Ala Leu Lys Asp Lys Asn Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Gln Asn Gln Tyr Asp Thr Lys Leu  
245 250 255

Ala Ala Ala Tyr Lys Ser Phe Ser  
260

<210> 55  
<211> 858  
<212> DNA  
<213> Burkholderia pseudomultivorans

<220>  
<221> misc\_feature  
<222> (28)..(834)  
<223> GN424 lysin

<220>  
<221> CDS  
<222> (28)..(834)

&lt;400&gt; 55

gtttaacttt aagaaggaga attcacc atg aat acc ctt cgt ttc aac agt cgc 54  
 Met Asn Thr Leu Arg Phe Asn Ser Arg  
 1 5

ggc gcc gaa gtc ggc gtg ctg cag caa cgg ctc gtg cgc gcc ggc tat 102  
 Gly Ala Glu Val Gly Val Leu Gln Gln Arg Leu Val Arg Ala Gly Tyr  
 10 15 20 25

ccg atc gac gtc acg cat ctc tat gac gaa gcg acg gag cag gcc gtg 150  
 Pro Ile Asp Val Thr His Leu Tyr Asp Glu Ala Thr Glu Gln Ala Val  
 30 35 40

aag gcg ttg cag gca gcg gcc gga atc gtc gtc gac gga atc gcc ggc 198  
 Lys Ala Leu Gln Ala Ala Ala Gly Ile Val Val Asp Gly Ile Ala Gly  
 45 50 55

ccg aac acc tat gcc gtg ttg tcg gcc ggc cag cgc gac cgc aag cac 246  
 Pro Asn Thr Tyr Ala Val Leu Ser Ala Gly Gln Arg Asp Arg Lys His  
 60 65 70

ttg acc gaa gcg gac atc gcc cgc gcc gca gac aag ctc ggt gtc tcg 294  
 Leu Thr Glu Ala Asp Ile Ala Arg Ala Ala Asp Lys Leu Gly Val Ser  
 75 80 85

ccg gca tgc gtc cgc gcc gtc aac gaa gtc gag tca cgc ggc tcg ggc 342  
 Pro Ala Cys Val Arg Ala Val Asn Glu Val Glu Ser Arg Gly Ser Gly  
 90 95 100 105

ttt ctg gcg gac ggc cgg ccc gtg att ctc ttc gag cgg cac gtg atg 390  
 Phe Leu Ala Asp Gly Arg Pro Val Ile Leu Phe Glu Arg His Val Met  
 110 115 120

tac aac cgc ctc gtc gcg gcg aag cgt gcc gtc gac gca gcg agc gca 438  
 Tyr Asn Arg Leu Val Ala Ala Lys Arg Ala Val Asp Ala Ala Ser Ala  
 125 130 135

gcg cag cgc ttt ccg aac gtc gtc agc gcg aag ccg ggc gga tac cag 486  
 Ala Gln Arg Phe Pro Asn Val Val Ser Ala Lys Pro Gly Gly Tyr Gln  
 140 145 150

ggc ggc gca gcc gaa tat gtg cga ctc gac acc gcc gcg cgc atc gat 534  
 Gly Gly Ala Ala Glu Tyr Val Arg Leu Asp Thr Ala Ala Arg Ile Asp  
 155 160 165

gcg gca atc gcg tac gaa tcg gcg agc tgg ggc gca ttt cag gtg atg 582  
 Ala Ala Ile Ala Tyr Glu Ser Ala Ser Trp Gly Ala Phe Gln Val Met  
 170 175 180 185

ggc tat cac tgg gaa cgc ctg ggc tac tcg agc atc gac gag ttc gtt 630  
 Gly Tyr His Trp Glu Arg Leu Gly Tyr Ser Ser Ile Asp Glu Phe Val  
 190 195 200

0341\_0021-00-304\_ST25 (1).txt

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| gcc cgg atg gag acg agc gaa ggc gaa cag ctc gac gcg ttt gtg cgg | 678 |
| Ala Arg Met Glu Thr Ser Glu Gly Glu Gln Leu Asp Ala Phe Val Arg |     |
| 205 210 215                                                     |     |
| ttc gtc gcc gcc gac tcg tcg ctg cgc acg gcg ctg aaa aac cgg aag | 726 |
| Phe Val Ala Ala Asp Ser Ser Leu Arg Thr Ala Leu Lys Asn Arg Lys |     |
| 220 225 230                                                     |     |
| tgg gct gca ttc gcg aag ggc tac aac ggc ccg gac tat gcg cgc aac | 774 |
| Trp Ala Ala Phe Ala Lys Gly Tyr Asn Gly Pro Asp Tyr Ala Arg Asn |     |
| 235 240 245                                                     |     |
| ctc tac gac gcg aag ctc gcc cag gcg tac gaa cgg tat gcc ggc acg | 822 |
| Leu Tyr Asp Ala Lys Leu Ala Gln Ala Tyr Glu Arg Tyr Ala Gly Thr |     |
| 250 255 260 265                                                 |     |
| aag gcg gcc gcg tgataaaagc ttggctgttt tggc                      | 858 |
| Lys Ala Ala Ala                                                 |     |

<210> 56  
 <211> 269  
 <212> PRT  
 <213> Burkholderia pseudomultivorans

<400> 56

|                                                                 |
|-----------------------------------------------------------------|
| Met Asn Thr Leu Arg Phe Asn Ser Arg Gly Ala Glu Val Gly Val Leu |
| 1 5 10 15                                                       |

|                                                                 |
|-----------------------------------------------------------------|
| Gln Gln Arg Leu Val Arg Ala Gly Tyr Pro Ile Asp Val Thr His Leu |
| 20 25 30                                                        |

|                                                                 |
|-----------------------------------------------------------------|
| Tyr Asp Glu Ala Thr Glu Gln Ala Val Lys Ala Leu Gln Ala Ala Ala |
| 35 40 45                                                        |

|                                                                 |
|-----------------------------------------------------------------|
| Gly Ile Val Val Asp Gly Ile Ala Gly Pro Asn Thr Tyr Ala Val Leu |
| 50 55 60                                                        |

|                                                                 |
|-----------------------------------------------------------------|
| Ser Ala Gly Gln Arg Asp Arg Lys His Leu Thr Glu Ala Asp Ile Ala |
| 65 70 75 80                                                     |

|                                                                 |
|-----------------------------------------------------------------|
| Arg Ala Ala Asp Lys Leu Gly Val Ser Pro Ala Cys Val Arg Ala Val |
| 85 90 95                                                        |

0341\_0021-00-304\_ST25 (1).txt

Asn Glu Val Glu Ser Arg Gly Ser Gly Phe Leu Ala Asp Gly Arg Pro  
100 105 110

Val Ile Leu Phe Glu Arg His Val Met Tyr Asn Arg Leu Val Ala Ala  
115 120 125

Lys Arg Ala Val Asp Ala Ala Ser Ala Ala Gln Arg Phe Pro Asn Val  
130 135 140

Val Ser Ala Lys Pro Gly Gly Tyr Gln Gly Gly Ala Ala Glu Tyr Val  
145 150 155 160

Arg Leu Asp Thr Ala Ala Arg Ile Asp Ala Ala Ile Ala Tyr Glu Ser  
165 170 175

Ala Ser Trp Gly Ala Phe Gln Val Met Gly Tyr His Trp Glu Arg Leu  
180 185 190

Gly Tyr Ser Ser Ile Asp Glu Phe Val Ala Arg Met Glu Thr Ser Glu  
195 200 205

Gly Glu Gln Leu Asp Ala Phe Val Arg Phe Val Ala Ala Asp Ser Ser  
210 215 220

Leu Arg Thr Ala Leu Lys Asn Arg Lys Trp Ala Ala Phe Ala Lys Gly  
225 230 235 240

Tyr Asn Gly Pro Asp Tyr Ala Arg Asn Leu Tyr Asp Ala Lys Leu Ala  
245 250 255

Gln Ala Tyr Glu Arg Tyr Ala Gly Thr Lys Ala Ala Ala  
260 265

<210> 57  
<211> 864  
<212> DNA  
<213> Pseudomonas flexibilis

<220>

<221> misc\_feature  
 <222> (28)..(840)  
 <223> GN425 lysin

<220>  
 <221> CDS  
 <222> (28)..(840)

<400> 57

gtttaacttt aagaaggaga attcacc atg acc ctg cgc ctc gat gac gtc ggc 54  
 Met Thr Leu Arg Leu Asp Asp Val Gly  
 1 5

ctc gac gtg ctc cat ctg cag aag cgc ctc aac gag ctg ggc gcg aat 102  
 Leu Asp Val Leu His Leu Gln Lys Arg Leu Asn Glu Leu Gly Ala Asn  
 10 15 20 25

ccg cgg ctg ctg ccc gat ggc cag ttc ggc gag gtc acc gag cgc gcc 150  
 Pro Arg Leu Leu Pro Asp Gly Gln Phe Gly Glu Val Thr Glu Arg Ala  
 30 35 40

gtg cgg gcc ttc cag caa cgt gcc ggc ctg gtg gtc gat ggc gtg gcc 198  
 Val Arg Ala Phe Gln Gln Arg Ala Gly Leu Val Val Asp Gly Val Ala  
 45 50 55

gga ccc aag acg atg gcc gcc ctg tcc ggc cat tcc acc agc cgc ctg 246  
 Gly Pro Lys Thr Met Ala Ala Leu Ser Gly His Ser Thr Ser Arg Leu  
 60 65 70

ctc ggc cag cgc gac ctg caa cgc gcc gcc gac cgc ttg ggc gtg ccg 294  
 Leu Gly Gln Arg Asp Leu Gln Arg Ala Ala Asp Arg Leu Gly Val Pro  
 75 80 85

ctg gcc agc gtc atg gcc ctc aat gcc gtg gaa agt cgc ggc gag ggc 342  
 Leu Ala Ser Val Met Ala Leu Asn Ala Val Glu Ser Arg Gly Glu Gly  
 90 95 100 105

ttc gcc gcc aat ggc cgg ccg gtg atc ctg ttc gag cgg cac gtg atg 390  
 Phe Ala Ala Asn Gly Arg Pro Val Ile Leu Phe Glu Arg His Val Met  
 110 115 120

cac gaa cgc ttg cag gtc aac ggc ctg agc gaa gcc gag gcg gac gcc 438  
 His Glu Arg Leu Gln Val Asn Gly Leu Ser Glu Ala Glu Ala Asp Ala  
 125 130 135

ctg gcg gca cgc cac ccc ggc ctg gtg agt cgc cgg cca ggc ggc tac 486  
 Leu Ala Ala Arg His Pro Gly Leu Val Ser Arg Arg Pro Gly Gly Tyr  
 140 145 150

gtc ggc gac acc gcc gag cat cag cgc ctg gcc aat gcc cgc ctg ttg 534  
 Val Gly Asp Thr Ala Glu His Gln Arg Leu Ala Asn Ala Arg Leu Leu  
 155 160 165

0341\_0021-00-304\_ST25 (1).txt

cat gac acc gct gcc ctg gaa tcc gcc agt tgg gga ctg ttc cag gtg 582  
His Asp Thr Ala Ala Leu Glu Ser Ala Ser Trp Gly Leu Phe Gln Val  
170 175 180 185

atg ggc tac cac tgg cag gcc ctg ggc tac gac acc acc cag gac ttc 630  
Met Gly Tyr His Trp Gln Ala Leu Gly Tyr Asp Thr Thr Gln Asp Phe  
190 195 200

acc gag cgc atg gcc cgc cac gaa gcc gag cac ctg gaa gcg ttc gtg 678  
Thr Glu Arg Met Ala Arg His Glu Ala Glu His Leu Glu Ala Phe Val  
205 210 215

cgc ttc atc gaa gcc gat ccg gca ctg cac aag gca ctc aag ggc cgt 726  
Arg Phe Ile Glu Ala Asp Pro Ala Leu His Lys Ala Leu Lys Gly Arg  
220 225 230

aag tgg gcc gag ttc gcc cgc cgc tac aac ggc ccg gcc tac gcc cgc 774  
Lys Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Arg  
235 240 245

aat ttg tac gac gtg aag ctg gct cgg gca ttc gag caa ttc agc gac 822  
Asn Leu Tyr Asp Val Lys Leu Ala Arg Ala Phe Glu Gln Phe Ser Asp  
250 255 260 265

gca ctg cag gcc gcc gca tgataaaagc ttggctgttt tggc 864  
Ala Leu Gln Ala Ala Ala  
270

<210> 58  
<211> 271  
<212> PRT  
<213> Pseudomonas flexibilis

<400> 58

Met Thr Leu Arg Leu Asp Asp Val Gly Leu Asp Val Leu His Leu Gln  
1 5 10 15

Lys Arg Leu Asn Glu Leu Gly Ala Asn Pro Arg Leu Leu Pro Asp Gly  
20 25 30

Gln Phe Gly Glu Val Thr Glu Arg Ala Val Arg Ala Phe Gln Gln Arg  
35 40 45

Ala Gly Leu Val Val Asp Gly Val Ala Gly Pro Lys Thr Met Ala Ala  
50 55 60

0341\_0021-00-304\_ST25 (1).txt

Leu Ser Gly His Ser Thr Ser Arg Leu Leu Gly Gln Arg Asp Leu Gln  
65 70 75 80

Arg Ala Ala Asp Arg Leu Gly Val Pro Leu Ala Ser Val Met Ala Leu  
85 90 95

Asn Ala Val Glu Ser Arg Gly Glu Gly Phe Ala Ala Asn Gly Arg Pro  
100 105 110

Val Ile Leu Phe Glu Arg His Val Met His Glu Arg Leu Gln Val Asn  
115 120 125

Gly Leu Ser Glu Ala Glu Ala Asp Ala Leu Ala Ala Arg His Pro Gly  
130 135 140

Leu Val Ser Arg Arg Pro Gly Gly Tyr Val Gly Asp Thr Ala Glu His  
145 150 155 160

Gln Arg Leu Ala Asn Ala Arg Leu Leu His Asp Thr Ala Ala Leu Glu  
165 170 175

Ser Ala Ser Trp Gly Leu Phe Gln Val Met Gly Tyr His Trp Gln Ala  
180 185 190

Leu Gly Tyr Asp Thr Thr Gln Asp Phe Thr Glu Arg Met Ala Arg His  
195 200 205

Glu Ala Glu His Leu Glu Ala Phe Val Arg Phe Ile Glu Ala Asp Pro  
210 215 220

Ala Leu His Lys Ala Leu Lys Gly Arg Lys Trp Ala Glu Phe Ala Arg  
225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Arg Asn Leu Tyr Asp Val Lys Leu  
245 250 255

Ala Arg Ala Phe Glu Gln Phe Ser Asp Ala Leu Gln Ala Ala Ala  
260 265 270

```
<210> 59
<211> 843
<212> DNA
<213> Escherichia virus
```

```
<220>
<221> misc_feature
<222> (28)..(819)
<223> GN428 lysin
```

```
<220>
<221> CDS
<222> (28)..(819)
```

|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|-------------------------------------------------------------------|----|--|--|--|--|--|--|--|--|--|--|--|--|--|--|-----|
| <400>                                                             | 59 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| gtttaacttt aagaaggaga attcacc atg gcc att cta aaa ctt ggc aac cga |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 54  |
| Met Ala Ile Leu Lys Leu Gly Asn Arg                               |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 1 5                                                               |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| ggt tct gaa gtc aaa gca ctt caa caa agc ctc aac aaa atc ggt ttc   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 102 |
| Gly Ser Glu Val Lys Ala Leu Gln Gln Ser Leu Asn Lys Ile Gly Phe   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 10 15 20 25                                                       |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| tct ctt aca gcc gat ggc ata ttt ggt aag gca aca gag aat gcc gtc   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 150 |
| Ser Leu Thr Ala Asp Gly Ile Phe Gly Lys Ala Thr Glu Asn Ala Val   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 30 35 40                                                          |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| aaa tcc gtt cag gca ggt gct gga ttg gtt att gat ggt att gct ggg   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 198 |
| Lys Ser Val Gln Ala Gly Ala Gly Leu Val Ile Asp Gly Ile Ala Gly   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 45 50 55                                                          |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| cca aag acc ttc tat gct atc cgc aac gct gga gac gct cac cag gaa   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 246 |
| Pro Lys Thr Phe Tyr Ala Ile Arg Asn Ala Gly Asp Ala His Gln Glu   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 60 65 70                                                          |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| cat ctg acc gaa gcg gac ttg gtt gac gca gca cgt gaa ctt ggt gtt   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 294 |
| His Leu Thr Glu Ala Asp Leu Val Asp Ala Ala Arg Glu Leu Gly Val   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 75 80 85                                                          |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| gag ctg gcc agt atg aaa gcg gtg aac cag gta gaa tcc cgt ggt acg   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 342 |
| Glu Leu Ala Ser Met Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 90 95 100 105                                                     |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| ggt ttt acc aaa act ggc aag atc aaa act ctg ttt gag cgc cac atc   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 390 |
| Gly Phe Thr Lys Thr Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 110 115 120                                                       |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
|                                                                   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| atg tac aaa aag gtg acg gcc aaa ttc ggg caa gca aga gcc aat gct   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 438 |
| Met Tyr Lys Lys Val Thr Ala Lys Phe Gly Gln Ala Arg Ala Asn Ala   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |
| 125 130 135                                                       |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |

0341\_0021-00-304\_ST25 (1).txt

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| ctg tac caa ctc tac cca aca ttg gtt aac ccc aat tct ggc ggg tat | 486 |
| Leu Tyr Gln Leu Tyr Pro Thr Leu Val Asn Pro Asn Ser Gly Gly Tyr |     |
| 140 145 150                                                     |     |
| atc ggc gga gac gcg gag ttg gaa cgc ctt cag ggt gca atc gcc ctt | 534 |
| Ile Gly Gly Asp Ala Glu Leu Glu Arg Leu Gln Gly Ala Ile Ala Leu |     |
| 155 160 165                                                     |     |
| gac gag gac tgc gct tac gag agt gct tcc tac ggc cta ttc cag atc | 582 |
| Asp Glu Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile |     |
| 170 175 180 185                                                 |     |
| atg ggg ttc aac tgc caa atc tgt ggc tat tca aat gcc aaa gag atg | 630 |
| Met Gly Phe Asn Cys Gln Ile Cys Gly Tyr Ser Asn Ala Lys Glu Met |     |
| 190 195 200                                                     |     |
| ttc act gat ttc ctg act ggt gaa cgc gct cat ctt ctg gca ttt gtc | 678 |
| Phe Thr Asp Phe Leu Thr Gly Glu Arg Ala His Leu Leu Ala Phe Val |     |
| 205 210 215                                                     |     |
| aag ttc atc aag gct gat gcc aat atg tgg aaa gcc ctg aag aac aag | 726 |
| Lys Phe Ile Lys Ala Asp Ala Asn Met Trp Lys Ala Leu Lys Asn Lys |     |
| 220 225 230                                                     |     |
| aat tgg gcc gag ttt gct cgt cgg tac aat ggt ccg gca tat gcg aaa | 774 |
| Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Ala Lys |     |
| 235 240 245                                                     |     |
| aac cag tat gat act aaa ctg gcg gca gca tac aag agt ttc tgt     | 819 |
| Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Lys Ser Phe Cys     |     |
| 250 255 260                                                     |     |
| taataaaagc ttggctgttt tggc                                      | 843 |

<210> 60  
 <211> 264  
 <212> PRT  
 <213> Escherichia virus

<400> 60

|                                                                 |
|-----------------------------------------------------------------|
| Met Ala Ile Leu Lys Leu Gly Asn Arg Gly Ser Glu Val Lys Ala Leu |
| 1 5 10 15                                                       |

|                                                                 |
|-----------------------------------------------------------------|
| Gln Gln Ser Leu Asn Lys Ile Gly Phe Ser Leu Thr Ala Asp Gly Ile |
| 20 25 30                                                        |

|                                                                 |
|-----------------------------------------------------------------|
| Phe Gly Lys Ala Thr Glu Asn Ala Val Lys Ser Val Gln Ala Gly Ala |
|-----------------------------------------------------------------|

35

40

45

Gly Leu Val Ile Asp Gly Ile Ala Gly Pro Lys Thr Phe Tyr Ala Ile  
 50 55 60

Arg Asn Ala Gly Asp Ala His Gln Glu His Leu Thr Glu Ala Asp Leu  
 65 70 75 80

Val Asp Ala Ala Arg Glu Leu Gly Val Glu Leu Ala Ser Met Lys Ala  
 85 90 95

Val Asn Gln Val Glu Ser Arg Gly Thr Gly Phe Thr Lys Thr Gly Lys  
 100 105 110

Ile Lys Thr Leu Phe Glu Arg His Ile Met Tyr Lys Lys Val Thr Ala  
 115 120 125

Lys Phe Gly Gln Ala Arg Ala Asn Ala Leu Tyr Gln Leu Tyr Pro Thr  
 130 135 140

Leu Val Asn Pro Asn Ser Gly Gly Tyr Ile Gly Gly Asp Ala Glu Leu  
 145 150 155 160

Glu Arg Leu Gln Gly Ala Ile Ala Leu Asp Glu Asp Cys Ala Tyr Glu  
 165 170 175

Ser Ala Ser Tyr Gly Leu Phe Gln Ile Met Gly Phe Asn Cys Gln Ile  
 180 185 190

Cys Gly Tyr Ser Asn Ala Lys Glu Met Phe Thr Asp Phe Leu Thr Gly  
 195 200 205

Glu Arg Ala His Leu Leu Ala Phe Val Lys Phe Ile Lys Ala Asp Ala  
 210 215 220

Asn Met Trp Lys Ala Leu Lys Asn Lys Asn Trp Ala Glu Phe Ala Arg  
 225 230 235 240

Arg Tyr Asn Gly Pro Ala Tyr Ala Lys Asn Gln Tyr Asp Thr Lys Leu

Ala Ala Ala Tyr Lys Ser Phe Cys  
260

<210> 61

<211> 660

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (13)..(639)

<223> GN93 lysin

<220>

<221> CDS

<222> (13)..(639)

<400> 61

ggagaattca cc atg aaa ttc ttt aag ttc ttt aag ttt ttt aaa gcc ggc 51  
Met Lys Phe Phe Lys Phe Phe Lys Phe Phe Lys Ala Gly  
1 5 10

gca gga gct ggt gca gga gct ggt gca gga gct ggt gca gga gct agc 99  
Ala Gly Ala Gly Ala Gly Ala Gly Ala Gly Ala Gly Ala Gly Ala Ser  
15 20 25

aat aac gaa ctt cct tgg gta gcc gaa gcc cga aag tat atc ggc ctt 147  
Asn Asn Glu Leu Pro Trp Val Ala Glu Ala Arg Lys Tyr Ile Gly Leu  
30 35 40 45

cgc gaa gac act tcg aag act tcg cat aac ccg aaa ctt ctt gcc atg 195  
Arg Glu Asp Thr Ser Lys Thr Ser His Asn Pro Lys Leu Leu Ala Met  
50 55 60

ctt gac cgc atg ggc gaa ttt tcc aac gaa tcc cgc gct tgg tgg cac 243  
Leu Asp Arg Met Gly Glu Phe Ser Asn Glu Ser Arg Ala Trp Trp His  
65 70 75

gac gac gaa acg cct tgg tgc gga ctg ttc gtc ggc tat tgc ttg ggc 291  
Asp Asp Glu Thr Pro Trp Cys Gly Leu Phe Val Gly Tyr Cys Leu Gly  
80 85 90

gtt gcc ggg cgc tac gtc gtc cgc gaa tgg tac agg gcg cgg gca tgg 339  
Val Ala Gly Arg Tyr Val Val Arg Glu Trp Tyr Arg Ala Arg Ala Trp

95

100

105

gaa gcc ccg cag ctt acg aag ctt gac cgg ccc gca tac ggc gcg ctt 387  
 Glu Ala Pro Gln Leu Thr Lys Leu Asp Arg Pro Ala Tyr Gly Ala Leu  
 110 115 120 125

gtg acc ttc acg cga agc ggc ggc ggc cac gtc ggt ttt att gtg ggc 435  
 Val Thr Phe Thr Arg Ser Gly Gly Gly His Val Gly Phe Ile Val Gly  
 130 135 140

aag gat gcg cgc gga aat ctt atg gtt ctt ggc ggt aat cag tcg aac 483  
 Lys Asp Ala Arg Gly Asn Leu Met Val Leu Gly Gly Asn Gln Ser Asn  
 145 150 155

gcc gta agt atc gca ccg ttc gca gta tcc cgc gta acc ggc tat ttc 531  
 Ala Val Ser Ile Ala Pro Phe Ala Val Ser Arg Val Thr Gly Tyr Phe  
 160 165 170

tgg ccg tcg ttc tgg cga aac aag acc gca gtt aaa agc gtt ccg ttt 579  
 Trp Pro Ser Phe Trp Arg Asn Lys Thr Ala Val Lys Ser Val Pro Phe  
 175 180 185

gaa gaa cgt tat tcg ctg ccg ctg ttg aag tcg aac ggc gaa ctt tcg 627  
 Glu Glu Arg Tyr Ser Leu Pro Leu Leu Lys Ser Asn Gly Glu Leu Ser  
 190 195 200 205

acg aat gaa gcg taataagctt ggctgttttg g 660  
 Thr Asn Glu Ala

&lt;210&gt; 62

&lt;211&gt; 209

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Construct

&lt;400&gt; 62

Met Lys Phe Phe Lys Phe Phe Lys Phe Phe Lys Ala Gly Ala Gly Ala  
 1 5 10 15

Gly Ala Gly Ala Gly Ala Gly Ala Gly Ala Gly Ala Ser Asn Asn Glu  
 20 25 30

Leu Pro Trp Val Ala Glu Ala Arg Lys Tyr Ile Gly Leu Arg Glu Asp  
 35 40 45

0341\_0021-00-304\_ST25 (1).txt

Thr Ser Lys Thr Ser His Asn Pro Lys Leu Leu Ala Met Leu Asp Arg  
50 55 60

Met Gly Glu Phe Ser Asn Glu Ser Arg Ala Trp Trp His Asp Asp Glu  
65 70 75 80

Thr Pro Trp Cys Gly Leu Phe Val Gly Tyr Cys Leu Gly Val Ala Gly  
85 90 95

Arg Tyr Val Val Arg Glu Trp Tyr Arg Ala Arg Ala Trp Glu Ala Pro  
100 105 110

Gln Leu Thr Lys Leu Asp Arg Pro Ala Tyr Gly Ala Leu Val Thr Phe  
115 120 125

Thr Arg Ser Gly Gly Gly His Val Gly Phe Ile Val Gly Lys Asp Ala  
130 135 140

Arg Gly Asn Leu Met Val Leu Gly Gly Asn Gln Ser Asn Ala Val Ser  
145 150 155 160

Ile Ala Pro Phe Ala Val Ser Arg Val Thr Gly Tyr Phe Trp Pro Ser  
165 170 175

Phe Trp Arg Asn Lys Thr Ala Val Lys Ser Val Pro Phe Glu Glu Arg  
180 185 190

Tyr Ser Leu Pro Leu Leu Lys Ser Asn Gly Glu Leu Ser Thr Asn Glu  
195 200 205

Ala

<210> 63

<211> 843

<212> DNA

<213> Dickeya phage phiD3

<220>

```
<221> misc_feature
<222> (28)..(819)
<223> GN431 lysin
```

```
<220>
<221> CDS
<222> (28)..(819)
```

<400> 63

gtttaacttt aagaaggaga attcacc atg gcc att cta aaa ctt ggc aac cgt 54  
Met Ala Ile Leu Lys Leu Gly Asn Arg  
1 5

ggc act gaa gtg aag gca ctt cag gat agc ctc aac aaa atc ggc ttc 102  
Gly Thr Glu Val Lys Ala Leu Gln Asp Ser Leu Asn Lys Ile Gly Phe  
10 15 20 25

acc ctc gtc gct gac ggc atc ttt ggt aag gca aca gag aac gct gtc 150  
Thr Leu Val Ala Asp Gly Ile Phe Gly Lys Ala Thr Glu Asn Ala Val  
30 35 40

aag acc gtt cag gcg ggt gcg ggg ctt gtc att gat ggt atc gtg ggt 198  
Lys Thr Val Gln Ala Gly Ala Gly Leu Val Ile Asp Gly Ile Val Gly  
45 50 55

cca aag acc tcc tat gct att cgc aac gcc ggg gaa gcg cat cag gat 246  
Pro Lys Thr Ser Tyr Ala Ile Arg Asn Ala Gly Glu Ala His Gln Asp  
60 65 70

cac ctg act gag gct gac ctt atc gag gcg gcc aat cag ctg ggc gtc 294  
 His Leu Thr Glu Ala Asp Leu Ile Glu Ala Ala Asn Gln Leu Gly Val  
 75 80 85

gac ctc gct tct gtg aag gca gtc aac cag gtt gaa tcc cgt ggc aca 342  
Asp Leu Ala Ser Val Lys Ala Val Asn Gln Val Glu Ser Arg Gly Thr  
90 95 100 105

ggc ttc acc aag tca ggc aag atc aag aca ttg ttc gag cgt cac atc 390  
Gly Phe Thr Lys Ser Gly Lys Ile Lys Thr Leu Phe Glu Arg His Ile  
110 115 120

atg tat aag aaa ctg atg gca aag ttc gga cag gct cga gcg aat gcc 438  
Met Tyr Lys Lys Leu Met Ala Lys Phe Gly Gln Ala Arg Ala Asn Ala  
125 130 135

atg ggt cag atg tat ccg act ctg gtc agc ccg gtt gca ggc ggg tac 486  
Met Gly Gln Met Tyr Pro Thr Leu Val Ser Pro Val Ala Gly Gly Tyr  
140 145 150

acg gga ggt gac gca gaa ttg gat cga ctc cac gca gcg atc aac atc 534  
Thr Gly Gly Asp Ala Glu Leu Asp Arg Leu His Ala Ala Ile Asn Ile  
155 160 165

## 0341\_0021-00-304\_ST25 (1).txt

gac gag gat tgt gcg tac gag agc gct tca tac ggc ctc ttc cag atc 582  
 Asp Glu Asp Cys Ala Tyr Glu Ser Ala Ser Tyr Gly Leu Phe Gln Ile  
 170 175 180 185

atg ggc ttc aac tgc cag gtc tgc ggg tat gcc aac gcc aag gag atg 630  
 Met Gly Phe Asn Cys Gln Val Cys Gly Tyr Ala Asn Ala Lys Glu Met  
 190 195 200

ttc aat gac ttc ctg acg gga gaa cgt gct cac ctg atg gca ttc gtg 678  
 Phe Asn Asp Phe Leu Thr Gly Glu Arg Ala His Leu Met Ala Phe Val  
 205 210 215

aag ttc atc aag gct gat gcc aag ctc tgg cag gct ctg aag gac aag 726  
 Lys Phe Ile Lys Ala Asp Ala Lys Leu Trp Gln Ala Leu Lys Asp Lys  
 220 225 230

aat tgg gct gag ttc gcg cgg cgc tat aat ggt ccg gcg tat acc aag 774  
 Asn Trp Ala Glu Phe Ala Arg Arg Tyr Asn Gly Pro Ala Tyr Thr Lys  
 235 240 245

aac cag tac gac acg aag ctc gca gca gca tac aac agc ttc aat 819  
 Asn Gln Tyr Asp Thr Lys Leu Ala Ala Ala Tyr Asn Ser Phe Asn  
 250 255 260

taataaaagc ttggctgttt tggc 843

<210> 64

<211> 264

<212> PRT

<213> Dickeya phage phiD3

<400> 64

Met Ala Ile Leu Lys Leu Gly Asn Arg Gly Thr Glu Val Lys Ala Leu  
 1 5 10 15

Gln Asp Ser Leu Asn Lys Ile Gly Phe Thr Leu Val Ala Asp Gly Ile  
 20 25 30

Phe Gly Lys Ala Thr Glu Asn Ala Val Lys Thr Val Gln Ala Gly Ala  
 35 40 45

Gly Leu Val Ile Asp Gly Ile Val Gly Pro Lys Thr Ser Tyr Ala Ile  
 50 55 60

Arg Asn Ala Gly Glu Ala His Gln Asp His Leu Thr Glu Ala Asp Leu

|            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 65         |            |            |            |            | 70         | —          |            |            |            | 75         | ✓          |            |            |            | 80         |
| Ile        | Glu        | Ala        | Ala        | Asn<br>85  | Gln        | Leu        | Gly        | Val        | Asp<br>90  | Leu        | Ala        | Ser        | Val        | Lys<br>95  | Ala        |
| Val        | Asn        | Gln        | Val<br>100 | Glu        | Ser        | Arg        | Gly        | Thr<br>105 | Gly        | Phe        | Thr        | Lys        | Ser<br>110 | Gly        | Lys        |
| Ile        | Lys        | Thr<br>115 | Leu        | Phe        | Glu        | Arg        | His<br>120 | Ile        | Met        | Tyr        | Lys        | Lys<br>125 | Leu        | Met        | Ala        |
| Lys        | Phe<br>130 | Gly        | Gln        | Ala        | Arg        | Ala<br>135 | Asn        | Ala        | Met        | Gly        | Gln<br>140 | Met        | Tyr        | Pro        | Thr        |
| Leu<br>145 | Val        | Ser        | Pro        | Val<br>150 | Ala        | Gly        | Gly        | Tyr        | Thr        | Gly<br>155 | Gly        | Asp        | Ala        | Glu        | Leu<br>160 |
| Asp        | Arg        | Leu        | His<br>165 | Ala        | Ala        | Ile        | Asn        | Ile        | Asp<br>170 | Glu        | Asp        | Cys        | Ala        | Tyr<br>175 | Glu        |
| Ser        | Ala        | Ser        | Tyr<br>180 | Gly        | Leu        | Phe        | Gln        | Ile<br>185 | Met        | Gly        | Phe        | Asn        | Cys<br>190 | Gln        | Val        |
| Cys        | Gly        | Tyr<br>195 | Ala        | Asn        | Ala        | Lys        | Glu<br>200 | Met        | Phe        | Asn        | Asp        | Phe<br>205 | Leu        | Thr        | Gly        |
| Glu        | Arg<br>210 | Ala        | His        | Leu        | Met        | Ala<br>215 | Phe        | Val        | Lys        | Phe        | Ile<br>220 | Lys        | Ala        | Asp        | Ala        |
| Lys<br>225 | Leu        | Trp        | Gln        | Ala        | Leu<br>230 | Lys        | Asp        | Lys        | Asn        | Trp<br>235 | Ala        | Glu        | Phe        | Ala        | Arg        |
| Arg        | Tyr        | Asn        | Gly<br>245 | Pro        | Ala        | Tyr        | Thr        | Lys        | Asn<br>250 | Gln        | Tyr        | Asp        | Thr        | Lys<br>255 | Leu        |
| Ala        | Ala        | Ala        | Tyr<br>260 | Asn        | Ser        | Phe        | Asn        |            |            |            |            |            |            |            |            |

<210> 65

<211> 510  
 <212> DNA  
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (10)..(510)

<223> GN486 lysin

<220>

<221> CDS

<222> (10)..(510)

<400> 65

|           |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |    |
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|----|
| gaattcacc | atg | gga | tcc | cat | cat | cac | cac | cat | cat | ggt | ggt | ccg | cgt | cgt |  | 51 |
|           | Met | Gly | Ser | His | His | His | His | His | His | Gly | Gly | Pro | Arg | Arg |  |    |
| 1         |     |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     |  |    |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |    |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| ccg | cgt | cgt | ccg | ggt | cgt | cgt | gct | ccg | gtt | cgt | acc | tct | cag | cgt | ggt | 99 |
| Pro | Arg | Arg | Pro | Gly | Arg | Arg | Ala | Pro | Val | Arg | Thr | Ser | Gln | Arg | Gly |    |
| 15  |     |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |    |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| atc | gac | ctg | atc | aaa | tct | ttc | gaa | ggt | ctg | cgt | ctg | tct | gct | tac | cag | 147 |
| Ile | Asp | Leu | Ile | Lys | Ser | Phe | Glu | Gly | Leu | Arg | Leu | Ser | Ala | Tyr | Gln |     |
|     |     |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| gac | tct | gtt | ggt | gtt | tgg | acc | atc | ggt | tac | ggt | acc | acc | cgt | ggt | gtt | 195 |
| Asp | Ser | Val | Gly | Val | Trp | Thr | Ile | Gly | Tyr | Gly | Thr | Thr | Arg | Gly | Val |     |
|     |     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| acc | cgt | tac | atg | acc | atc | acc | gtt | gaa | cag | gct | gaa | cgt | atg | ctg | tct | 243 |
| Thr | Arg | Tyr | Met | Thr | Ile | Thr | Val | Glu | Gln | Ala | Glu | Arg | Met | Leu | Ser |     |
|     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| aac | gac | atc | cag | cgt | ttc | gaa | ccg | gaa | ctg | gac | cgt | ctg | gct | aaa | gtt | 291 |
| Asn | Asp | Ile | Gln | Arg | Phe | Glu | Pro | Glu | Leu | Asp | Arg | Leu | Ala | Lys | Val |     |
|     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| ccg | ctg | aac | cag | aac | cag | tgg | gac | gct | ctg | atg | tct | ttc | gtt | tac | aac | 339 |
| Pro | Leu | Asn | Gln | Asn | Gln | Trp | Asp | Ala | Leu | Met | Ser | Phe | Val | Tyr | Asn |     |
| 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| ctg | ggt | gct | gct | aac | ctg | gct | tct | tct | acc | ctg | ctg | aaa | ctg | ctg | aac | 387 |
| Leu | Gly | Ala | Ala | Asn | Leu | Ala | Ser | Ser | Thr | Leu | Leu | Lys | Leu | Leu | Asn |     |
|     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| aaa | ggt | gac | tac | cag | ggt | gct | gct | gac | cag | ttc | ccg | cgt | tgg | gtt | aac | 435 |
| Lys | Gly | Asp | Tyr | Gln | Gly | Ala | Ala | Asp | Gln | Phe | Pro | Arg | Trp | Val | Asn |     |

130

135

140

gct ggt ggt aaa cgt ctg gac ggt ctg gtt aaa cgt cgt gct gct gaa 483  
 Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Arg Ala Ala Glu  
           145                  150                  155

cgt gct ctg ttc ctg gaa ccg ctg tct 510  
 Arg Ala Leu Phe Leu Glu Pro Leu Ser  
       160                  165

&lt;210&gt; 66

&lt;211&gt; 167

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic Construct

&lt;400&gt; 66

Met Gly Ser His His His His His His Gly Gly Pro Arg Arg Pro Arg  
 1                  5                  10                  15

Arg Pro Gly Arg Arg Ala Pro Val Arg Thr Ser Gln Arg Gly Ile Asp  
           20                  25                  30

Leu Ile Lys Ser Phe Glu Gly Leu Arg Leu Ser Ala Tyr Gln Asp Ser  
       35                  40                  45

Val Gly Val Trp Thr Ile Gly Tyr Gly Thr Thr Arg Gly Val Thr Arg  
       50                  55                  60

Tyr Met Thr Ile Thr Val Glu Gln Ala Glu Arg Met Leu Ser Asn Asp  
 65                  70                  75                  80

Ile Gln Arg Phe Glu Pro Glu Leu Asp Arg Leu Ala Lys Val Pro Leu  
           85                  90                  95

Asn Gln Asn Gln Trp Asp Ala Leu Met Ser Phe Val Tyr Asn Leu Gly  
           100                  105                  110

Ala Ala Asn Leu Ala Ser Ser Thr Leu Leu Lys Leu Leu Asn Lys Gly  
       115                  120                  125

Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro Arg Trp Val Asn Ala Gly  
 130 135 140

Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Arg Ala Ala Glu Arg Ala  
 145 150 155 160

Leu Phe Leu Glu Pro Leu Ser  
 165

<210> 67

<211> 219

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (1)..(216)

<223> GN485 lysin

<220>

<221> CDS

<222> (1)..(216)

<400> 67

atg ccg ggt ctg tct ggt ttc atc cgt aac gct gac acc ccg gtt acc 48  
 Met Pro Gly Leu Ser Gly Phe Ile Arg Asn Ala Asp Thr Pro Val Thr  
 1 5 10 15

tct ctg ggt tct gct ggt cac gtt cac gtt ccg gaa ggt ccg ctg atc 96  
 Ser Leu Gly Ser Ala Gly His Val His Val Pro Glu Gly Pro Leu Ile  
 20 25 30

cgt atc aac ccg gac tgc ctg ctg ggt acc ccg ttc aaa ttc ttc aag 144  
 Arg Ile Asn Pro Asp Cys Leu Leu Gly Thr Pro Phe Lys Phe Phe Lys  
 35 40 45

ttc ttc aag ttc ttc aag ttc ttt aag ttc ttt aag ttt ttc aag ttc 192  
 Phe Phe Lys Phe Phe Lys Phe Phe Lys Phe Phe Lys Phe Phe Lys Phe  
 50 55 60

ttc aag aac gaa tgc gtt ctg ctg taa 219  
 Phe Lys Asn Glu Cys Val Leu Leu  
 65 70

<210> 68  
 <211> 72  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Synthetic Construct

<400> 68

Met Pro Gly Leu Ser Gly Phe Ile Arg Asn Ala Asp Thr Pro Val Thr  
 1 5 10 15

Ser Leu Gly Ser Ala Gly His Val His Val Pro Glu Gly Pro Leu Ile  
 20 25 30

Arg Ile Asn Pro Asp Cys Leu Leu Gly Thr Pro Phe Lys Phe Phe Lys  
 35 40 45

Phe Phe Lys Phe Phe Lys Phe Phe Lys Phe Phe Lys Phe Phe Lys Phe  
 50 55 60

Phe Lys Asn Glu Cys Val Leu Leu  
 65 70

<210> 69  
 <211> 132  
 <212> DNA  
 <213> Chlamydia phage 2

<400> 69  
 atgaggttaa aaatggcacg aagaagatac agacttccgc gacgtagaag tcgaagactt 60

ttttcaagaa ctgcattgag gatgcatcca agaaataggc ttcgaagaat tatgcgtggc 120

ggcattaggt tc 132

<210> 70  
 <211> 44  
 <212> PRT  
 <213> Chlamydia phage 2

<400> 70

Met Arg Leu Lys Met Ala Arg Arg Arg Tyr Arg Leu Pro Arg Arg Arg

1 5 10 15

Ser Arg Arg Leu Phe Ser Arg Thr Ala Leu Arg Met His Pro Arg Asn  
20 25 30

Arg Leu Arg Arg Ile Met Arg Gly Gly Ile Arg Phe  
35 40

<210> 71  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>  
<221> misc\_feature  
<222> (1)..(24)  
<223> linker

<400> 71  
accgcgggcg gcaccgcggg cggc

24

<210> 72  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic peptide

<220>  
<221> MISC\_FEATURE  
<222> (1)..(8)  
<223> linker

<400> 72

Thr Ala Gly Gly Thr Ala Gly Gly  
1 5

<210> 73  
<211> 435  
<212> DNA

<213> Pseudomonas phage PAJU2

<220>

<221> misc\_feature

<222> (1)..(435)

<223> GN4

<400> 73

```

atgcgtacat cccaacgagg catcgacctc atcaaattct tcgagggcct gcgcctgtcc      60
gcttaccagg actcggtggg tgtctggacc ataggttacg gcaccactcg gggcgtcacc      120
cgctacatga cgatcacctg cgagcaggcc gagcggatgc tgtcgaacga cattcagcgc      180
ttcgagccag agctagacag gctggcgaag gtgccactga accagaacca gtgggatgcc      240
ctgatgagct tcgtgtacaa cctgggcgcg gccaatctgg cgtcgtccac gctgctcaag      300
ctgctgaaca aggggtgacta ccaggagca gcggaccagt tcccgcgctg ggtgaatgcg      360
ggcggtaagc gcttgatgg tctggttaag cgtcgagcag ccgagcgtgc gctgttcctg      420
gagccactat cgtga                                     435

```

<210> 74

<211> 144

<212> PRT

<213> Pseudomonas phage PAJU2

<220>

<221> MISC\_FEATURE

<222> (1)..(144)

<223> GN4

<400> 74

```

Met Arg Thr Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser Phe Glu Gly
1           5           10           15

```

```

Leu Arg Leu Ser Ala Tyr Gln Asp Ser Val Gly Val Trp Thr Ile Gly
          20           25           30

```

```

Tyr Gly Thr Thr Arg Gly Val Thr Arg Tyr Met Thr Ile Thr Val Glu
          35           40           45

```

```

Gln Ala Glu Arg Met Leu Ser Asn Asp Ile Gln Arg Phe Glu Pro Glu

```

50

55

60

Leu Asp Arg Leu Ala Lys Val Pro Leu Asn Gln Asn Gln Trp Asp Ala  
65 70 75 80

Leu Met Ser Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu Ala Ser Ser  
85 90 95

Thr Leu Leu Lys Leu Leu Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp  
100 105 110

Gln Phe Pro Arg Trp Val Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu  
115 120 125

Val Lys Arg Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu Pro Leu Ser  
130 135 140

&lt;210&gt; 75

&lt;211&gt; 63

&lt;212&gt; DNA

<213> *Penaeus chinensis*

&lt;400&gt; 75

atgagcttta acgtgacccc gaaatttaaa cgctggcagc tgtatttttcg cggccgcatg 60

tgg 63

&lt;210&gt; 76

&lt;211&gt; 21

&lt;212&gt; PRT

<213> *Penaeus chinensis*

&lt;400&gt; 76

Met Ser Phe Asn Val Thr Pro Lys Phe Lys Arg Trp Gln Leu Tyr Phe  
1 5 10 15

Arg Gly Arg Met Trp  
20

&lt;210&gt; 77

&lt;211&gt; 438

&lt;212&gt; DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>

<221> misc\_feature

<222> (1)..(438)

<223> Modified GN4 lysin, GN146

<400> 77

```

atgcgtacat cccaacgagg catcgacctc atcaaatacct tcgagggcct ggcgcctgtcc      60
gcttaccagg actcgggtggg tgtctggacc ataggttacg gcaccactcg gggcgtcacc      120
cgctacatga cgatcacctg cgagcaggcc gagcggatgc tgtcgaacga cattcagcgc      180
ttcgagccag agctagacag gctggcgaag gtgccactga accagaacca gtgggatgcc      240
ctgatgagct tcgtgtacaa cctgggcgcg gccaatctgg cgtcgtccac gctgctcgac      300
ctgctgaaca agggtgacta ccaggagca gcggaccagt tcccgcattg ggtgaatgcg      360
ggcggtaagc gcttggatgg tctggttaag cgtcgagcag ccgagcgtgc gctgttcctg      420
gagccactat cgtgataa                                     438

```

<210> 78

<211> 144

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<220>

<221> MISC\_FEATURE

<222> (1)..(144)

<223> Modified GN4 lysin, GN146

<400> 78

```

Met Arg Thr Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser Phe Glu Gly
1           5           10           15

```

```

Leu Arg Leu Ser Ala Tyr Gln Asp Ser Val Gly Val Trp Thr Ile Gly
          20           25           30

```

Tyr Gly Thr Thr Arg Gly Val Thr Arg Tyr Met Thr Ile Thr Val Glu  
35 40 45

Gln Ala Glu Arg Met Leu Ser Asn Asp Ile Gln Arg Phe Glu Pro Glu  
50 55 60

Leu Asp Arg Leu Ala Lys Val Pro Leu Asn Gln Asn Gln Trp Asp Ala  
65 70 75 80

Leu Met Ser Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu Ala Ser Ser  
85 90 95

Thr Leu Leu Asp Leu Leu Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp  
100 105 110

Gln Phe Pro His Trp Val Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu  
115 120 125

Val Lys Arg Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu Pro Leu Ser  
130 135 140

<210> 79  
<211> 57  
<212> DNA  
<213> Pelophylax esculentus

<400> 79  
atttttagca aactggcggg caaaaaaatt aaaaacctgc tgattagcgg cctgaaa 57

<210> 80  
<211> 19  
<212> PRT  
<213> Pelophylax esculentus

<400> 80

Ile Phe Ser Lys Leu Ala Gly Lys Lys Ile Lys Asn Leu Leu Ile Ser  
1 5 10 15

Gly Leu Lys

<210> 81  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>  
 <221> misc\_feature  
 <222> (1)..(36)  
 <223> BBa\_K1485002

<400> 81  
 ggcggtagcg gcagcggtag cggtagcggc agccccg 36

<210> 82  
 <211> 12  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic peptide

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(12)  
 <223> BBa\_K1485002

<400> 82  
 Gly Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Pro  
 1 5 10

<210> 83  
 <211> 381  
 <212> DNA  
 <213> Micavibrio aeruginosavorus

<220>  
 <221> misc\_feature  
 <222> (1)..(381)  
 <223> GN37

<400> 83  
 atgacataca ccctgagcaa aagaagcctg gataacctaa aaggcgttca tcccgatctg 60

0341\_0021-00-304\_ST25 (1).txt

gttgccgttg tccatcgcg ccatccagctt 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 aatacatgatg a 381

<210> 84  
<211> 126  
<212> PRT  
<213> Micavibrio aeruginosavorus

<400> 84

Met Thr Tyr Thr Leu Ser Lys Arg Ser Leu Asp Asn Leu Lys Gly Val  
1 5 10 15

His Pro Asp Leu Val Ala Val Val His Arg Ala Ile Gln Leu Thr Pro  
20 25 30

Val Asp Phe Ala Val Ile Glu Gly Leu Arg Ser Val Ser Arg Gln Lys  
35 40 45

Glu Leu Val Ala Ala Gly Ala Ser Lys Thr Met Asn Ser Arg His Leu  
50 55 60

Thr Gly His Ala Val Asp Leu Ala Ala Tyr Val Asn Gly Ile Arg Trp  
65 70 75 80

Asp Trp Pro Leu Tyr Asp Ala Ile Ala Val Ala Val Lys Ala Ala Ala  
85 90 95

Lys Glu Leu Gly Val Ala Ile Val Trp Gly Gly Asp Trp Thr Thr Phe  
100 105 110

Lys Asp Gly Pro His Phe Glu Leu Asp Arg Ser Lys Tyr Arg  
115 120 125

<210> 85  
 <211> 39  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>  
 <221> misc\_feature  
 <222> (1)..(39)  
 <223> IGEM linker (BBA\_K1486037)

<400> 85  
 ggcggtggct ctggaggtgg tgggtccggc ggtggctct 39

<210> 86  
 <211> 13  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic peptide

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(13)  
 <223> IGEM linker (BBA\_K1486037)

<400> 86  
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser  
 1 5 10

<210> 87  
 <211> 36  
 <212> DNA  
 <213> Sus scrofa

<400> 87  
 cgcctgaaaa aaattggcaa agtgctgaaa tggatt 36

<210> 88  
 <211> 12  
 <212> PRT  
 <213> Sus scrofa

<400> 88

Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
1 5 10

<210> 89

<211> 102

<212> DNA

<213> Unknown

<220>

<223> Description of Unknown: Gokushovirinae sequence

<220>

<221> misc\_feature

<222> (1)..(102)

<223> gkh2

<220>

<221> misc\_feature

<222> (1)..(102)

<223> Description of Unknown: Gokushovirinae sequence

<400> 89

atgtcgaaga aggcgtcgag gaagagtttt actaagggtg ccgtaaggt tcataagaaa 60

aatgttccta ctcgtgttcc tatgcgtggc ggtattaggc tt 102

<210> 90

<211> 34

<212> PRT

<213> Unknown

<220>

<223> Description of Unknown: Gokushovirinae sequence

<400> 90

Met Ser Lys Lys Ala Ser Arg Lys Ser Phe Thr Lys Gly Ala Val Lys  
1 5 10 15

Val His Lys Lys Asn Val Pro Thr Arg Val Pro Met Arg Gly Gly Ile  
20 25 30

Arg Leu

<210> 91  
 <211> 54  
 <212> DNA  
 <213> Sus scrofa

<400> 91  
 cgtaaaaaa cccgtaaacg tctgaaaaaa atcggtaaag ttctgaaatg gatc 54

<210> 92  
 <211> 18  
 <212> PRT  
 <213> Sus scrofa

<400> 92  
 Arg Lys Lys Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys  
 1 5 10 15

Trp Ile

<210> 93  
 <211> 45  
 <212> DNA  
 <213> Sus scrofa

<400> 93  
 acccgcaaac gcctgaaaaa aattggcaaa gtgctgaaat ggatt 45

<210> 94  
 <211> 15  
 <212> PRT  
 <213> Sus scrofa

<400> 94  
 Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
 1 5 10 15

<210> 95  
 <211> 348  
 <212> DNA  
 <213> Pseudomonas phage PaP2

<400> 95

0341\_0021-00-304\_ST25 (1).txt

atgaaactca gcgaaaaacg agcactgttc acccagctgc ttgcccagtt aattctttgg 60  
gcaggaactc aggatcgagt gtcagtagcc ttggatcaag tgaaaaggac acaggctgaa 120  
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

<210> 96

<211> 116

<212> PRT

<213> Pseudomonas phage PaP2

<400> 96

Met Lys Leu Ser Glu Lys Arg Ala Leu Phe Thr Gln Leu Leu Ala Gln  
1 5 10 15

Leu Ile Leu Trp Ala Gly Thr Gln Asp Arg Val Ser Val Ala Leu Asp  
20 25 30

Gln Val Lys Arg Thr Gln Ala Glu Ala Asp Ala Asn Ala Lys Ser Gly  
35 40 45

Ala Gly Ile Arg Asn Ser Leu His Leu Leu Gly Leu Ala Gly Asp Leu  
50 55 60

Ile Leu Tyr Lys Asp Gly Lys Tyr Met Asp Lys Ser Glu Asp Tyr Lys  
65 70 75 80

Phe Leu Gly Asp Tyr Trp Lys Ser Leu His Pro Leu Cys Arg Trp Gly  
85 90 95

Gly Asp Phe Lys Ser Arg Pro Asp Gly Asn His Phe Ser Leu Glu His  
100 105 110

Glu Gly Val Gln  
115

<210> 97  
 <211> 30  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>  
 <221> misc\_feature  
 <222> (1)..(30)  
 <223> linker

<400> 97  
 ccaccaaccg cgggcggcac cgcgggcggc

30

<210> 98  
 <211> 10  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 98

Pro Pro Thr Ala Gly Gly Thr Ala Gly Gly  
 1 5 10

<210> 99  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>  
 <221> misc\_feature  
 <222> (1)..(27)  
 <223> purification tag GSHHHHHHG

<400> 99  
 ggatcccatc atcaccacca tcatggt

27

<210> 100  
 <211> 9

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Synthetic peptide

&lt;400&gt; 100

Gly Ser His His His His His Gly

1 5

&lt;210&gt; 101

&lt;211&gt; 120

&lt;212&gt; DNA

&lt;213&gt; Chlamydia phage 4

&lt;400&gt; 101

atggcacgaa gatacagact ttcgcgacgc agaagtcgac gacttttttc aagaactgca 60

ttaagaatgc atcgaagaaa tagacttcga agaattatgc gtggcggcat taggttttag 120

&lt;210&gt; 102

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Chlamydia phage 4

&lt;400&gt; 102

Met Ala Arg Arg Tyr Arg Leu Ser Arg Arg Arg Ser Arg Arg Leu Phe

1 5 10 15

Ser Arg Thr Ala Leu Arg Met His Arg Arg Asn Arg Leu Arg Arg Ile

20 25 30

Met Arg Gly Gly Ile Arg Phe

35

&lt;210&gt; 103

&lt;211&gt; 126

&lt;212&gt; DNA

&lt;213&gt; Escherichia coli

&lt;400&gt; 103

atggctcgtt cccgtagacg tatgtctaag cggttcttccc gccgttcgtt ccgcaagtat 60

gcgaagtcgc ataagaagaa ctttaaagcc cgctcaatgc gtggcgggtat ccgtttatga 120

taataa

126

<210> 104  
 <211> 39  
 <212> PRT  
 <213> Escherichia coli

<400> 104

Met Ala Arg Ser Arg Arg Arg Met Ser Lys Arg Ser Ser Arg Arg Ser  
 1 5 10 15

Phe Arg Lys Tyr Ala Lys Ser His Lys Lys Asn Phe Lys Ala Arg Ser  
 20 25 30

Met Arg Gly Gly Ile Arg Leu  
 35

<210> 105  
 <211> 114  
 <212> DNA  
 <213> Chlamydia trachomatis

<400> 105  
 aaacgtagaa aaatgacaag aaaaggttct aagcgtcttt ttactgcaac tgctgataaa 60

actaaatcta tcaatactgc cccgccgccca atgcgtggcg gtatccggtt gtag 114

<210> 106  
 <211> 37  
 <212> PRT  
 <213> Chlamydia trachomatis

<400> 106

Lys Arg Arg Lys Met Thr Arg Lys Gly Ser Lys Arg Leu Phe Thr Ala  
 1 5 10 15

Thr Ala Asp Lys Thr Lys Ser Ile Asn Thr Ala Pro Pro Pro Met Arg  
 20 25 30

Gly Gly Ile Arg Leu  
 35

<210> 107  
 <211> 114  
 <212> DNA  
 <213> Oscillibacter sp. PC13

<400> 107  
 atgagaaagc gaatgtctaa gcgtgttgac aagaaggtgt tccgtcgtac tgccgcatct 60  
 gccaagaaga ttaacattga cccaagatt taccgtggag gtattcgctt atga 114

<210> 108  
 <211> 37  
 <212> PRT  
 <213> Oscillibacter sp. PC13

<400> 108  
 Met Arg Lys Arg Met Ser Lys Arg Val Asp Lys Lys Val Phe Arg Arg  
 1 5 10 15

Thr Ala Ala Ser Ala Lys Lys Ile Asn Ile Asp Pro Lys Ile Tyr Arg  
 20 25 30

Gly Gly Ile Arg Leu  
 35

<210> 109  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>  
 <221> misc\_feature  
 <222> (1)..(36)  
 <223> RR12

<400> 109  
 cgccgcctga ttgcctgtg gctgcgcctg ctgcgc 36

<210> 110  
 <211> 12  
 <212> PRT  
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 110

Arg Arg Leu Ile Arg Leu Trp Leu Arg Leu Leu Arg  
1 5 10

<210> 111

<211> 12

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>

<221> misc\_feature

<222> (1)..(12)

<223> structure moiety

<400> 111

atgatcgacc gt

12

<210> 112

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 112

Met Ile Asp Arg

1

<210> 113

<211> 12

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>

<221> misc\_feature  
 <222> (1)..(12)  
 <223> moiety (outer membrane binding peptide from PMID: 22628248)

<400> 113  
 ttcattcgtc tg 12

<210> 114  
 <211> 4  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 114

Phe Ile Arg Leu  
 1

<210> 115  
 <211> 12  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>  
 <221> misc\_feature  
 <222> (1)..(12)  
 <223> structure moiety

<400> 115  
 aatccgaccc at 12

<210> 116  
 <211> 4  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 116

Asn Pro Thr His  
 1

<210> 117  
 <211> 477  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
 <221> misc\_feature  
 <222> (1)..(477)  
 <223> GN202 lysin

<400> 117  
 ggtccgcgtc gtccgcgtcg tccgggtcgt cgtgctccgg ttcgtacatc ccaacgaggc 60  
 atcgacctca tcaaatcctt cgagggcctg cgcctgtccg cttaccagga ctcggtgggt 120  
 gtctggacca taggttacgg caccactcgg ggcgtcacc gctacatgac gatcaccgtc 180  
 gagcaggccg agcggatgct gtcgaacgac attcagcgct tcgagccaga gctagacagg 240  
 ctggcggaagg tgccactgaa ccagaaccag tgggatgccc tgatgagctt cgtgtacaac 300  
 ctgggcgcgg ccaatctggc gtcgtccacg ctgctcgacc tgctgaacaa gggtgactac 360  
 caggagcag cggaccagtt cccgcattgg gtgaatgcgg gcggtaagcg cttggatggt 420  
 ctggttaagc gtcgagcagc cgagcgtgcg ctgttcctgg agccactatc gtgataa 477

<210> 118  
 <211> 158  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 118  
 Met Gly Pro Arg Arg Pro Arg Arg Pro Gly Arg Arg Ala Pro Val Arg  
 1 5 10 15  
 Thr Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser Phe Glu Gly Leu Arg  
 20 25 30

0341\_0021-00-304\_ST25 (1).txt

Leu Ser Ala Tyr Gln Asp Ser Val Gly Val Trp Thr Ile Gly Tyr Gly  
35 40 45

Thr Thr Arg Gly Val Thr Arg Tyr Met Thr Ile Thr Val Glu Gln Ala  
50 55 60

Glu Arg Met Leu Ser Asn Asp Ile Gln Arg Phe Glu Pro Glu Leu Asp  
65 70 75 80

Arg Leu Ala Lys Val Pro Leu Asn Gln Asn Gln Trp Asp Ala Leu Met  
85 90 95

Ser Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu Ala Ser Ser Thr Leu  
100 105 110

Leu Asp Leu Leu Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe  
115 120 125

Pro His Trp Val Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys  
130 135 140

Arg Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu Pro Leu Ser  
145 150 155

<210> 119  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>  
<221> misc\_feature  
<222> (1)..(30)  
<223> cationic peptide

<400> 119  
aaattcttta agttcttta gttttttaaa

30

<210> 120  
<211> 10

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Synthetic peptide

&lt;400&gt; 120

|     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Phe | Phe | Lys | Phe | Phe | Lys | Phe | Phe | Lys |
| 1   |     |     | 5   |     |     |     |     |     | 10  |

&lt;210&gt; 121

&lt;211&gt; 54

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Synthetic oligonucleotide

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(54)

&lt;223&gt; linker

&lt;400&gt; 121

|            |            |            |            |            |      |    |
|------------|------------|------------|------------|------------|------|----|
| gccggcgcag | gagctggtgc | aggagctggt | gcaggagctg | gtgcaggagc | tagc | 54 |
|------------|------------|------------|------------|------------|------|----|

&lt;210&gt; 122

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Synthetic peptide

&lt;400&gt; 122

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Gly | Ala | Gly | Ala | Gly | Ala | Gly | Ala | Gly | Ala | Gly | Ala | Gly | Ala | Gly |
| 1   |     |     | 5   |     |     |     | 10  |     |     |     |     | 15  |     |     |     |

Ala Ser

&lt;210&gt; 123

&lt;211&gt; 543

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Synthetic polynucleotide

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)..(543)

&lt;223&gt; GN14 lysin

&lt;400&gt; 123

```

aataacgaac ttccttgggt agccgaagcc cgaaagtata tcggccttcg cgaagacact      60
tcgaagactt cgcataaccc gaaacttctt gccatgcttg accgcatggg cgaattttcc      120
aacgaatccc gcgcttgggt 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

```

&lt;210&gt; 124

&lt;211&gt; 180

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Synthetic polypeptide

&lt;400&gt; 124

```

Asn Asn Glu Leu Pro Trp Val Ala Glu Ala Arg Lys Tyr Ile Gly Leu
1           5           10           15

```

```

Arg Glu Asp Thr Ser Lys Thr Ser His Asn Pro Lys Leu Leu Ala Met
          20           25           30

```

```

Leu Asp Arg Met Gly Glu Phe Ser Asn Glu Ser Arg Ala Trp Trp His
          35           40           45

```

Asp Asp Glu Thr Pro Trp Cys Gly Leu Phe Val Gly Tyr Cys Leu Gly  
50 55 60

Val Ala Gly Arg Tyr Val Val Arg Glu Trp Tyr Arg Ala Arg Ala Trp  
65 70 75 80

Glu Ala Pro Gln Leu Thr Lys Leu Asp Arg Pro Ala Tyr Gly Ala Leu  
85 90 95

Val Thr Phe Thr Arg Ser Gly Gly Gly His Val Gly Phe Ile Val Gly  
100 105 110

Lys Asp Ala Arg Gly Asn Leu Met Val Leu Gly Gly Asn Gln Ser Asn  
115 120 125

Ala Val Ser Ile Ala Pro Phe Ala Val Ser Arg Val Thr Gly Tyr Phe  
130 135 140

Trp Pro Ser Phe Trp Arg Asn Lys Thr Ala Val Lys Ser Val Pro Phe  
145 150 155 160

Glu Glu Arg Tyr Ser Leu Pro Leu Leu Lys Ser Asn Gly Glu Leu Ser  
165 170 175

Thr Asn Glu Ala  
180

<210> 125  
<211> 471  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
<221> misc\_feature  
<222> (1)..(471)  
<223> GN156

```

<400> 125
gggccgcgtc gtccgcgtcg tccgggtcgt cgtgctccgg ttcgtacctc tcagcgtggt      60
atcgacctga tcaaattctt cgaaggctct cgtctgtctg cttaccagga ctctgttggt      120
gtttggacca tcggttacgg taccacccgt ggtgttacct gttacatgac catcacctt      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

```

```

<210> 126
<211> 157
<212> PRT
<213> Artificial Sequence

```

```

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

```

```

<400> 126

Gly Pro Arg Arg Pro Arg Arg Pro Gly Arg Arg Ala Pro Val Arg Thr
1              5              10              15

Ser Gln Arg Gly Ile Asp Leu Ile Lys Ser Phe Glu Gly Leu Arg Leu
      20              25              30

Ser Ala Tyr Gln Asp Ser Val Gly Val Trp Thr Ile Gly Tyr Gly Thr
      35              40              45

Thr Arg Gly Val Thr Arg Tyr Met Thr Ile Thr Val Glu Gln Ala Glu
      50              55              60

Arg Met Leu Ser Asn Asp Ile Gln Arg Phe Glu Pro Glu Leu Asp Arg
65              70              75              80

Leu Ala Lys Val Pro Leu Asn Gln Asn Gln Trp Asp Ala Leu Met Ser
      85              90              95

```

0341\_0021-00-304\_ST25 (1).txt

Phe Val Tyr Asn Leu Gly Ala Ala Asn Leu Ala Ser Ser Thr Leu Leu  
100 105 110

Lys Leu Leu Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro  
115 120 125

Arg Trp Val Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg  
130 135 140

Arg Ala Ala Glu Arg Ala Leu Phe Leu Glu Pro Leu Ser  
145 150 155

<210> 127  
<211> 39  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polypeptide

<220>  
<221> MISC\_FEATURE  
<222> (1)..(39)  
<223> PGN4

<400> 127

Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro Arg Trp Val  
1 5 10 15

Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Arg Ala Ser  
20 25 30

Gln Ser Arg Glu Ser Gln Cys  
35

<210> 128  
<211> 42  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polypeptide

<220>

<221> MISC\_FEATURE

<222> (1)..(42)

<223> FGN4-1

<400> 128

Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro Arg Trp Val  
1 5 10 15

Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Arg Ala Ala  
20 25 30

Glu Arg Ala Leu Phe Leu Glu Pro Leu Ser  
35 40

<210> 129

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<220>

<221> MISC\_FEATURE

<222> (1)..(31)

<223> FGN4-2

<400> 129

Asn Lys Gly Asp Tyr Gln Gly Ala Ala Asp Gln Phe Pro Arg Trp Val  
1 5 10 15

Asn Ala Gly Gly Lys Arg Leu Asp Gly Leu Val Lys Arg Arg Ala  
20 25 30

<210> 130

<211> 54

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic oligonucleotide

<220>

<221> misc\_feature

<222> (1)..(54)

<223> RI18

<400> 130

cgtaaaaaaa cccgtaaacg tctgaaaaaa atcggtaaag ttctgaaatg gatc

54

<210> 131

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 131

Arg Lys Lys Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys  
1 5 10 15

Trp Ile

<210> 132

<211> 111

<212> DNA

<213> Chlamydia virus Chp1

<400> 132

atggttcgta gaagacgttt gagaagaaga ataagtagaa gaatttttag aagaacagta

60

gctagagttg gtagaaggcg aaggtctttt cgtggtggta ttagatttta a

111

<210> 133

<211> 36

<212> PRT

<213> Chlamydia virus Chp1

<400> 133

Met Val Arg Arg Arg Arg Leu Arg Arg Arg Ile Ser Arg Arg Ile Phe  
1 5 10 15

Arg Arg Thr Val Ala Arg Val Gly Arg Arg Arg Arg Ser Phe Arg Gly  
20 25 30

Gly Ile Arg Phe  
35

<210> 134  
<211> 108  
<212> DNA  
<213> Chlamydia virus CPAR39

<400> 134  
ttgtgcaaaa aagtgtgcaa aaaatgccca aaaaaagggc caaaaaatgc ccccaaatc 60  
ggagcatttt acgagagaaa aacacctaga cttaaacagt ctacttga 108

<210> 135  
<211> 35  
<212> PRT  
<213> Chlamydia virus CPAR39

<400> 135  
Met Cys Lys Lys Val Cys Lys Lys Cys Pro Lys Lys Gly Pro Lys Asn  
1 5 10 15

Ala Pro Lys Ile Gly Ala Phe Tyr Glu Arg Lys Thr Pro Arg Leu Lys  
20 25 30

Gln Ser Thr  
35

<210> 136  
<211> 135  
<212> DNA  
<213> Chlamydia phage 3

<400> 136  
atgaggttaa aaatggcacg aagaagatac agacttccgc gacgtagaag tcgaagactt 60  
ttttcaagaa ctgcattaag gatgcatcca agaaataggc ttcgaagaat tatgcgtggc 120  
ggcattaggt tctag 135

<210> 137  
<211> 44  
<212> PRT

<213> Chlamydia phage 3

<400> 137

Met Arg Leu Lys Met Ala Arg Arg Arg Tyr Arg Leu Pro Arg Arg Arg  
1 5 10 15

Ser Arg Arg Leu Phe Ser Arg Thr Ala Leu Arg Met His Pro Arg Asn  
20 25 30

Arg Leu Arg Arg Ile Met Arg Gly Gly Ile Arg Phe  
35 40

<210> 138

<211> 117

<212> DNA

<213> Chlamydia trachomatis

<400> 138

atgaaacgta gaaaaatgac aagaaaaggt tctaagcgtc tttttactgc aactgctgat 60

aaaactaaat ctatcaatac tgccccgccg ccaatgcgtg gcggtatccg gttgtaa 117

<210> 139

<211> 38

<212> PRT

<213> Chlamydia trachomatis

<400> 139

Met Lys Arg Arg Lys Met Thr Arg Lys Gly Ser Lys Arg Leu Phe Thr  
1 5 10 15

Ala Thr Ala Asp Lys Thr Lys Ser Ile Asn Thr Ala Pro Pro Pro Met  
20 25 30

Arg Gly Gly Ile Arg Leu  
35

<210> 140

<211> 120

<212> DNA

<213> Chlamydia trachomatis

<400> 140

atgtctaaaa agcgttctcg catgtctcgc cgccgttcta agaagttggt ctgaaaacg 60

gctctccgca cgaagagtgt caacacccgt ccgcctatgc gcggagggtt ccggttctga 120

<210> 141

<211> 39

<212> PRT

<213> Chlamydia trachomatis

<400> 141

Met Ser Lys Lys Arg Ser Arg Met Ser Arg Arg Arg Ser Lys Lys Leu  
1 5 10 15

Phe Ser Lys Thr Ala Leu Arg Thr Lys Ser Val Asn Thr Arg Pro Pro  
20 25 30

Met Arg Gly Gly Phe Arg Phe  
35

<210> 142

<211> 123

<212> DNA

<213> Chlamydia trachomatis

<400> 142

atgtctcttc gtcgtcataa gctttctcgt aaggcgtcta agcgtatattt tcgtaaaggt 60

gcatcacgca cgaagacttt gaatactcgt gctacgccta tgcgcggcgg tttccgtatt 120

taa 123

<210> 143

<211> 40

<212> PRT

<213> Chlamydia trachomatis

<400> 143

Met Ser Leu Arg Arg His Lys Leu Ser Arg Lys Ala Ser Lys Arg Ile  
1 5 10 15

Phe Arg Lys Gly Ala Ser Arg Thr Lys Thr Leu Asn Thr Arg Ala Thr  
20 25 30

Pro Met Arg Gly Gly Phe Arg Ile  
           35                  40

<210> 144  
 <211> 117  
 <212> DNA  
 <213> Chlamydia trachomatis

<400> 144  
 gtgaaacgtc gtaaactgtc caaaaagaaa tctcgcaaga ttttcactcg cggtgctgta 60  
 aatgtgaaaa agcgtaacct tcgcgctcgc ccaatgcgcg gcggtttccg gatctaa 117

<210> 145  
 <211> 38  
 <212> PRT  
 <213> Chlamydia trachomatis

<400> 145

Met Lys Arg Arg Lys Leu Ser Lys Lys Lys Ser Arg Lys Ile Phe Thr  
 1                  5                  10                  15

Arg Gly Ala Val Asn Val Lys Lys Arg Asn Leu Arg Ala Arg Pro Met  
           20                  25                  30

Arg Gly Gly Phe Arg Ile  
           35

<210> 146  
 <211> 114  
 <212> DNA  
 <213> Chlamydia trachomatis

<400> 146  
 atggctaaaa aaatgactaa aggcaaggat cgtcagggtt ttcgtaaaac cgctgacgt 60  
 actaagaaac tcaatgtag accgttgtag tatcgaggag gtatcagatt atga 114

<210> 147  
 <211> 37  
 <212> PRT  
 <213> Chlamydia trachomatis

<400> 147

0341\_0021-00-304\_ST25 (1).txt

Met Ala Lys Lys Met Thr Lys Gly Lys Asp Arg Gln Val Phe Arg Lys  
1 5 10 15

Thr Ala Asp Arg Thr Lys Lys Leu Asn Val Arg Pro Leu Leu Tyr Arg  
20 25 30

Gly Gly Ile Arg Leu  
35

<210> 148  
<211> 120  
<212> DNA  
<213> Chlamydia trachomatis

<400> 148  
atggcaggaa aaaaaatggt atcaaaagga aaagatagac agattttccg aaaaactgct 60  
gatcgacta aaaaaatgaa tgtgcgcccc ctattatattc gtggagggtat tagattatga 120

<210> 149  
<211> 39  
<212> PRT  
<213> Chlamydia trachomatis

<400> 149

Met Ala Gly Lys Lys Met Val Ser Lys Gly Lys Asp Arg Gln Ile Phe  
1 5 10 15

Arg Lys Thr Ala Asp Arg Thr Lys Lys Met Asn Val Arg Pro Leu Leu  
20 25 30

Tyr Arg Gly Gly Ile Arg Leu  
35

<210> 150  
<211> 126  
<212> DNA  
<213> Marine gokushovirus

<400> 150  
atgagaagac caagaaaaat gaactataaa aaatcaaaaa gaatgttttc acgcacagca 60  
gcgagaacac acagaaaaaa ctctctaaga ggtagccgac ctatgagagg cggaatacgt 120

ctttaa

<210> 151  
 <211> 41  
 <212> PRT  
 <213> Marine gokushovirus

<400> 151

Met Arg Arg Pro Arg Lys Met Asn Tyr Lys Lys Ser Lys Arg Met Phe  
 1 5 10 15

Ser Arg Thr Ala Ala Arg Thr His Arg Lys Asn Ser Leu Arg Gly Ser  
 20 25 30

Arg Pro Met Arg Gly Gly Ile Arg Leu  
 35 40

<210> 152  
 <211> 108  
 <212> DNA  
 <213> Unknown

<220>

<223> Description of Unknown: Bacteria; environmental sample sequence

<400> 152  
 atgaaaatgc gtaagcggac ggacaagcga gtgtttaccc gcaccgctgc taagtccaag 60  
 aaagtgaaca ttgccccgaa aatttttaga ggaggtatcc gtctgtga 108

<210> 153  
 <211> 35  
 <212> PRT  
 <213> Unknown

<220>

<223> Description of Unknown: Bacteria; environmental sample sequence

<400> 153

Met Lys Met Arg Lys Arg Thr Asp Lys Arg Val Phe Thr Arg Thr Ala  
 1 5 10 15

Ala Lys Ser Lys Lys Val Asn Ile Ala Pro Lys Ile Phe Arg Gly Gly  
 20 25 30

Ile Arg Leu  
35

<210> 154  
<211> 120  
<212> DNA  
<213> Escherichia sp.

<400> 154  
atggctcgtt ctcgccgtcg tatgtccaag cgttcttccc gtcgttcggt ccgtaagtac 60  
gcaaagacgc ataaacgtaa ctttaaagcc cgctctatgc gtgggtggaat tcgtctttga 120

<210> 155  
<211> 39  
<212> PRT  
<213> Escherichia sp.

<400> 155  
Met Ala Arg Ser Arg Arg Arg Met Ser Lys Arg Ser Ser Arg Arg Ser  
1 5 10 15

Phe Arg Lys Tyr Ala Lys Thr His Lys Arg Asn Phe Lys Ala Arg Ser  
20 25 30

Met Arg Gly Gly Ile Arg Leu  
35

<210> 156  
<211> 144  
<212> DNA  
<213> Cognatishimia maritima

<400> 156  
atggaaagcc cgaacagccg cagccagctg ggcattaccc tgtatctgct gagcaccatt 60  
tttccggatg cgtgctttcg ctatcgccgc gaactgccgt atccgctggt gatttggggc 120  
gtggcgaccc tgtgcctgca gtaa 144

<210> 157  
<211> 47  
<212> PRT

<213> Cognatishimia maritima

<400> 157

Met Glu Ser Pro Asn Ser Arg Ser Gln Leu Gly Ile Thr Leu Tyr Leu  
1 5 10 15

Leu Ser Thr Ile Phe Pro Asp Ala Cys Phe Arg Tyr Arg Arg Glu Leu  
20 25 30

Pro Tyr Pro Leu Val Ile Trp Gly Val Ala Thr Leu Cys Leu Gln  
35 40 45

<210> 158

<211> 114

<212> DNA

<213> Unknown

<220>

<223> Description of Unknown: Bacteria; environmental sample sequence

<400> 158

atgagacgtc gtcgtctatc ccgcagaact tcccgccgtt ttttccgtaa aggacttaag 60

gttcgccgtc gtaacctccg cgcgagaccc atgagaggcg gattcagaat ttga 114

<210> 159

<211> 37

<212> PRT

<213> Unknown

<220>

<223> Description of Unknown: Bacteria; environmental sample sequence

<400> 159

Met Arg Arg Arg Arg Leu Ser Arg Arg Thr Ser Arg Arg Phe Phe Arg  
1 5 10 15

Lys Gly Leu Lys Val Arg Arg Arg Asn Leu Arg Ala Arg Pro Met Arg  
20 25 30

Gly Gly Phe Arg Ile  
35

<210> 160  
<211> 120  
<212> DNA  
<213> Unknown

<220>

<223> Description of Unknown: Bacteria; environmental sample sequence

<400> 160  
atggcacgac gcaagaagat gaaaggcaag cgggataaac ggggtgtttaa gcagacagcc 60  
aacaaaacca aggctatcaa catcagccca aaaaacatga gaggggggtac gagactgtga 120

<210> 161  
<211> 39  
<212> PRT  
<213> Unknown

<220>

<223> Description of Unknown: Bacteria; environmental sample sequence

<400> 161

Met Ala Arg Arg Lys Lys Met Lys Gly Lys Arg Asp Lys Arg Val Phe  
1 5 10 15

Lys Gln Thr Ala Asn Lys Thr Lys Ala Ile Asn Ile Ser Pro Lys Asn  
20 25 30

Met Arg Gly Gly Thr Arg Leu  
35

<210> 162  
<211> 162  
<212> DNA  
<213> Marine gokushovirus

<400> 162  
atgttaactg tgtggagtga caccctacc ataaaaagga gaaaagacat gtatagaaag 60  
agaatgtcaa gaaagaaaag taaaaagggtt ttgcaaaaaa ccgcaatgaa agtaaataaa 120  
agaaaccacg ttaaacctat gcgtggtgga tatagaatat aa 162

<210> 163  
<211> 53  
<212> PRT

<213> Marine gokushovirus

<400> 163

Met Leu Thr Val Trp Ser Asp Thr Pro Thr Ile Lys Arg Arg Lys Asp  
1 5 10 15

Met Tyr Arg Lys Arg Met Ser Arg Lys Lys Ser Lys Lys Val Phe Ala  
20 25 30

Lys Thr Ala Met Lys Val Asn Lys Arg Asn His Val Lys Pro Met Arg  
35 40 45

Gly Gly Tyr Arg Ile  
50

<210> 164

<211> 120

<212> DNA

<213> Marine gokushovirus

<400> 164

atgatgaagt acagaaaaa aatgagcgct aaaagtagcc gaaagcaatt tacaaaaggc 60

gccatgaaag tgaagggtaa aaacttcaca aaaccaatgc gcggaggcat ccgtctatag 120

<210> 165

<211> 39

<212> PRT

<213> Marine gokushovirus

<400> 165

Met Met Lys Tyr Arg Lys Lys Met Ser Ala Lys Ser Ser Arg Lys Gln  
1 5 10 15

Phe Thr Lys Gly Ala Met Lys Val Lys Gly Lys Asn Phe Thr Lys Pro  
20 25 30

Met Arg Gly Gly Ile Arg Leu  
35

<210> 166

<211> 117

&lt;212&gt; DNA

&lt;213&gt; Marine gokushovirus

&lt;400&gt; 166

atgcgacgtt acaatgtaaa taaaggtaaa tctgctaaga agtttcgaaa gcaggtaagt 60

aagacgaagg ttgcaaacct acgttctaata ccaatgcgag gtgggttgag actctaa 117

&lt;210&gt; 167

&lt;211&gt; 38

&lt;212&gt; PRT

&lt;213&gt; Marine gokushovirus

&lt;400&gt; 167

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Arg | Arg | Tyr | Asn | Val | Asn | Lys | Gly | Lys | Ser | Ala | Lys | Lys | Phe | Arg |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Gln | Val | Ser | Lys | Thr | Lys | Val | Ala | Asn | Leu | Arg | Ser | Asn | Pro | Met |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|
| Arg | Gly | Gly | Trp | Arg | Leu |
|     |     |     | 35  |     |     |

&lt;210&gt; 168

&lt;211&gt; 87

&lt;212&gt; DNA

&lt;213&gt; Spiroplasma virus SpV4

&lt;400&gt; 168

atggcctatc gtggttttaa aacgagtcgt gttgtaaaac atagagtacg tagaagatgg 60

tttaatcata gaagacgtta tagatag 87

&lt;210&gt; 169

&lt;211&gt; 28

&lt;212&gt; PRT

&lt;213&gt; Spiroplasma virus SpV4

&lt;400&gt; 169

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Tyr | Arg | Gly | Phe | Lys | Thr | Ser | Arg | Val | Val | Lys | His | Arg | Val |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Arg | Arg | Trp | Phe | Asn | His | Arg | Arg | Arg | Tyr | Arg |
|     |     |     | 20  |     |     |     | 25  |     |     |     |     |

<210> 170  
 <211> 117  
 <212> DNA  
 <213> Spiroplasma virus SpV4

<400> 170  
 gtgagacgca aggttaagaa cacaaagcgt catcagtgga ggttgactca ttctgcacgt 60  
 tcaattaaac gtgctaatat aatgccgtca aatcctcgtg gtggacgtcg ttttttag 117

<210> 171  
 <211> 38  
 <212> PRT  
 <213> Spiroplasma virus SpV4

<400> 171  
 Met Arg Arg Lys Val Lys Asn Thr Lys Arg His Gln Trp Arg Leu Thr  
 1 5 10 15

His Ser Ala Arg Ser Ile Lys Arg Ala Asn Ile Met Pro Ser Asn Pro  
 20 25 30

Arg Gly Gly Arg Arg Phe  
 35

<210> 172  
 <211> 798  
 <212> DNA  
 <213> Pseudomonas phage PhiPA3

<400> 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 acaaattccc agcaatggca atgccaacgt tgactgaaat aggtcgactg 300  
 acaaacgttg atcctaaatt gctagcgaca ttctgttcta tcgaaagcgc gtttgattac 360  
 acagctaaac cctacaagcc cgatggcaca gtgtacagct ccgccgaagg ttggttccag 420

0341\_0021-00-304\_ST25 (1).txt

|                                                                    |     |
|--------------------------------------------------------------------|-----|
| ttcctggatg caacatggga tgacgaagtg cgtaaacacg gtaagcaata tagcttcct   | 480 |
| gttgatcctg gtcgttcttt gcgtaaagat ccacgggcta atggcttgat gggcgctgag  | 540 |
| ttcctcaaag ggaatgctgc tattctgcgg ccagtactgg gtcatgaacc gagcgacaca  | 600 |
| gatctttatc tagcccatctt catgggagca ggtggcgcaa aacagttcct tatggccgat | 660 |
| caaaataaat tggctgccga attgttcctt ggtccagcta aggctaatacc taacatcttc | 720 |
| tataaatccg gaaatattgc ccgcacttta gcagaggctt atgcagtcct cgatgctaag  | 780 |
| gtagccaagc atagagct                                                | 798 |

<210> 173  
 <211> 266  
 <212> PRT  
 <213> Pseudomonas phage PhiPA3

<400> 173

|                                                                 |  |
|-----------------------------------------------------------------|--|
| Met Thr Leu Leu Lys Lys Gly Asp Lys Gly Asp Ala Val Lys Gln Leu |  |
| 1 5 10 15                                                       |  |

|                                                                 |  |
|-----------------------------------------------------------------|--|
| Gln Gln Lys Leu Lys Asp Leu Gly Tyr Thr Leu Gly Val Asp Gly Asn |  |
| 20 25 30                                                        |  |

|                                                                 |  |
|-----------------------------------------------------------------|--|
| Phe Gly Asn Gly Thr Asp Thr Val Val Arg Ser Phe Gln Thr Lys Met |  |
| 35 40 45                                                        |  |

|                                                                 |  |
|-----------------------------------------------------------------|--|
| Lys Leu Ser Val Asp Gly Val Val Gly Asn Gly Thr Met Ser Thr Ile |  |
| 50 55 60                                                        |  |

|                                                                 |  |
|-----------------------------------------------------------------|--|
| Asp Ser Thr Leu Ala Gly Ile Lys Ala Trp Lys Thr Ser Val Pro Phe |  |
| 65 70 75 80                                                     |  |

|                                                                 |  |
|-----------------------------------------------------------------|--|
| Pro Ala Thr Asn Lys Ser Arg Ala Met Ala Met Pro Thr Leu Thr Glu |  |
| 85 90 95                                                        |  |

|                                                                 |  |
|-----------------------------------------------------------------|--|
| Ile Gly Arg Leu Thr Asn Val Asp Pro Lys Leu Leu Ala Thr Phe Cys |  |
| 100 105 110                                                     |  |

|                                                                 |  |
|-----------------------------------------------------------------|--|
| Ser Ile Glu Ser Ala Phe Asp Tyr Thr Ala Lys Pro Tyr Lys Pro Asp |  |
| 115 120 125                                                     |  |

Gly Thr Val Tyr Ser Ser Ala Glu Gly Trp Phe Gln Phe Leu Asp Ala  
130 135 140

Thr Trp Asp Asp Glu Val Arg Lys His Gly Lys Gln Tyr Ser Phe Pro  
145 150 155 160

Val Asp Pro Gly Arg Ser Leu Arg Lys Asp Pro Arg Ala Asn Gly Leu  
165 170 175

Met Gly Ala Glu Phe Leu Lys Gly Asn Ala Ala Ile Leu Arg Pro Val  
180 185 190

Leu Gly His Glu Pro Ser Asp Thr Asp Leu Tyr Leu Ala His Phe Met  
195 200 205

Gly Ala Gly Gly Ala Lys Gln Phe Leu Met Ala Asp Gln Asn Lys Leu  
210 215 220

Ala Ala Glu Leu Phe Pro Gly Pro Ala Lys Ala Asn Pro Asn Ile Phe  
225 230 235 240

Tyr Lys Ser Gly Asn Ile Ala Arg Thr Leu Ala Glu Val Tyr Ala Val  
245 250 255

Leu Asp Ala Lys Val Ala Lys His Arg Ala  
260 265

<210> 174  
<211> 435  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>  
<221> misc\_feature  
<222> (1)..(435)  
<223> GN37 and RI18

<400> 174  
 atgacataca ccctgagcaa aagaagcctg gataacctaa aaggcgttca tcccgatctg 60  
 gttgccgttg tccatcgcg ccatccagctt 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

<210> 175  
 <211> 144  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 175  
 Met Thr Tyr Thr Leu Ser Lys Arg Ser Leu Asp Asn Leu Lys Gly Val  
 1 5 10 15  
 His Pro Asp Leu Val Ala Val Val His Arg Ala Ile Gln Leu Thr Pro  
 20 25 30  
 Val Asp Phe Ala Val Ile Glu Gly Leu Arg Ser Val Ser Arg Gln Lys  
 35 40 45  
 Glu Leu Val Ala Ala Gly Ala Ser Lys Thr Met Asn Ser Arg His Leu  
 50 55 60  
 Thr Gly His Ala Val Asp Leu Ala Ala Tyr Val Asn Gly Ile Arg Trp  
 65 70 75 80  
 Asp Trp Pro Leu Tyr Asp Ala Ile Ala Val Ala Val Lys Ala Ala Ala  
 85 90 95

0341\_0021-00-304\_ST25 (1).txt

Lys Glu Leu Gly Val Ala Ile Val Trp Gly Gly Asp Trp Thr Thr Phe  
100 105 110

Lys Asp Gly Pro His Phe Glu Leu Asp Arg Ser Lys Tyr Arg Arg Lys  
115 120 125

Lys Thr Arg Lys Arg Leu Lys Lys Ile Gly Lys Val Leu Lys Trp Ile  
130 135 140

<210> 176  
<211> 120  
<212> DNA  
<213> Escherichia sp.

<400> 176  
atggctcggtt ctcgtcgtcg tatgtctaaa cgttcttctc gtcgttcttt tcgtaaatat 60  
gctaaaactc ataaaaaaaa ttttaaagct cgttctatgc gtggaggaat tcgtttataa 120

<210> 177  
<211> 39  
<212> PRT  
<213> Escherichia sp.

<400> 177  
Met Ala Arg Ser Arg Arg Arg Met Ser Lys Arg Ser Ser Arg Arg Ser  
1 5 10 15

Phe Arg Lys Tyr Ala Lys Thr His Lys Lys Asn Phe Lys Ala Arg Ser  
20 25 30

Met Arg Gly Gly Ile Arg Leu  
35

<210> 178  
<211> 117  
<212> DNA  
<213> Escherichia coli

<400> 178  
atggcgcgca gccgccgccg catgagcaaa cgcagcagcc gccgcagctt tcgcaaatat 60  
gcgaaaagcc ataaaaaaaa ctttaaagcg cgcagcatgc gcggcggcat tcgcctg 117

<210> 179  
 <211> 39  
 <212> PRT  
 <213> Escherichia coli

<400> 179

Met Ala Arg Ser Arg Arg Arg Met Ser Lys Arg Ser Ser Arg Arg Ser  
 1 5 10 15

Phe Arg Lys Tyr Ala Lys Ser His Lys Lys Asn Phe Lys Ala Arg Ser  
 20 25 30

Met Arg Gly Gly Ile Arg Leu  
 35

<210> 180  
 <211> 117  
 <212> DNA  
 <213> Alces alces faeces associated microvirus MP12 5423

<400> 180  
 atggcaaaga aaattagaaa caaagcacgt gatagacgta tcttcacaag aacagcttca 60  
 cgcatgcaca aggcaaaccg cacaccaaga tttatgagag gcggtattag gttatga 117

<210> 181  
 <211> 38  
 <212> PRT  
 <213> Alces alces faeces associated microvirus MP12 5423

<400> 181

Met Ala Lys Lys Ile Arg Asn Lys Ala Arg Asp Arg Arg Ile Phe Thr  
 1 5 10 15

Arg Thr Ala Ser Arg Met His Lys Ala Asn Arg Thr Pro Arg Phe Met  
 20 25 30

Arg Gly Gly Ile Arg Leu  
 35

<210> 182  
 <211> 117

<212> DNA  
<213> Unknown

<220>

<223> Description of Unknown: Gokushovirinae environmental sample sequence

<400> 182  
atgctgcgta aaaaaatgtc acgcggtaaa tcaaaaaaac tctttcgccg aacagcaaaa 60  
cgcggttcac gaaaaaacct acgagctcgc ccaatgcgtg gcggcatacg catgtag 117

<210> 183  
<211> 38  
<212> PRT  
<213> Unknown

<220>

<223> Description of Unknown: Gokushovirinae environmental sample sequence

<400> 183

Met Arg Arg Lys Lys Met Ser Arg Gly Lys Ser Lys Lys Leu Phe Arg  
1 5 10 15

Arg Thr Ala Lys Arg Val His Arg Lys Asn Leu Arg Ala Arg Pro Met  
20 25 30

Arg Gly Gly Ile Arg Met  
35

<210> 184  
<211> 120  
<212> DNA  
<213> Unknown

<220>

<223> Description of Unknown: Gokushovirinae environmental sample sequence

<400> 184  
atggcgaagc gacacaaaat cccgcaacgc gcgtcacaac attccttcac gcgccatgcg 60  
caaaaggtcc accctaagaa cggtcccccgc ctgccaatgc gaggcgggtat ccgtctctaa 120

<210> 185

<211> 39  
<212> PRT  
<213> Unknown

<220>

<223> Description of Unknown: Gokushovirinae environmental sample sequence

<400> 185

Met Ala Lys Arg His Lys Ile Pro Gln Arg Ala Ser Gln His Ser Phe  
1 5 10 15

Thr Arg His Ala Gln Lys Val His Pro Lys Asn Val Pro Arg Leu Pro  
20 25 30

Met Arg Gly Gly Ile Arg Leu  
35

<210> 186  
<211> 114  
<212> DNA  
<213> Unknown

<220>

<223> Description of Unknown: uncultured bacterium sequence

<400> 186

atgcgtaaaa aaatgcacaa atcattagac aagcgagtgt ttaaccgcac tgcaaaaaaa 60

tcaaaaaaaa taaatgttaa tcctgtagtt tatcgtggag gtattagatt atga 114

<210> 187  
<211> 37  
<212> PRT  
<213> Unknown

<220>

<223> Description of Unknown: uncultured bacterium sequence

<400> 187

Met Arg Lys Lys Met His Lys Ser Leu Asp Lys Arg Val Phe Asn Arg  
1 5 10 15

Thr Ala Lys Lys Ser Lys Lys Ile Asn Val Asn Pro Val Val Tyr Arg  
20 25 30

Gly Gly Ile Arg Leu  
35

<210> 188  
<211> 117  
<212> DNA  
<213> Marine gokushovirus

<400> 188  
atgcgacgtt acaatgtaaa taaaggtaaa tctgctaaga agtttcgaaa gcaggtaagt 60  
aagacgaagg ttgcaaacct acgttctaata ccaatgcgag gtgggttgag actctaa 117

<210> 189  
<211> 38  
<212> PRT  
<213> Marine gokushovirus

<400> 189  
Met Arg Arg Tyr Asn Val Asn Lys Gly Lys Ser Ala Lys Lys Phe Arg  
1 5 10 15

Lys Gln Val Ser Lys Thr Lys Val Ala Asn Leu Arg Ser Asn Pro Met  
20 25 30

Arg Gly Gly Trp Arg Leu  
35

<210> 190  
<211> 126  
<212> DNA  
<213> Richelia intracellularis HH01

<400> 190  
atgcgtccag ttaaaagatc aagagtaaata aaggcccgat ctgcaggcaa gtttcgtaag 60  
caggtcggta aaacaaagat ggcaaatactg cgtagtaatc cgatgcgcgg cggatggcgg 120  
ctgtga 126

<210> 191  
<211> 41  
<212> PRT

<213> Richelia intracellularis HH01

<400> 191

Met Arg Pro Val Lys Arg Ser Arg Val Asn Lys Ala Arg Ser Ala Gly  
1 5 10 15

Lys Phe Arg Lys Gln Val Gly Lys Thr Lys Met Ala Asn Leu Arg Ser  
20 25 30

Asn Pro Met Arg Gly Gly Trp Arg Leu  
35 40

<210> 192

<211> 126

<212> DNA

<213> Gokushovirinae Fen7875\_21

<400> 192

atgaagccat tgaagcgtaa gccggttcag aaggcgcggt cagcagccaa gttccgtcga 60

aatgtgtcta ccgttaaggc tgccaatatg gcggtgaagc cgatgcgcgg cggttggcgg 120

ttctga 126

<210> 193

<211> 41

<212> PRT

<213> Gokushovirinae Fen7875\_21

<400> 193

Met Lys Pro Leu Lys Arg Lys Pro Val Gln Lys Ala Arg Ser Ala Ala  
1 5 10 15

Lys Phe Arg Arg Asn Val Ser Thr Val Lys Ala Ala Asn Met Ala Val  
20 25 30

Lys Pro Met Arg Gly Gly Trp Arg Phe  
35 40

<210> 194

<211> 135

<212> DNA

<213> Mycobacterium phage BabyRay

<400> 194  
atgaccaaga gagacatcga gtaccggaaa gctttggggc tcaacccatc tgagccgctc 60  
ccgaagattg tgggtgccgt caccgccac ggggccactc tgaaacgccc acgggtcacc 120  
gcactggccc gatag 135

<210> 195  
<211> 44  
<212> PRT  
<213> Mycobacterium phage BabyRay

<400> 195  
Met Thr Lys Arg Asp Ile Glu Tyr Arg Lys Ala Leu Gly Leu Asn Pro  
1 5 10 15  
Ser Glu Pro Leu Pro Lys Ile Val Gly Ala Val Thr Arg His Gly Ala  
20 25 30  
Thr Leu Lys Arg Pro Arg Val Thr Ala Leu Ala Arg  
35 40

<210> 196  
<211> 117  
<212> DNA  
<213> Bdellovibrio phage phiMH2K

<400> 196  
atgaaaagaa aaccaatgag ccgcaaggcc tctcaaaaaa ccttcaaaaa gaacacaggc 60  
gttcaacgca tgaaccatct caaccacgc gccatgcgtg gtggcattag actataa 117

<210> 197  
<211> 38  
<212> PRT  
<213> Bdellovibrio phage phiMH2K

<400> 197  
Met Lys Arg Lys Pro Met Ser Arg Lys Ala Ser Gln Lys Thr Phe Lys  
1 5 10 15  
Lys Asn Thr Gly Val Gln Arg Met Asn His Leu Asn Pro Arg Ala Met  
20 25 30

Arg Gly Gly Ile Arg Leu  
35

<210> 198  
<211> 168  
<212> DNA  
<213> Pseudomonas phage PP7

<400> 198  
ttgtcgtcaa ctttgtgccg ctgggccgtt aaggccctgc ggtgtacccg tgtgtataag 60  
gagtttatat ggaaaccctt agtagcgctc agttacgtga cgttgtatct tctgagctcg 120  
gtcttcctgt cccaactcag ctaccccatc gggagctggg cgggtgtag 168

<210> 199  
<211> 55  
<212> PRT  
<213> Pseudomonas phage PP7

<400> 199  
Met Ser Ser Thr Leu Cys Arg Trp Ala Val Lys Ala Leu Arg Cys Thr  
1 5 10 15

Arg Val Tyr Lys Glu Phe Ile Trp Lys Pro Leu Val Ala Leu Ser Tyr  
20 25 30

Val Thr Leu Tyr Leu Leu Ser Ser Val Phe Leu Ser Gln Leu Ser Tyr  
35 40 45

Pro Ile Gly Ser Trp Ala Val  
50 55

<210> 200  
<211> 108  
<212> DNA  
<213> Acinetobacter phage AP205

<400> 200  
atgaagaaaa ggacaaaagc cttgcttccc tatgcggttt tcatcatact cagctttcaa 60  
ctaacattgt tgactgcctt gtttatgtat taccattata ccttttag 108

<210> 201  
 <211> 35  
 <212> PRT  
 <213> Acinetobacter phage AP205

<400> 201

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Lys | Lys | Arg | Thr | Lys | Ala | Leu | Leu | Pro | Tyr | Ala | Val | Phe | Ile | Ile |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Ser | Phe | Gln | Leu | Thr | Leu | Leu | Thr | Ala | Leu | Phe | Met | Tyr | Tyr | His |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |
|-----|-----|-----|
| Tyr | Thr | Phe |
|     |     | 35  |

<210> 202  
 <211> 558  
 <212> DNA  
 <213> Acinetobacter phage vB\_AbaP\_CEB1

<400> 202

|                                                                    |     |
|--------------------------------------------------------------------|-----|
| atgattctga ctaaagatgg gtttggtatt atccgtaatg aactattcgg aggtaagtta  | 60  |
| gatcaaactc aagtagatgc aataaacttt attgtagaga aagctactga gtctggttta  | 120 |
| tcttatccag aggcagccta tttagtagct accatctatc atgagactgg tctaccaagc  | 180 |
| ggttatcgaa ctatgcaacc tattaaagaa gctgggttctg ataactacct tcgatctaag | 240 |
| aagtactacc cgtacattgg ttatgggttat gtacagttaa cttggaagga gaactatgga | 300 |
| cggattggta aacttattgg aattgaccta attaagaatc ctgagaaagc gctagaacct  | 360 |
| ttaattgcta ttcagattgc tatcaaaggc atgttgaatg gttgggtcac aggtggttga  | 420 |
| ttccgacgta aacgtccagt tagtaaatac aacaaacagc agtacatagc tgcgcgtaat  | 480 |
| atcattaatg ggaaagataa ggctgagctt atagcgaagt acgctattat ctttgaacgc  | 540 |
| gctctacgga gcttataa                                                | 558 |

<210> 203  
 <211> 185  
 <212> PRT  
 <213> Acinetobacter phage vB\_AbaP\_CEB1

&lt;400&gt; 203

Met Ile Leu Thr Lys Asp Gly Phe Gly Ile Ile Arg Asn Glu Leu Phe  
 1 5 10 15

Gly Gly Lys Leu Asp Gln Thr Gln Val Asp Ala Ile Asn Phe Ile Val  
 20 25 30

Glu Lys Ala Thr Glu Ser Gly Leu Ser Tyr Pro Glu Ala Ala Tyr Leu  
 35 40 45

Leu Ala Thr Ile Tyr His Glu Thr Gly Leu Pro Ser Gly Tyr Arg Thr  
 50 55 60

Met Gln Pro Ile Lys Glu Ala Gly Ser Asp Asn Tyr Leu Arg Ser Lys  
 65 70 75 80

Lys Tyr Tyr Pro Tyr Ile Gly Tyr Gly Tyr Val Gln Leu Thr Trp Lys  
 85 90 95

Glu Asn Tyr Gly Arg Ile Gly Lys Leu Ile Gly Ile Asp Leu Ile Lys  
 100 105 110

Asn Pro Glu Lys Ala Leu Glu Pro Leu Ile Ala Ile Gln Ile Ala Ile  
 115 120 125

Lys Gly Met Leu Asn Gly Trp Phe Thr Gly Val Gly Phe Arg Arg Lys  
 130 135 140

Arg Pro Val Ser Lys Tyr Asn Lys Gln Gln Tyr Ile Ala Ala Arg Asn  
 145 150 155 160

Ile Ile Asn Gly Lys Asp Lys Ala Glu Leu Ile Ala Lys Tyr Ala Ile  
 165 170 175

Ile Phe Glu Arg Ala Leu Arg Ser Leu  
 180 185

&lt;210&gt; 204

&lt;211&gt; 36

<212> PRT  
<213> Sus scrofa

<220>  
<221> MISC\_FEATURE  
<222> (1)..(36)  
<223> PMAP-36

<400> 204

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Arg | Phe | Arg | Arg | Leu | Arg | Lys | Lys | Thr | Arg | Lys | Arg | Leu | Lys | Lys |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Gly | Lys | Val | Leu | Lys | Trp | Ile | Pro | Pro | Ile | Val | Gly | Ser | Ile | Pro |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |
|-----|-----|-----|-----|
| Leu | Gly | Cys | Gly |
|     |     |     | 35  |