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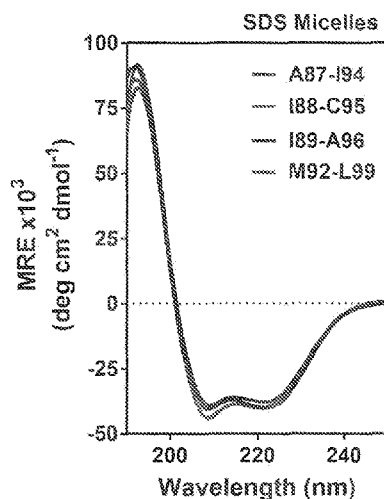
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(54) Title: STABILIZED POLYPEPTIDES AND USES THEREOF

FIG. 1A



(57) Abstract: The present invention features polypeptides which inhibit dimerization of small multidrug resistance transporters including a stabilized α -helix, and the use of such polypeptides in the treatment of bacterial infections.

STABILIZED POLYPEPTIDES AND USES THEREOF

Cross-Reference to Related Applications

This application claims the benefit of U.S. Provisional Patent Application No. 62/613,994, filed on January 5, 2018 and also claims the benefit of U.S. Provisional Patent Application No. 62/714,464, filed on August 3, 2018, which the entire contents of both are incorporated herein by reference.

Government Interest

This invention was made with government support under grant AI111416 awarded by the National Institutes of Health. The government has certain rights in the invention.

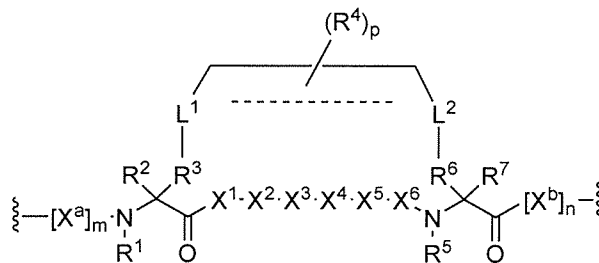
Background of the Invention

Multidrug resistance poses serious challenges for the treatment of many infectious diseases. A common mechanism by which multidrug resistance is conferred to bacteria is based on the active efflux of a wide range of cytotoxic compounds by transmembrane pumps. Some of these systems utilize supplier proteins, such as multidrug transporter EmrE in *E. coli*, which transport compounds into the periplasm from the cytoplasm. The various suppliers have overlapping specificities, and collectively form a multidrug resistance network of proteins that renders bacteria effectively immune to a broad range of compounds. The small multidrug resistance family of membrane bound transporters is ubiquitous in bacteria. Accordingly, compounds capable of inhibiting these transporters could be useful in the treatment of bacterial infections.

Summary of the Invention

The present invention features polypeptides which inhibit dimerization of small multidrug resistance transporters containing a stabilized α -helix, and the use of such polypeptides in the treatment of bacterial infections.

Accordingly, in an aspect, the invention features a polypeptide, or a pharmaceutically acceptable salt thereof, including a stabilized α -helix, wherein the polypeptide includes the structure of Formula I:



Formula I

wherein the dotted line represents an optional double bond;

m is 1, 2, 3, 4, 5, or 6;

n is 6-m;

p is 0, 1, or 2;

each of $[X^a]_m$, $[X^b]_n$, and X^1 - X^6 consist of consecutive amino acids of an α -helix of a monomer of a small multidrug resistance transporter (e.g., an α -helix of any one of SEQ ID NOs: 1-421), or conservative substitutions thereof;

5 R^1 and R^5 are, independently, hydrogen, optionally substituted acyl, or optionally substituted C_1 - C_6 alkyl;

R^2 and R^7 are, independently, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkenyl, optionally substituted C_1 - C_6 alkynyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_6 carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl;

10 R^3 and R^6 are, independently, optionally substituted C_1 - C_6 alkylene, optionally substituted C_1 - C_6 heteroalkylene, optionally substituted C_3 - C_6 carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl, or R^1 and R^3 or R^5 and R^6 combine with the atoms to which they are attached to form an optionally substituted C_5 - C_6 heterocyclyl;

L^1 and L^2 are, independently, absent, optionally substituted C_1 - C_6 alkylene, or –
15 $C(=O)OR^{L1}$ –, wherein each R^{L1} is, independently, an optionally substituted C_1 - C_6 alkyl; and each R^4 is, independently, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_6 - C_{10} alkyl,

wherein the polypeptide binds to the monomer of a small multidrug resistance transporter.

In some embodiments, the structure of Formula I includes the sequence of an α -helix of a
20 monomer of a small multidrug resistance transporter (e.g., an α -helix of any one of SEQ ID NOs: 1-421) in which two of the amino acids are replaced with a cross-link.

In some embodiments, R^2 is optionally substituted C_1 - C_6 alkyl (e.g., methyl). In some
embodiments, R^7 is optionally substituted C_1 - C_6 alkyl (e.g., methyl). In some embodiments, R^1 is
hydrogen. In some embodiments, R^5 is hydrogen. In some embodiments, p is 0. In some
25 embodiments, R^6 is optionally substituted C_1 - C_6 alkylene (e.g., methylene). In some
embodiments, R^3 is optionally substituted C_1 - C_6 alkylene (e.g., methylene). In some
embodiments, L^1 is optionally substituted C_1 - C_6 alkylene (e.g., pentylene). In some embodiments,
 L^2 is optionally substituted C_1 - C_6 alkylene (e.g., ethylene). In some embodiments, the dotted line
represents a double bond.

30 In some embodiments, X^1 is glycine, alanine, valine, leucine, or isoleucine; X^2 is glycine,
alanine, valine, leucine, or isoleucine; X^3 is glycine, alanine, valine, leucine, or isoleucine; X^4 is
serine, cysteine, selenocysteine, threonine, or methionine; X^5 is serine, cysteine, selenocysteine,
threonine, or methionine; and/or X^6 is histidine, lysine, or arginine.

In some embodiments, X^1 is glycine, alanine, valine, leucine, or isoleucine; X^2 is glycine,
35 alanine, valine, leucine, or isoleucine; X^3 is serine, cysteine, selenocysteine, threonine, or
methionine; X^4 is serine, cysteine, selenocysteine, threonine, or methionine; X^5 is histidine, lysine,
or arginine, and/or X^6 is glycine, alanine, valine, leucine, or isoleucine.

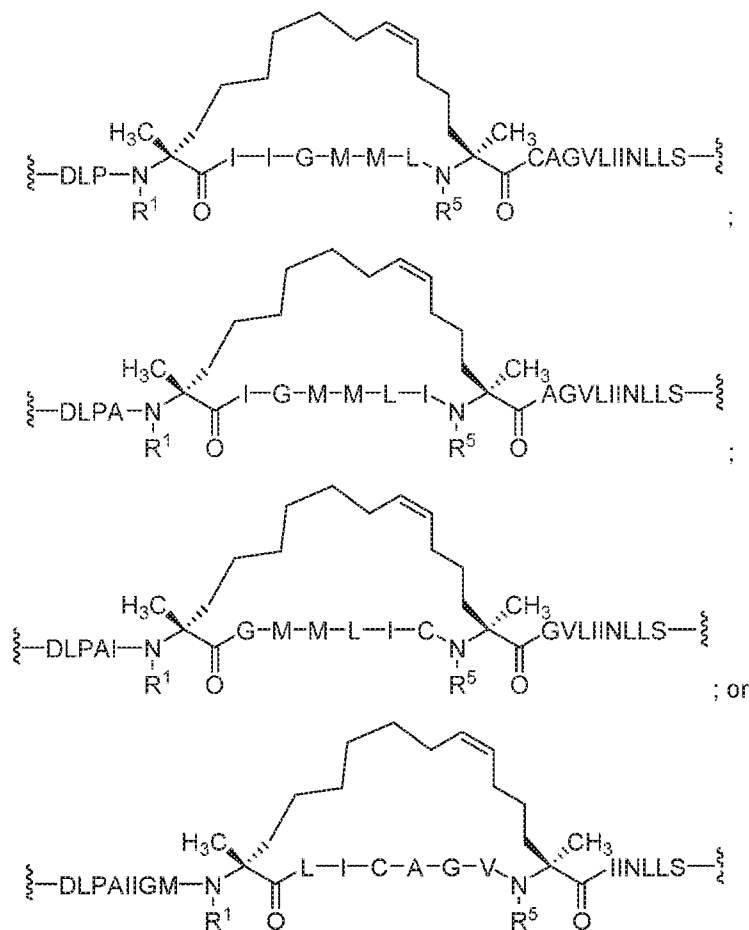
In some embodiments, X^1 is glycine, alanine, valine, leucine, or isoleucine; X^2 is serine,
cysteine, selenocysteine, threonine, or methionine; X^3 is serine, cysteine, selenocysteine,
40 threonine, or methionine;

X⁴ is histidine, lysine, or arginine; X⁵ is glycine, alanine, valine, leucine, or isoleucine; and/or X⁶ is serine, cysteine, selenocysteine, threonine, or methionine.

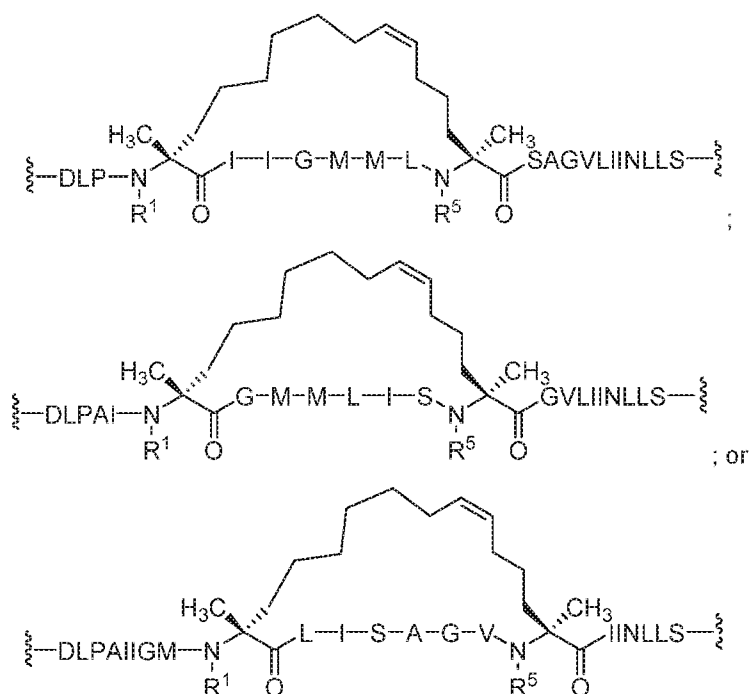
In some embodiments, X¹ is histidine, lysine, or arginine; X² is glycine, alanine, valine, leucine, or isoleucine; X³ is serine, cysteine, selenocysteine, threonine, or methionine; X⁴ is glycine, alanine, valine, leucine, or isoleucine; X⁵ is glycine, alanine, valine, leucine, or isoleucine; and/or X⁶ is glycine, alanine, valine, leucine, or isoleucine.

In some embodiments, [X^b]_n includes the sequence lysine-lysine-serine, or conservative substitutions thereof. In some embodiments, [X^b]_n includes the sequence isoleucine-isoleucine-asparagine-lysine-lysine-serine, or conservative substitutions thereof. In some embodiments, X¹-X⁶ or [X^b]_n includes the sequence cysteine-alanine-glycine, or conservative substitutions thereof. In some embodiments, [X^b]_n includes the sequence cysteine-alanine-glycine-valine-leucine-isoleucine-isoleucine-asparagine-lysine-lysine-serine, or conservative substitutions thereof. In some embodiments, [X^a]_m includes the sequence Aspartic acid-leucine-proline, or conservative substitutions thereof. In some embodiments, [X^a]_m includes the sequence Aspartic acid-leucine-proline-alanine-isoleucine-isoleucine-glycine-methionine, or conservative substitutions thereof.

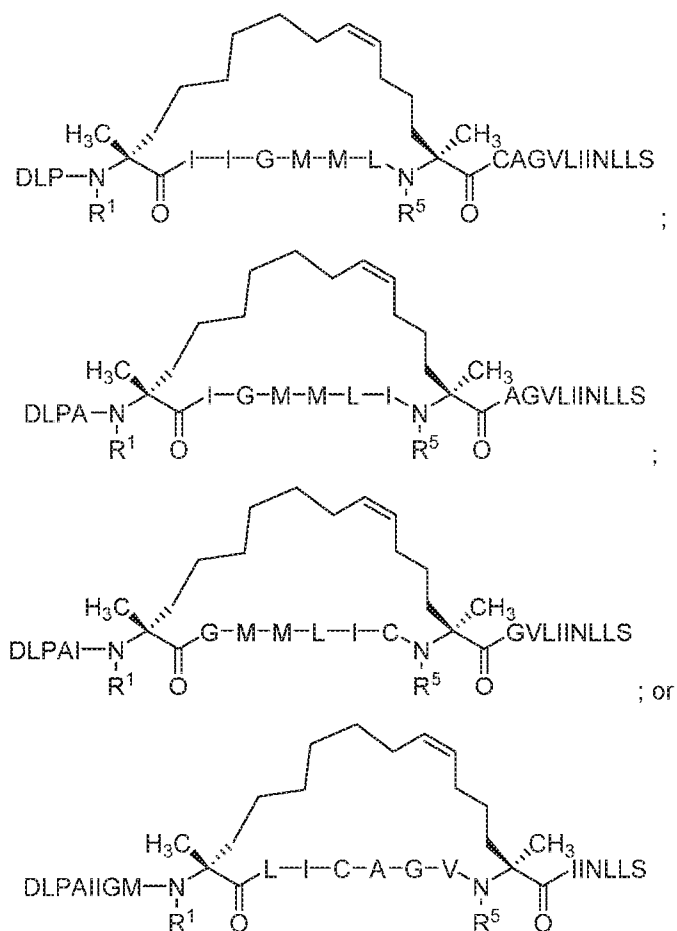
In some embodiments, the polypeptide includes the structure:



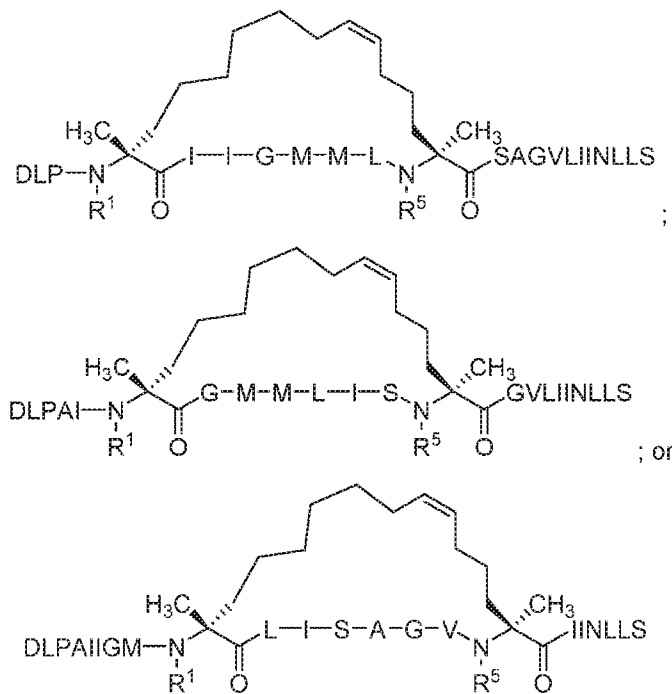
In some embodiments, the polypeptide includes the structure:



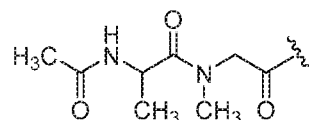
In some embodiments, the polypeptide consists of the structure:



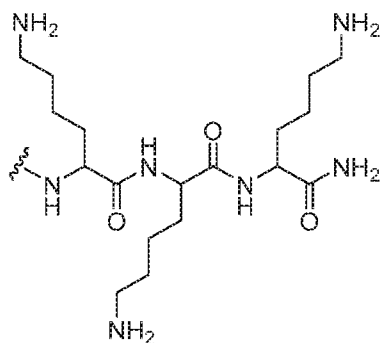
In some embodiments, the polypeptide consists of the structure:



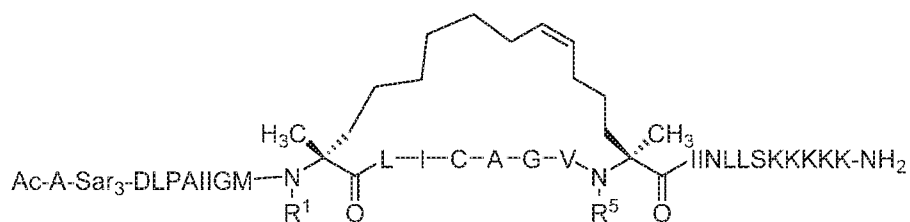
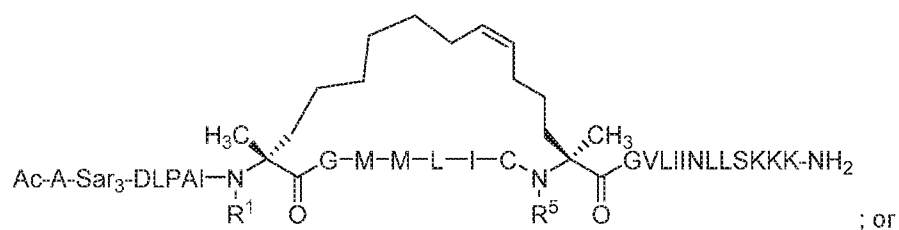
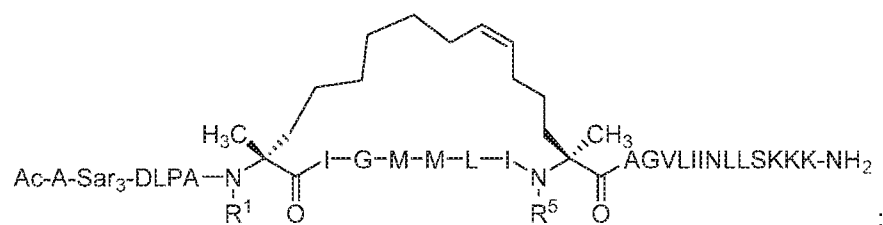
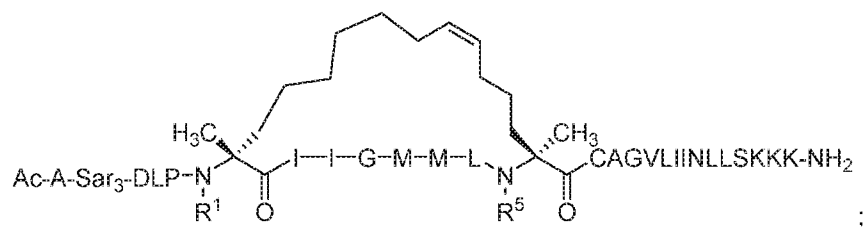
- 5 In some embodiments, the polypeptide includes a solubility tag (e.g., one or more lysine residues or a sarcosine-containing tag) at the N- and/or C-terminus. In some embodiments, the polypeptide is acetylated at the N-terminus. In some embodiments, the polypeptide is amidated at the C-terminus. In some embodiments, the polypeptide includes a solubility tag including at least one lysine (e.g., at least two, at least three, at least four, at least five) at the C-terminus. In some
- 10 embodiments, the polypeptide includes (e.g., at the N-terminus) the structure:



In some embodiments, the polypeptide includes (e.g., at the C-terminus) the structure:

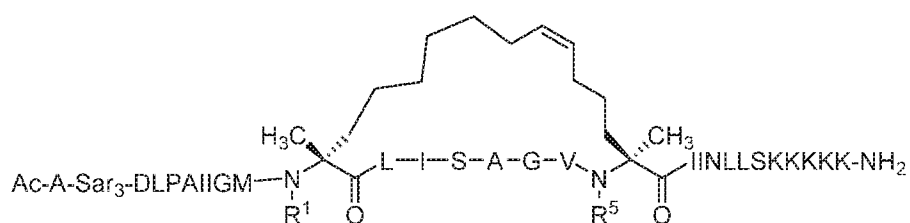
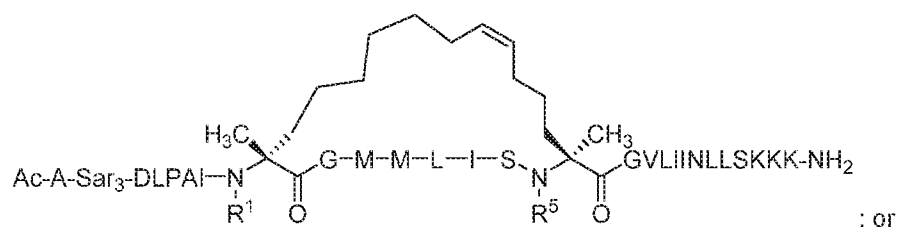
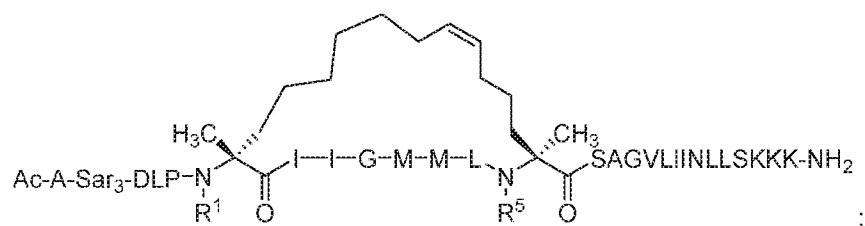


In some embodiments, the polypeptide consists of the structure:



5

In some embodiments, the polypeptide consists of the structure:



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In another aspect, the invention features a pharmaceutical composition including any of the foregoing polypeptides and a pharmaceutically acceptable carrier.

In another aspect, the invention features, a method of reducing efflux in a bacterial cell, the method including contacting the cell with any of the foregoing polypeptides or pharmaceutical
5 compositions. In some embodiments, the bacterial cell is a gram-negative bacteria (e.g., *E. coli*, *P. aeruginosa*, *B. pertussis*, or *N. meningitidis*). In some embodiments, the bacterial cell is a gram-positive bacteria (e.g., *S. aureus* or *B. anthracis*).

In another aspect, the invention features a method of treating a bacterial infection in a subject in need thereof, the method including administering any of the foregoing polypeptides or
10 pharmaceutical compositions. In some embodiments, the bacterial infection includes bacteria which are resistant to one or more antibacterial agents or the bacterial infection has failed to respond to treatment with one or more antibacterial agents. In some embodiments, the bacterial infection includes bacteria which express one or more small molecule resistance membrane-bound transporters. In some embodiments, the method further includes administering one or more
15 antibacterial agents (e.g., ampicillin, erythromycin, or tetracycline). In some embodiments, the one or more antibacterial agents is a β -lactam antibiotic, a cephalosporin antibiotic, a carbapenem antibiotic, a polymyxin antibiotic, a rifamycin antibiotic, a lipiarycin antibiotic, a quinolone antibiotic, a sulfonamide antibiotic, a macrolide antibiotic, a lincosamide antibiotic, a tetracycline antibiotic, an aminoglycoside antibiotic, a cyclic lipopeptide antibiotic, a glycylcycline antibiotic, an oxazolidinone
20 antibiotic, or a combination thereof. In some embodiments, the one or more antibacterial agent and any of the foregoing polypeptides or pharmaceutical compositions are administered within 28 days of each other (e.g., within 21, 14, 10, 7, 5, 4, 3, 2, or 1 days) or within 24 hours (e.g., 12, 6, 3, 2, or 1 hours; or concomitantly) each in an amount that together are effective to treat the subject.

Brief Description of the Drawings

25 FIGs. 1A and 1B are CD spectra of polypeptides of the invention. FIG. 1A is a CD spectrum of polypeptides of the invention in micelles. FIG. 1B is a CD spectrum of polypeptides of the invention in lipid bilayers.

FIG. 2 is a graph illustrating the toxicity of polypeptides of the invention to *E. coli* cells.

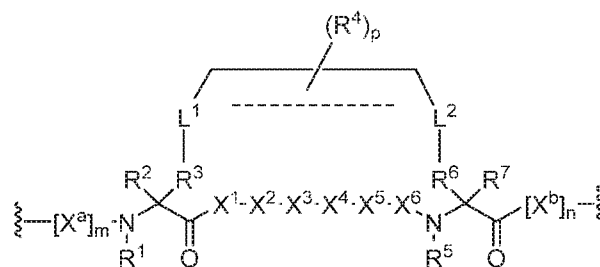
FIG. 3 is a graph illustrating the efflux of ethidium bromide from *E. coli* cells in the
30 presence and absence of polypeptides of the invention.

Detailed Description

Peptide stapling and stitching is a synthetic strategy known to increase helix stabilization, in which adjacent or subsequent turns of an α -helix are cross-linked by a macrocyclic bridge. See, e.g., Kim *et al.*, *Nat. Protoc.* (2011) 6:761-771. This incorporated staple can enforce the bioactive
35 α -helical conformation of a synthetic peptide and confer on it increased target affinity, robust cell penetration, and/or extended *in vivo* half-life. The present invention features polypeptides which inhibit dimerization of small multidrug resistance transporters including a stabilized α -helix, and the use of such polypeptides in the treatment of bacterial infections.

Polypeptides

Exemplary polypeptides of the invention comprise the structure of Formula I:



Formula I

5 wherein the dotted line represents an optional double bond;

m is 1, 2, 3, 4, 5, or 6;

n is 6-m;

p is 0, 1, or 2;

10 each of $[X^a]_m$, $[X^b]_n$, and X^1 - X^6 consist of consecutive amino acids of an α -helix of a monomer of a small multidrug resistance transporter, or conservative substitutions thereof;

R^1 and R^5 are, independently, hydrogen, optionally substituted acyl, or optionally substituted C_1 - C_6 alkyl;

15 R^2 and R^7 are, independently, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkenyl, optionally substituted C_1 - C_6 alkynyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_6 carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl;

R^3 and R^6 are, independently, optionally substituted C_1 - C_6 alkylene, optionally substituted C_1 - C_6 heteroalkylene, optionally substituted C_3 - C_6 carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl, or R^1 and R^3 or R^5 and R^6 combine with the atoms to which they are attached to form an optionally substituted C_5 - C_6 heterocyclyl;

20 L^1 and L^2 are, independently, absent, optionally substituted C_1 - C_6 alkylene, or $-C(=O)OR^{L1}-$, wherein each R^{L1} is, independently, an optionally substituted C_1 - C_6 alkyl; and

each R^4 is, independently, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_6 - C_{10} alkyl,

wherein the polypeptide binds to the monomer of a small multidrug resistance transporter.

25

Peptide Staples

Groups R^2 , R^3 , R^6 , R^7 , L^1 , and L^2

As generally defined above, R^2 is substituted or unsubstituted alkyl; substituted or unsubstituted alkenyl; substituted or unsubstituted alkynyl; substituted or unsubstituted heteroalkyl; substituted or unsubstituted carbocyclyl; substituted or unsubstituted heterocyclyl. In certain 30 embodiments, R^2 is substituted or unsubstituted C_{1-10} alkyl. In certain embodiments, R^2 is substituted methyl. In certain embodiments, R^2 is unsubstituted methyl. In certain embodiments, R^2 is substituted ethyl. In certain embodiments, R^2 is unsubstituted ethyl. In certain embodiments, R^2 is substituted n -propyl. In certain embodiments, R^2 is unsubstituted n -propyl. In certain

embodiments, R^2 is substituted *iso*-propyl. In certain embodiments, R^2 is unsubstituted *iso*-propyl. In certain embodiments, R^2 is substituted or unsubstituted heteroalkyl. In certain embodiments, R^2 is substituted or unsubstituted heteroalkyl with at least one nitrogen. In certain embodiments, R^2 is unsubstituted heteroalkyl containing at least one nitrogen. In certain embodiments, R^2 is

5 substituted heteroalkyl containing at least one nitrogen.

As generally defined above, R^3 is substituted or unsubstituted alkylene; substituted or unsubstituted heteroalkylene; substituted or unsubstituted carbocyclylene; or substituted or unsubstituted heterocyclylene; or optionally R^2 , R^3 and the carbon to which R^2 and R^3 are attached are joined to form a ring. In certain embodiments, R^3 is substituted or unsubstituted alkylene. In certain embodiments, R^3 is substituted or unsubstituted C_{1-10} alkylene. In certain embodiments, R^3 is substituted C_{1-10} alkylene. In certain embodiments, R^3 is unsubstituted C_{1-10} alkylene. In certain embodiments, R^3 is substituted or unsubstituted heteroalkylene. In certain embodiments, R^3 is substituted heteroalkylene. In certain embodiments, R^3 is unsubstituted heteroalkylene. In certain embodiments, R^3 is substituted or unsubstituted heteroalkylene containing at least one nitrogen. In certain embodiments, R^3 is $-(CH_2)_j-Y_1-$, wherein j is an integer between 0 and 10, inclusive; and Y_1 is a bond, $-CR^8R^9-$ or $-NR^{10}-$, wherein each of R^8 and R^9 is independently hydrogen, halogen, or C_{1-6} alkyl; and R^{10} is hydrogen; acyl; optionally substituted C_{1-6} alkyl; or an amino protecting group. In certain embodiments, R^3 is $-(CH_2)_j-$. In certain embodiments, R^3 is $-(CH_2)_j-NR^{10}-$. In certain embodiments, R^3 is $-(CH_2)_j-NH-$. In certain embodiments, R^3 is $-(CH_2)_{j+1}-$. In certain embodiments, j is 0. In certain embodiments, j is 1. In certain embodiments, j is 2. In certain embodiments, j is 3. In certain embodiments, j is 4. In certain embodiments, j is 5. In certain embodiments, j is 6. In certain embodiments, j is 7. In certain embodiments, j is 8. In certain embodiments, j is 9. In certain embodiments, j is 10.

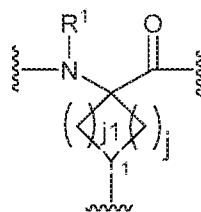
As generally defined above, each instance of R^{10} is, independently, hydrogen; acyl; optionally substituted C_{1-6} alkyl; or an amino protecting group. In certain embodiments, R^{10} is hydrogen. In certain embodiments, R^{10} is acyl; optionally substituted C_{1-6} alkyl; or an amino protecting group. In certain embodiments, R^{10} is acyl or optionally substituted C_{1-6} alkyl. In certain embodiments, R^{10} is substituted or unsubstituted alkyl. In certain embodiments, R^{10} is substituted or unsubstituted C_{1-6} alkyl. In certain embodiments, R^{10} is unsubstituted C_{1-6} alkyl. In certain embodiments, R^{10} is methyl, ethyl, or propyl. In certain embodiments, R^{10} is acyl. In certain embodiments, R^{10} is acetyl ($-C(=O)CH_3$). In certain embodiments, R^{10} is an amino protecting group. In certain embodiments, R^{10} is TBS, TBPS, Bn, BOC, Cbz, Fmoc, trifluoroacetyl, triphenylmethyl, or Ts.

In certain embodiments, at least one instance of R^2 and R^3 together with the carbon atom to which they are attached, are joined to form a ring. In this instance, in certain embodiments, the ring formed by R^2 and R^3 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} carbocyclyl or heterocyclyl. In certain embodiments, the ring formed by R^2 and R^3 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} carbocyclyl. In certain embodiments, the ring formed by R^2 and R^3 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} heterocyclyl. In certain

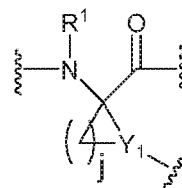
embodiments, the ring formed by R^2 and R^3 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} heterocyclyl containing at least one O, N, or S atom. In certain embodiments, the ring formed by R^2 and R^3 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} heterocyclyl containing at least one nitrogen atom.

- 5 In certain embodiments, the ring formed by R^2 and R^3 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} heterocyclyl containing one nitrogen atom. In certain embodiments, the ring formed by R^2 and R^3 together with the carbon atom to which they are attached is unsubstituted C_{3-6} heterocyclyl containing one nitrogen atom.

- 10 In certain embodiments, R^2 , R^3 , and the carbon to which R^2 and R^3 are attached are joined to form a ring. In certain embodiments, the ring formed by R^2 , R^3 , and the carbon to which R^2 and

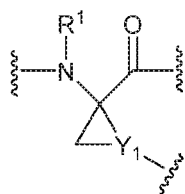


R^3 are attached is of the formula: , wherein Y_1 is $-CR^3-$ or $-N-$, each of j and j_1 is independently 0, 1, 2, 3, 4, 5, or 6. In certain embodiments, j_1 is zero, and the ring formed by

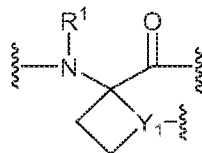


R^2 , R^3 and the carbon to which R^2 and R^3 are attached is of the formula: . In certain embodiments, j is 0 and Y_1 is directly linked to the alpha-carbon of the amino acid. In

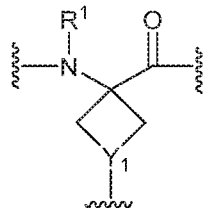
- 15 In certain embodiments, the ring formed by R^2 , R^3 and the carbon to which R^2 and R^3 are attached is



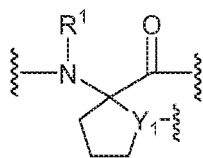
of the formula: . In certain embodiments, the ring formed by R^2 , R^3 and the carbon



to which R^2 and R^3 are attached is of the formula: . In certain embodiments, the ring formed by R^2 , R^3 and the carbon to which R^2 and R^3 are attached is of the formula:

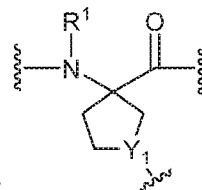


. In certain embodiments, the ring formed by R^2 , R^3 and the carbon to which R^2



and R^3 are attached is of the formula:

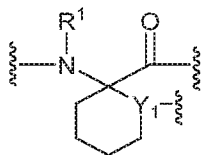
. In certain embodiments, the ring formed



by R^2 , R^3 and the carbon to which R^2 and R^3 are attached is of the formula:

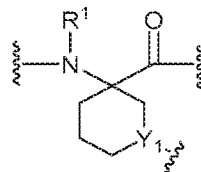
. In

certain embodiments, the ring formed by R^2 , R^3 and the carbon to which R^2 and R^3 are attached is



of the formula:

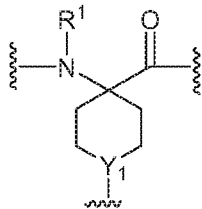
. In certain embodiments, the ring formed by R^{2a} , R^{3a} and the



5 carbon to which R^2 and R^3 are attached is of the formula:

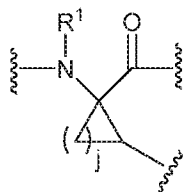
. In certain

embodiments, the ring formed by R^2 , R^3 and the carbon to which R^2 and R^3 are attached is of the



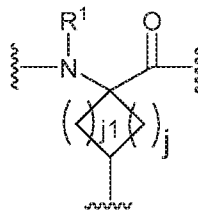
formula:

In certain embodiments, the ring formed by R^2 , R^3 and the carbon to which R^2 and R^3 are



attached is of the formula:

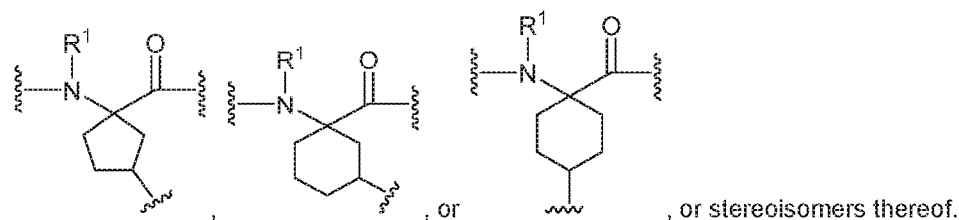
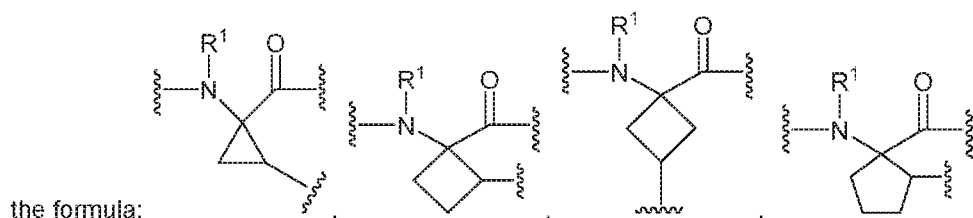
. In certain embodiments, the ring formed by R^2 , R^3 and



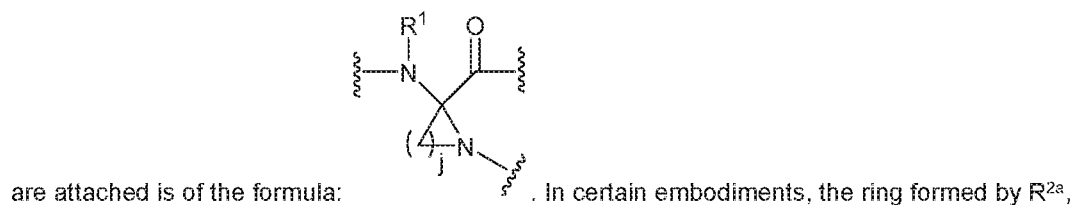
10 the carbon to which R^2 and R^3 are attached is of the formula:

. In certain

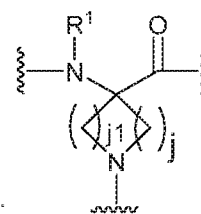
embodiments, the ring formed by R^{2a} , R^{3a} and the carbon to which R^{2a} and R^{3a} are attached is of



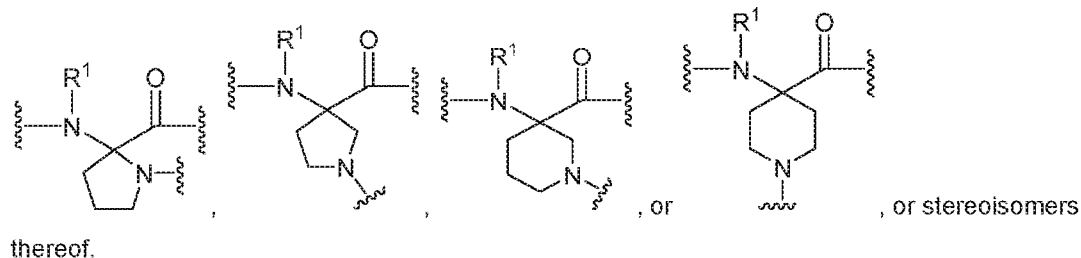
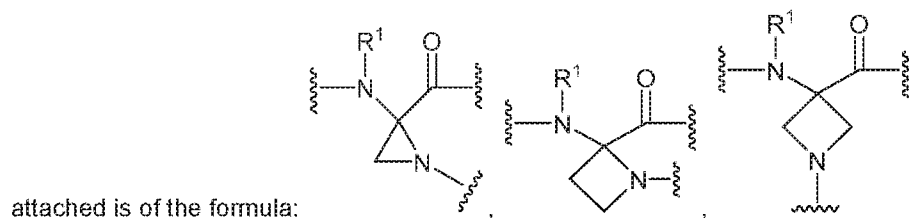
In certain embodiments, the ring formed by R^2 , R^3 and the carbon to which R^{2a} and R^{3a}



- 5 R^{3a} and the carbon to which R^{2a} and R^{3a} are attached is of the formula:



in certain embodiments, the ring formed by R^{2a} , R^{3a} and the carbon to which R^{2a} and R^{3a} are



- 10 As used herein, each of j and j_1 is independently an integer between 1 and 10, inclusive. In some embodiments, j is 1. In some embodiments, j is 2. In some embodiments, j is 3. In some embodiments, j is 4. In some embodiments, j is 5. In some embodiments, j is 6. In some embodiments, j is 7. In some embodiments, j is 8. In some embodiments, j is 9. In some embodiments, j is 10. In some embodiments, j_1 is 1. In some embodiments, j_1 is 2. In some

embodiments, j_1 is 3. In some embodiments, j_1 is 4. In some embodiments, j_1 is 5. In some embodiments, j_1 is 6. In some embodiments, j_1 is 7. In some embodiments, j_1 is 8. In some embodiments, j_1 is 9. In some embodiments, j_1 is 10.

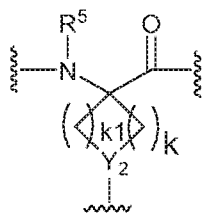
In some embodiments, R^2 , R^3 and the carbon to which R^2 and R^3 are attached are not
 5 joined to form a ring. In this instance, R^3 is substituted or unsubstituted alkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted heteroalkylene, or substituted or unsubstituted heterocyclylene. In some embodiments, R^3 is substituted or unsubstituted C_{1-10} alkylene. In some embodiments, R^3 is substituted C_{1-10} alkylene. In some embodiments, R^3 is $-(CH_2)_j-$, wherein j is an integer between 0 and 10, inclusive.

10 In some embodiments, R^2 , R^3 and the carbon to which R^2 and R^3 are attached are not joined to form a ring. In this instance, R^2 is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroalkyl, or substituted or unsubstituted heterocyclyl. In some embodiments, R^2 is substituted or unsubstituted C_{1-10} alkyl. In some embodiments, R^2 is substituted methyl. In some embodiments,
 15 R^2 is unsubstituted methyl. In some embodiments, R^2 is substituted ethyl. In some embodiments, R^2 is unsubstituted ethyl. In some embodiments, R^2 is substituted or unsubstituted C_{2-6} alkyl.

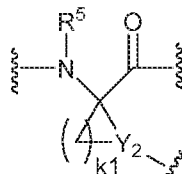
As generally described above, R^3 is substituted or unsubstituted alkylene; substituted or unsubstituted heteroalkylene; substituted or unsubstituted carbocyclylene; or substituted or unsubstituted heterocyclylene; or optionally R^6 , R^7 and the carbon to which R^6 and R^7 are attached
 20 are joined to form a ring. In some embodiments, R^6 is substituted or unsubstituted C_{1-10} alkylene. In some embodiments, R^6 is substituted C_{1-10} alkylene. In some embodiments, R^6 is unsubstituted C_{1-10} alkylene. In some embodiments, R^6 is substituted or unsubstituted heteroalkylene. In some embodiments, R^6 is substituted heteroalkylene. In some embodiments, R^6 is unsubstituted heteroalkylene. In some embodiments, R^6 is substituted or unsubstituted heteroalkylene with at
 25 least one nitrogen. In some embodiments, R^6 is $-(CH_2)_k-Y_2-$, wherein k is an integer between 0 and 10, inclusive, and Y_2 is a bond, $-CR^8R^9-$, or $-NR^{10}-$, wherein R^8 , R^9 and R^{10} are as defined herein. In some embodiments, R^6 is $-(CH_2)_k-$. In some embodiments, R^6 is $-(CH_2)_k-NR^{10}-$. In some embodiments, R^6 is $-(CH_2)_k-NH-$. In some embodiments, R^6 is $-(CH_2)_{k+1}-$. In some
 30 embodiments, k is 0. In some embodiments, k is 1. In some embodiments, k is 2. In some embodiments, k is 3. In some embodiments, k is 4. In some embodiments, k is 5. In some embodiments, k is 6. In some embodiments, k is 7. In some embodiments, k is 8. In some embodiments, k is 9. In some embodiments, k is 10.

As generally described above, R^7 is substituted or unsubstituted alkyl; substituted or unsubstituted alkenyl; substituted or unsubstituted alkynyl; substituted or unsubstituted heteroalkyl;
 35 substituted or unsubstituted carbocyclyl; or substituted or unsubstituted heterocyclyl. In some embodiments, R^7 is substituted or unsubstituted C_{1-10} alkyl. In some embodiments, R^7 is substituted or unsubstituted heteroalkyl. In some embodiments, R^7 is substituted or unsubstituted heteroalkyl with at least one nitrogen atom. In some embodiments, R^7 is unsubstituted heteroalkyl with at least one nitrogen atom. In some embodiments, R^7 is substituted heteroalkyl with at least
 40 one nitrogen atom.

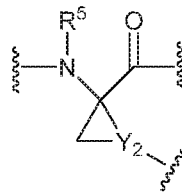
- In some embodiments, for at least one instance, R^6 , R^7 and the carbon to which R^6 and R^7 are attached are joined to form a ring. In this instance, in some embodiments, the ring formed by R^6 and R^7 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} carbocyclyl or heterocyclyl. In some embodiments, the ring formed by R^6 and R^7 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} carbocyclyl. In some embodiments, the ring formed by R^6 and R^7 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} heterocyclyl. In some embodiments, the ring formed by R^6 and R^7 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} heterocyclyl with at least one O, N, or S atom. In some embodiments, the ring formed by R^6 and R^7 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} heterocyclyl with at least one N. In some embodiments, the ring formed by R^6 and R^7 together with the carbon atom to which they are attached is substituted or unsubstituted C_{3-6} heterocyclyl with one N. In some embodiments, the ring formed by R^6 and R^7 together with the carbon atom to which they are attached is unsubstituted C_{3-6} heterocyclyl with one N.
- In some embodiments, the ring formed by R^6 , R^7 and the carbon to which R^6 and R^7 are



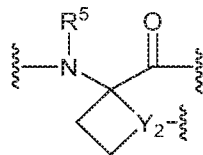
attached is of the formula: $\text{---N(R}^5\text{)---C(=O)---}$ $\left(\text{---CH}_2 \right)_k \text{---Y}_2 \text{---}$, wherein Y_2 is $\text{---CR}^6\text{---}$ or ---N--- ; k is 0, or an integer from 1 to 10, inclusive; and k_1 is an integer from 1 to 10, inclusive. In some embodiments, k_1 is zero, and the ring formed by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is of the



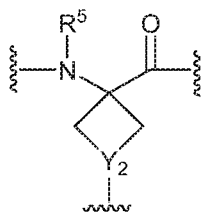
formula: $\text{---N(R}^5\text{)---C(=O)---}$ $\left(\text{---CH}_2 \right)_{k_1} \text{---Y}_2 \text{---}$. In some embodiments, the ring formed by R^{2b} , R^{3b} and the carbon to



- which R^{2b} and R^{3b} are attached is of the formula: $\text{---N(R}^5\text{)---C(=O)---}$ $\left(\text{---CH}_2 \right)_3 \text{---Y}_2 \text{---}$. In some embodiments, the ring formed by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is of the formula:

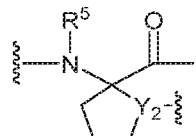


. In some embodiments, the ring formed by R^{2b} , R^{3b} and the carbon to which R^{2b}



and R^{3b} are attached is of the formula:

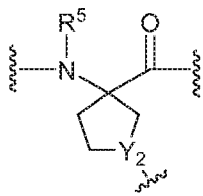
. In some embodiments, the ring formed



by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is of the formula:

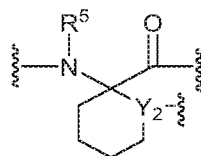
. In

some embodiments, the ring formed by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is



of the formula:

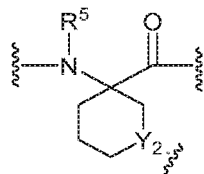
. In some embodiments, the ring formed by R^6 , R^7 and the carbon



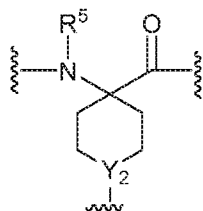
5 to which R^6 and R^7 are attached is of the formula:

. In some embodiments, the

ring formed by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is of the formula:

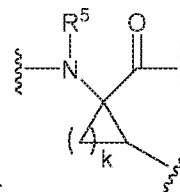


. In some embodiments, the ring formed by R^6 , R^7 and the carbon to which R^6



and R^7 are attached is of the formula:

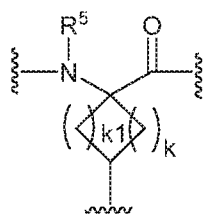
. In some embodiments, the ring formed



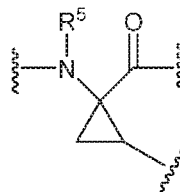
by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is of the formula:

. In

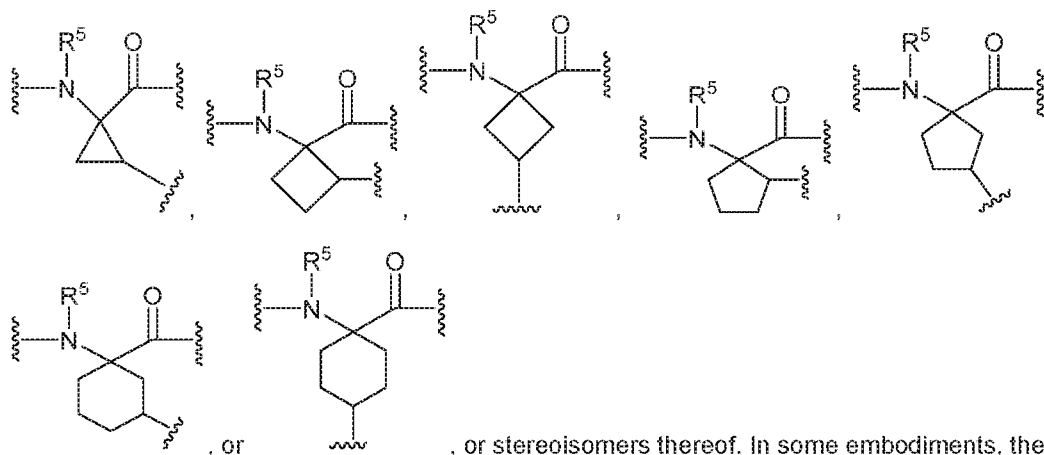
10 some embodiments, the ring formed by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is



of the formula: . In some embodiments, the ring formed by R^6 , R^7 and the carbon

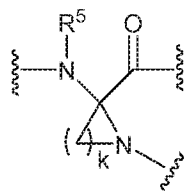


to which R^6 and R^7 are attached is of the formula: . In some embodiments, the ring formed by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is of the formula:

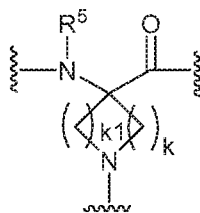


5

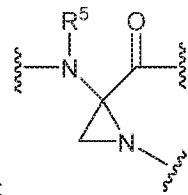
, or stereoisomers thereof. In some embodiments, the ring formed by R^6 , R^7 and the carbon to which R^6 and R^7 are attached is of the formula:



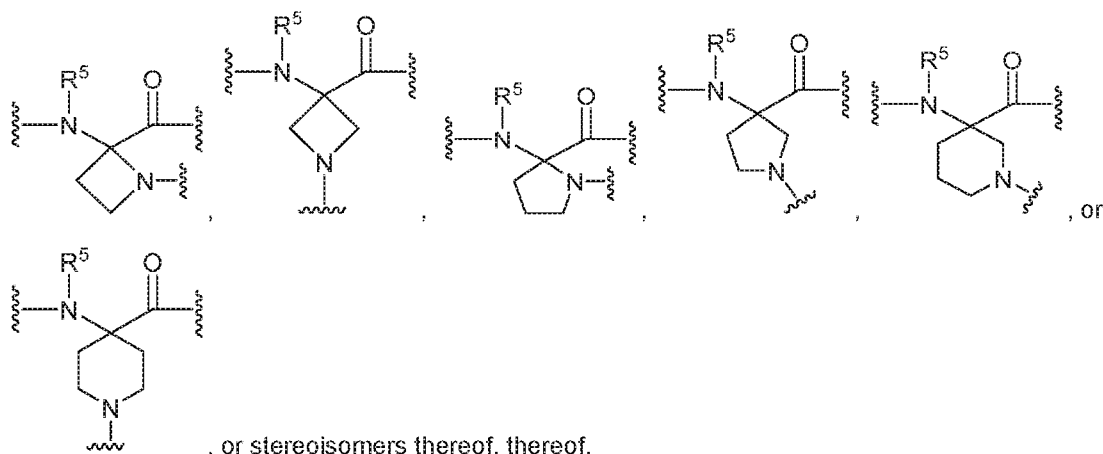
. In some embodiments, the ring formed by R^6 , R^7 and the carbon to which R^6 and



R^7 are attached is of the formula: . In some embodiments, the ring formed by R^6 ,



R^7 and the carbon to which R^6 and R^7 are attached is of the formula:



As used herein, k is an integer between 0 and 10, inclusive; and k_1 is an integer between 1 and 10, inclusive. In some embodiments, k is 0. In some embodiments, k is 1. In some
 5 embodiments, k is 2. In some embodiments, k is 3. In some embodiments, k is 4. In some
 embodiments, k is 5. In some embodiments, k is 6. In some embodiments, k is 7. In some
 embodiments, k is 8. In some embodiments, k is 9. In some embodiments, k is 10. In some
 embodiments, k_1 is 1. In some embodiments, k_1 is 2. In some embodiments, k_1 is 3. In some
 embodiments, k_1 is 4. In some embodiments, k_1 is 5. In some embodiments, k_1 is 6. In some
 10 embodiments, k_1 is 7. In some embodiments, k_1 is 8. In some embodiments, k_1 is 9. In some
 embodiments, k_1 is 10.

In some embodiments, R^6 , R^7 and the carbon to which R^6 and R^7 are attached are not
 joined to form a ring. In this instance, R^6 is substituted or unsubstituted alkylene, substituted or
 unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted
 15 heteroalkylene, or substituted or unsubstituted heterocyclylene. In some embodiments, R^6 is
 substituted or unsubstituted C_{1-10} alkylene. In some embodiments, R^6 is substituted C_{1-10} alkylene.
 In some embodiments, R^6 is $-(CH_2)_k-$, wherein k is as defined above.

In some embodiments, R^6 , R^7 and the carbon to which R^6 and R^7 are attached are not
 joined to form a ring. In this instance, in some embodiments, R^7 is substituted or unsubstituted C_{1-10}
 20 alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or
 unsubstituted heteroalkyl, or substituted or unsubstituted heterocyclyl. In some embodiments, R^7
 is substituted or unsubstituted C_{1-10} alkyl. In some embodiments, R^7 is substituted methyl. In some
 embodiments, R^7 is unsubstituted methyl. In some embodiments, R^7 is substituted ethyl. In some
 embodiments, R^7 is unsubstituted ethyl. In some embodiments, R^7 is substituted or unsubstituted
 25 C_{2-6} alkyl.

In some embodiments, for at least one instance, R^2 , R^3 , and the carbon to which R^2 and
 R^3 are attached are not joined to form a ring, and R^6 , R^7 , and the carbon to which R^6 and R^7 are
 attached are not joined form a ring. In some embodiments, R^2 , R^3 and the carbon to which R^2 and
 R^3 are attached are not joined to form a ring, and R^6 , R^7 and the carbon to which R^6 and R^7 are
 30 attached are joined form a ring. In some embodiments, R^2 , R^3 and the carbon to which R^2 and R^3
 are attached are joined to form a ring, and R^6 , R^7 and the carbon to which R^6 and R^7 are attached

are not joined form a ring. In some embodiments, for at least one instance, R^2 , R^3 and the carbon to which R^2 and R^3 are attached are joined to form a ring, and R^6 , R^7 and the carbon to which R^6 and R^7 are attached are joined form a ring.

In some embodiments, each instance of R^3 and R^6 are the same. In some embodiments,
5 each instance of R^3 and R^6 are different.

As generally described above, L_1 is a bond, substituted or unsubstituted C_{1-10} alkylene, or $-C(=O)OR^{L1}-$, wherein R^{L1} is optionally substituted C_{1-10} alkylene. In some embodiments, L_1 is substituted or unsubstituted C_{1-10} alkylene. In some embodiments, L_1 is substituted C_{1-10} alkylene. In some embodiments, L_1 is $-(CH_2)_g-$, wherein g is 0 or an integer between 1 and 10. In some
10 embodiments, g is 0, and L_1 is a bond. In some embodiments, g is 1. In some embodiments, g is 2. In some embodiments, g is 3. In some embodiments, g is 4. In some embodiments, g is 5. In some embodiments, g is 6. In some embodiments, g is 7. In some embodiments, g is 8. In some embodiments, g is 9. In some embodiments, g is 10. In some embodiments, R^{L1} is substituted C_{1-10} alkylene. In some embodiments, R^{L1} is $-C(=O)O(CH_2)_{g1}-$, wherein $g1$ is an integer between 1 and
15 10 inclusive. In some embodiments, $g1$ is 1. In some embodiments, $g1$ is 2. In some embodiments, $g1$ is 3. In some embodiments, $g1$ is 4. In some embodiments, $g1$ is 5. In some embodiments, $g1$ is 6. In some embodiments, $g1$ is 7. In some embodiments, $g1$ is 8. In some embodiments, $g1$ is 9. In some embodiments, $g1$ is 10.

As generally described above, L_2 is a bond, substituted or unsubstituted C_{1-10} alkylene, or $-C(=O)OR^{L2}-$, wherein R^{L2} is optionally substituted C_{1-10} alkylene. In some embodiments, L_2 is substituted or unsubstituted C_{1-10} alkylene. In some embodiments, L_2 is substituted C_{1-10} alkylene. In some embodiments, L_2 is $-(CH_2)_h-$, wherein h is 0 or an integer between 1 and 10 inclusive. In some embodiments, h is 0, and L_2 is a bond. In some embodiments, h is 1. In some embodiments, h is 2. In some embodiments, h is 3. In some embodiments, h is 4. In some embodiments, h is 5.
25 In some embodiments, h is 6. In some embodiments, h is 7. In some embodiments, h is 8. In some embodiments, h is 9. In some embodiments, h is 10. In some embodiments, R^{L2} is substituted C_{1-10} alkylene. In some embodiments, R^{L2} is $-C(=O)O(CH_2)_{h1}-$, wherein $h1$ is an integer between 1 and 10 inclusive. In some embodiments, $h1$ is 1. In some embodiments, $h1$ is 2. In some embodiments, $h1$ is 3. In some embodiments, $h1$ is 4. In some embodiments, $h1$ is 5. In some embodiments, $h1$
30 is 6. In some embodiments, $h1$ is 7. In some embodiments, $h1$ is 8. In some embodiments, $h1$ is 9. In some embodiments, $h1$ is 10.

In some embodiments, each instance of L_1 and L_2 is the same. In some embodiments, each instance of L_1 and L_2 is different.

35 *Group R^1 and R^5*

As generally defined above, R^1 and R^5 are, independently, hydrogen; acyl; optionally substituted C_{1-6} alkyl; or an amino protecting group.

In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is acyl; optionally substituted C_{1-6} alkyl; or an amino protecting group. In some embodiments, R^1 is acyl or optionally
40 substituted C_{1-6} alkyl.

In some embodiments, R¹ is substituted or unsubstituted alkyl. In some embodiments, R¹ is substituted or unsubstituted C₁₋₆ alkyl. In some embodiments, R¹ is unsubstituted C₁₋₆ alkyl. In some embodiments, R¹ is methyl, ethyl, or propyl.

In some embodiments, R¹ is acyl. In some embodiments, R¹ is acetyl (-C(=O)CH₃).

5 In some embodiments, R¹ is an amino protecting group. In some embodiments, R¹ is TBS, TBPS, Bn, BOC, Cbz, Fmoc, trifluoroacetyl, triphenylmethyl, or Ts.

In some embodiments, R⁵ is hydrogen. In some embodiments, R⁵ is acyl; optionally substituted C₁₋₆ alkyl; or an amino protecting group. In some embodiments, R⁵ is acyl or optionally substituted C₁₋₆alkyl.

10 In some embodiments, R⁵ is substituted or unsubstituted alkyl. In some embodiments, R⁵ is substituted or unsubstituted C₁₋₆ alkyl. In some embodiments, R⁵ is unsubstituted C₁₋₆ alkyl. In some embodiments, R⁵ is methyl, ethyl, or propyl.

In some embodiments, R⁵ is acyl. In some embodiments, R⁵ is acetyl (-C(=O)CH₃).

15 In some embodiments, R⁵ is an amino protecting group. In some embodiments, R⁵ is TBS, TBPS, Bn, BOC, Cbz, Fmoc, trifluoroacetyl, triphenylmethyl, or Ts.

In some embodiments, R¹ and R⁵ are, independently, hydrogen, C₁₋₆ alkyl (e.g., methyl), or acyl. In some embodiments, R¹ and R⁵ are hydrogen.

In some embodiments, R¹ and R⁵ are, independently, hydrogen, optionally substituted C₁₋₆ alkyl (e.g., methyl), or acyl. In some embodiments, R¹ and R⁵ are, independently, hydrogen, 20 methyl, or acetyl. In some embodiments, R¹ and R⁵ are, independently, hydrogen or methyl. In some embodiments, R¹ and R⁵ are hydrogen. In some embodiments, R¹ and R⁵ are methyl.

Groups =====, R⁴ and p

As generally defined above, ===== represents a single bond or a double bond. In some embodiments, ===== is a single bond. In some embodiments, ===== is a double bond.

25 As generally defined above, each instance of R⁴ is independently hydrogen; optionally substituted aliphatic; optionally substituted heteroaliphatic; substituted or unsubstituted aryl; optionally substituted heteroaryl; acyl; optionally substituted hydroxyl; optionally substituted thiol; optionally substituted amino; azido; cyano; isocyano; halo; or nitro.

As generally defined above, p is 0, 1, or 2.

30 In some embodiments, each instance of p is 0, and thus each instance of R⁴ is absent to provide an unsubstituted crosslink. In some embodiments at least one instance of p is 1, and thus at least one instance of R⁴ is a non-hydrogen substituent.

In some embodiments, after stapling of an inventive polypeptide, the method further comprises additional synthetic modification of the unsaturated staple or stitch of the cross-linked 35 peptides. Any chemical or biological modification to the stapled or stitched polypeptide may be made. In some embodiments, the modifications are carried out on the Alloc moiety of a polypeptide. In some embodiments, the modifications extrude CO₂ from the Alloc moiety from the stapled peptides. In some embodiments, the CO₂ extrusion is carried out in the presence of a palladium catalyst. In some embodiments, the CO₂ extrusion is carried out in the presence of

Pd(PPh₃)₄. In some embodiments, the modification comprises alkylation on the amide group of the staple or stitch.

In some embodiments, additional modifications of the stapled or stitched peptides include reduction, oxidation, and nucleophilic or electrophilic additions to the double bond provided from a
5 metathesis reaction to provide a synthetically modified polypeptide. Other modifications may include conjugation of a stapled polypeptide, or a synthetically modifying the stapled polypeptide with a therapeutically active agent, label, or diagnostic agent anywhere on the stapled polypeptide scaffold, e.g., such as at the N-terminus of the stapled polypeptide, the C-terminus of the stapled polypeptide, on an amino acid side chain of the stapled polypeptide, or at one or more modified or
10 unmodified stapled sites (i.e., to a staple). Such modification may be useful in delivery of the peptide or therapeutically active agent to a cell, tissue, or organ. Such modifications may, in some embodiments, allow for targeting to a particular type of cell or tissue.

The staples or stitches of the polypeptide may further comprise additional synthetic modification(s). Any chemical or biological modification may be made. In some embodiments, the
15 staple or stitch has an Alloc group. In some embodiments, the modifications are carried out on the Alloc moiety of a polypeptide. In some embodiments, the modifications extrude CO₂ from the Alloc moiety from the stapled peptides. In some embodiments, the CO₂ extrusion is carried out in the presence of a palladium catalyst. In some embodiments, the CO₂ extrusion is carried out in the presence of Pd(PPh₃)₄. In some embodiments, such modifications include reduction, oxidation,
20 and nucleophilic or electrophilic additions to the double bond provided from a metathesis reaction of the cross-link to provide a synthetically modified stapled or stitched polypeptide. One of ordinary skill in the art will appreciate that a wide variety of conditions may be employed to promote such transformations, therefore, a wide variety of conditions are envisioned; see generally, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, M.B.
25 Smith and J. March, 5th Edition, John Wiley & Sons, 2001; *Advanced Organic Chemistry, Part B: Reactions and Synthesis*, Carey and Sundberg, 3rd Edition, Plenum Press, New York, 1993; and *Comprehensive Organic Transformations*, R.C. Larock, 2nd Edition, John Wiley & Sons, 1999, the entirety of each of which is hereby incorporated herein by reference. In other embodiments, the staple(s) of the polypeptide are not further modified.

In some embodiments, the staple or stitch has a double bond. In some embodiments, the
30 modifications are carried out on the double bond of the stapled or stitched polypeptide. Exemplary conditions may be any reagent reactive with a double bond. In some embodiments, the reagent is able to react with a double bond, for example, via a hydrogenation, osmylation, hydroxylation (mono- or di-), amination, halogenation, cycloaddition (e.g., cyclopropanation, aziridination,
35 epoxidation), oxy-mercuration, and/or a hydroboration reaction, to provide a functionalized single bond. As one of ordinary skill in the art will clearly recognize, these above-described transformations will introduce functionalities compatible with the particular stabilized structures and the desired biological interactions; such functionalities include, but are not limited to, hydrogen; substituted or unsubstituted aliphatic; substituted or unsubstituted heteroaliphatic; substituted or
40 unsubstituted aryl; substituted or unsubstituted heteroaryl; acyl; substituted or unsubstituted

hydroxyl; substituted or unsubstituted amino; substituted or unsubstituted thiol, halo; cyano; nitro; azido; imino; oxo; and thiooxo.

Other modifications may further include conjugation of the stapled or stitched polypeptide, or a synthetically modified stapled or stitched polypeptide, with a biologically active agent, label, targeting moiety, diagnostic agent, anywhere on the polypeptide scaffold, *e.g.*, such as at the N-terminus of the polypeptide, the C-terminus of the polypeptide, on an amino acid side chain of the polypeptide, or at one or more modified or unmodified stapled sites. Such modification may be useful in delivery of the peptide or biologically active agent to a cell, tissue, or organ. Such modifications may allow for targeting of the stabilized polypeptide to a particular type of cell or tissue. Conjugation of an agent (*e.g.*, a label, a diagnostic agent, a biologically active agent, a targeting moiety) to the stapled polypeptide may be achieved in a variety of different ways. The agent may be covalently conjugated, directly or indirectly, to the polypeptide at the site of stapling, or to the N-terminus or the C-terminus of the polypeptide. Alternatively, the agent may be noncovalently conjugated, directly or indirectly, to the polypeptide at the site of stapling, or to the N-terminus or the C-terminus of the polypeptide, or any other site on the polypeptide. Indirect covalent conjugation is by means of one or more covalent bonds. Indirect non-covalent conjugation is by means of one or more non-covalent interactions. Conjugation may also be via a combination of non-covalent and covalent interactions. The agent may also be conjugated to the polypeptide through a linker. Any number of covalent bonds may be used in the conjugation of a biologically active agent and/or diagnostic agent to the inventive polypeptide of the present invention. Such bonds include amide linkages, ester linkages, disulfide linkages, carbon-carbon bonds, carbamate linkages, carbonate linkages, urea linkages, hydrazide linkages, and the like. In some embodiments, the bond is cleavable under physiological conditions (*e.g.*, enzymatically cleavable, cleavable at a high or low pH, with heat, light, ultrasound, x-ray, *etc.*). However, in some embodiments, the bond is not cleavable.

In some embodiments, the additional modification is PEGylation. The PEGylation of the stapled or stitched polypeptide can be carried out using any of the PEGylation reactions known in the art. Such reactions are described, for example, in the following references: Francis et al., (1992), Focus on Growth Factors 3: 4-10; European Patent Nos. 0 154 316 and 0 401 384; and U.S. Pat. No. 4,179,337. For example, PEGylation can be carried out via an acylation reaction or an alkylation reaction with a reactive polyethylene glycol molecule (or an analogous reactive water-soluble polymer) as described herein. For the acylation reactions, a selected polymer should have a single reactive ester group. For reductive alkylation, a selected polymer should have a single reactive aldehyde group. A reactive aldehyde is, for example, polyethylene glycol propionaldehyde, which is water stable, or mono C₁₋₁₀ alkoxy or aryloxy derivatives thereof (*see, e.g.*, U.S. Pat. No. 5,252,714).

The stapled peptides of the invention may be synthesized using methods known in the art, *e.g.*, general methods of preparing the stapled or stitched peptides and addition modifications are described in U.S. Patent Nos. 7,192,713; 7,723,469; 7,786,072, 8,198,405, 8,324,428, 8,592,377, 8,796,418, 8,889,632, 8,895,699, 9,074,009, 9,273,099, 9,556,227; 9,617,309; U.S. Patent

Application Publication Nos: 2010-0184645; 2010-0168388; 2010-0081611; 2009-0176964; 2009-0149630; 2006-0008848; 2014-0296160; 2014-162339; 2014-0011979; 2015-0239937, 2015-119951; 2016-0024153; 2016-0215036; 2016-0244494; 2017-0240604; 2017-0066799; PCT Application Publication Nos: WO 2010/011313; WO 2008/121767; WO 2008/095063; WO 2008/061192; WO2014/055564; and WO 2005/044839, as well as PCT Application No. PCT/US2014/025544; the synthetic methods of which are incorporated by references herein.

Small multidrug resistance transporters

The polypeptides of the invention include sequences of small multidrug resistance transporters of which two amino acids have been replaced with a cross-link. In some embodiments, the α -helix which is stabilized to produce the polypeptides of the invention is:

DLPAIIGMMLICAGVLIINLLS (SEQ ID NO: 1)

Exemplary sequences of small multidrug resistance transporters which include an α -helix include:

Multidrug transporter EmrE (*Escherichia coli* (strain K12)):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAIIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 2)

Antiseptic-resistance protein (*Escherichia coli*):

MKGWFLVIAIVGEVIATSALKSSEGFTKLAPSAVVIIGYGIIFYFLSLVLKSIPVGVAYAVWSGLGVVIIT
AIAWLLHGQKLDAGFVGMGLIIAFLARSPSWKSLRRPTPW (SEQ ID NO: 3)

Multidrug SMR transporter (*Escherichia coli*):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 4)

EmrE (*Mycobacterium tuberculosis*):

MYIRTQGEVLTYLFFPLCAIAEAAAATSLFKGSFGDFRVCSPGHGDAITAMPSVLAASRIRSS (SEQ ID
NO: 5)

EmrE protein (*Mycobacterium oryis*):

MIYLYLLCAIFAEVVATSLKSTEGFTRLWPTVGCLVGYGIAPALLALSISHGMQTDVAYALWSAIGTAAIV
LVAVLFLGSPISVMKVVGVLIVGVVTLNLAGAH (SEQ ID NO: 6)

Ethidium bromide resistance protein (*Enterobacter cloacae*):

MKGWFLVIAIVGEVIATSALKSSEGFTKLAPSAVVIIGYGIIFYFLSLVLKSIPVGVAYAVWSGLGVVIIT
AIAWLLHGQKLDAGFVGMGLIIAFLARSPSWKSLRRPTPW (SEQ ID NO: 7)

Orf3/QacEdelta1 fusion protein (*Klebsiella pneumoniae*):

MKGWFLVIAIVGEVIATSALKSSEGFTKLAPSAVVIIGYGIIFYFLSLVLKSIPVGVAYAVWSGLGVVIIT
AIAWLLHGQKLDAGFVGMGLIIAFLARSPSWKSLRRPTPW (SEQ ID NO: 8)

Antiseptic-resistance protein (*Escherichia coli*):

MKGWFLVIAIVGEVIATSALKSSEGFTKLAPSAVVIIGYGIIFYFLSLVLKSIPVGVAYAVWSGLGVVIIT
AIAWLLHGQKLDAGFVGMGLIIAFLARSPSWKSLRRPTPW (SEQ ID NO: 9)

Ethidium bromide resistance protein (*Pseudomonas aeruginosa*):

MKGWFLVIAIVGEVIATSALKSSEGFTKLAPSAVVIIGYGIIFYFLSLVLKSIPVGVAYAVWSGLGVVIIT
AIAWLLHGQKLDAGFVGMGLIIAFLARSPSWKSLRRPTPW (SEQ ID NO: 10)

Multidrug transporter (*Providencia rettgeri*):

MKGWLFVLVIAIVGEVIATSLKSSSEGFTKLAPSAVVIIGYGIIFYFLSLVLKSIPVGVAYAVWSGLGVVIIT
ATAWLLHGQKLDAGVFGMGLIIAFLARSPSWKSLRRPTPW (SEQ ID NO: 11)

Multidrug DMT transporter (*Pseudomonas citronellolis*):

5 MPGYLYLAIAIVAIVATASLKSVMKGLSTPLPLLLVIVGYAISFWMLTLVVRISIPVGIAYAIWAGLGIVLVS
VAALVLYQQKLDAPALLGMGLIVSGVVVIQLFSGSVSH (SEQ ID NO: 12)

Methyl viologen resistance protein C (*Pseudomonas aeruginosa*):

MTNYLYLAIAIAAEVATTSLKAVAGFSKPLPLLLVGGYVLAFSMLVLMRTLPVGVVYAIWSGLGIVLVS
LVAMFVYGQRLDPAALLGIGLIAGVLVIQLFSRASGH (SEQ ID NO: 13)

10 Methyl viologen resistance protein C (*Pseudomonas aeruginosa*):

MNPYIYLAAAIIVLEVIATSLKASDGMSRLWPTVAGLVGYGLCFYLLSVTMKSVPTGIAYAIWSGVGIVLIS
LIGLVVFKQRLDAPALIGIGLICAGVLVINLFSRSSAH (SEQ ID NO: 14)

Membrane transport protein (*Bordetella pertussis*):

15 MNSWIHLMAIAVAEIIATSLKSSSEGFTRLPLSLVTVAGYAIIFYFLALTLRVIPVGVAYAIWSGVGIVLIS
LVGALLFKQHLDLPAIIGIALILAGVVVMNVFSKSVGH (SEQ ID NO: 15)

Membrane transport protein (*Bordetella pertussis*):

MAGYAIIFYFLALTLRVIPVGVAYAIWSGVGIVLISLVGALLFKQHLDLPAIIGIALILAGVVVMNVFSKSV
GH (SEQ ID NO: 16)

Membrane transport protein (*Bordetella pertussis*):

20 MGVAIYAIWSGVGIVLISLVGALLFKQHLDLPAIIGIALILAGVVVMNVFSKSVGH (SEQ ID NO: 17)

Ethidium bromide-methyl viologen resistance protein EmrE (*Neisseria meningitidis* serogroup B):

MPLATAYAIWAGVGLVLTALVSVVFFGEKADFIGIVSIGLILLGVLLNTMSHMSGH (SEQ ID NO: 18)

Quaternary ammonium compound-resistance protein, small multidrug resistance protein family
(*Bacillus cereus* var. *anthracis* (strain CI)):

25 MKNKAWLYVILTCEFEVFWVFENTANTWWHIIILGVIAVDFHFLSKACEHLATGTVYAVFAGAGTVGTFL
MDVFLFGGSFSVGKLFIVMVVAGVIGLKLADNKEETVEGAA (SEQ ID NO: 19)

Quaternary ammonium compound-resistance protein QacC (*Staphylococcus aureus*):

MPYIYLIIAISTEVIGSAFLKSSEGFSKFIPSLGTIISFGICFYFLSKTMQHLPLNITYATWAGLGIVLTTV
VSIIFKEQINLITIVSIVLIIVGVVSLNIFGTSH (SEQ ID NO: 20)

30 Further exemplary polypeptides which include an α -helix include polypeptides which
include a sequence at least 80% identical to SEQ ID NO:1:

Membrane transporters of cations and cationic drugs domain-containing protein (*Fundulus
heteroclitus*):

35 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPALIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 21)

Multidrug transporter EmrE (*Escherichia coli* 2.3916):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPALIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 22)

Multidrug transporter EmrE (*Escherichia coli* UMN18):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 23)

QacE family quaternary ammonium compound efflux SMR transporter (Escherichia coli):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 24)

Multidrug transporter EmrE (Escherichia coli (strain K12)):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 25)

Hypothetical phage protein (Escherichia coli (strain SE11)):

10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 26)

Multidrug transporter EmrE (Escherichia coli H591):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 27)

15 **Multidrug transporter EmrE (Escherichia coli KTE75):**

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 28)

Multidrug transporter EmrE (Escherichia coli B088):

20 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 29)

EmrE protein (Escherichia coli (strain 55989/EAEC)):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 30)

Multidrug transporter EmrE (Escherichia coli 2-427-07_S4_C3):

25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 31)

Multidrug transporter EmrE (Escherichia coli 4.0967):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 32)

30 **Multidrug transporter EmrE (Escherichia coli 3-267-03_S4_C1):**

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 33)

Multidrug transporter (Escherichia coli O146:H21 str. 2010C-3325):

35 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 34)

Multidrug transporter EmrE (Escherichia coli MS 145-7):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 35)

Multidrug transporter EmrE (Escherichia coli 2-011-08_S1_C1):

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 36)
- Multidrug transporter EmrE (Escherichia coli KTE66):**
- 5 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 37)
- Multidrug transporter EmrE (Escherichia coli B185):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 38)
- EmrE protein (Escherichia coli O139:H28 (strain E24377A/ETEC)):**
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 39)
- Multidrug transporter EmrE (Escherichia coli 1-392-07_S4_C3):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 40)
- 15 **Multidrug transporter EmrE (Escherichia coli 1-392-07_S4_C1):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 41)
- Multidrug transporter EmrE (Escherichia coli UMEA 3718-1):**
- 20 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 42)
- Multidrug SMR transporter (Escherichia coli):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 43)
- Multidrug resistance protein DLP12 prophage (Escherichia coli NCCP15648):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 44)
- Multidrug efflux protein (Escherichia coli O83:H1 (strain NRG 857C/AIEC)):**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 45)
- 30 **Multidrug SMR transporter (Escherichia coli O157):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 46)
- Multidrug transporter EmrE (Escherichia coli KTE100):**
- 35 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 47)
- Multidrug transporter EmrE (Escherichia sp. KTE159):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 48)
- Multidrug efflux protein (Escherichia coli Xuzhou21):**

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 49)
- Ethidium bromide-methyl viologen resistance protein EmrE (Escherichia coli O157:H7 str. SS52):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 50)
- EmrE protein (Escherichia coli O157:H7 (strain EC869)):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 51)
- Multidrug SMR transporter (Escherichia coli):**
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 52)
- Integral membrane drug resistance protein EmrE (Escherichia coli O157:H7):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 53)
- 15 **Multidrug transporter EmrE (Escherichia coli):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDMPAIIIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 54)
- Multidrug transporter EmrE (Escherichia coli HVH 70 (4-2963531)):**
- MNPYIYLGGAILAQVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 55)
- Multidrug transporter EmrE (Escherichia coli (strain UMEA 3162-1)):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 56)
- Multidrug transporter EmrE (Escherichia coli 2-005-03_S4_C3):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 57)
- Multidrug transporter EmrE (Escherichia coli H420):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 58)
- 30 **Multidrug transporter EmrE (Escherichia coli DEC6A):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 59)
- Multidrug transporter EmrE (Escherichia coli 97.0246):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 60)
- Multidrug efflux protein (Escherichia coli O104:H4 (strain 2011C-3493)):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 61)
- Multidrug efflux protein (Escherichia coli O111:H8 str. CVM9634):**

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 62)

Multidrug transporter EmrE (Escherichia coli KTE73):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 63)

Multidrug transporter EmrE (Escherichia coli HVH 70 (4-2963531)):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 64)

Multidrug transporter EmrE (Escherichia coli UMNK88):

10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 65)

Multidrug transporter (Escherichia fergusonii):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 66)

15 **Multidrug transporter EmrE (Escherichia coli B088):**

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 67)

Ethidium bromide-methyl viologen resistance protein EmrE (Escherichia coli ISC7):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 68)

Multidrug transporter EmrE (Escherichia coli TA054):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 69)

Multidrug transporter (Escherichia coli ATCC BAA-2209):

25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 70)

Multidrug transporter EmrE (Escherichia sp. KTE114):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 71)

30 **Multidrug transporter EmrE (Escherichia coli HVH 25 (4-5851939)):**

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 72)

Multidrug transporter EmrE (Escherichia coli H461):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 73)

Multidrug transporter EmrE (Escherichia coli M718):

MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 74)

Methyl viologen resistance protein C (Achromobacter sp.):

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 75)
- Multidrug transporter EmrE (Escherichia coli KOEGE 71 (186a)):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 76)
- Multidrug transporter EmrE (Escherichia coli 2-427-07_S4_C3):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 77)
- Multidrug transporter (Escherichia coli O111:NM str. K6722):**
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 78)
- Quaternary ammonium transporter (Escherichia coli APEC O2-211):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 79)
- Multidrug transporter EmrE (Escherichia coli KTE21):**
- 15 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 80)
- Multidrug resistance protein (Escherichia coli (strain ATCC 9637/CCM 2024/DSM 1116/NCIMB 8666/NRRL B-766/W)):**
- 20 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 81)
- Multidrug transporter EmrE (Escherichia coli 2-177-06_S3_C3):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 82)
- Multidrug transporter EmrE (Escherichia coli 3-267-03_S4_C1):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 83)
- Multidrug transporter EmrE (Escherichia coli HVH 50 (4-2593475)):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
30 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 84)
- Multidrug transporter EmrE (Escherichia coli 1.2264):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 85)
- Multidrug transporter EmrE (Shigella flexneri K-227):**
- 35 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 86)
- Multidrug transporter EmrE (Shigella flexneri 2a str. 301):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPH (SEQ ID NO: 87)
- Methylviologen resistance (Shigella sunnier (strain Ss046)):**
- 40

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 88)
- Multidrug transporter (Escherichia coli O174:H8 str. 04-3038):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 89)
- Multidrug transporter EmrE (Escherichia coli KTE108):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 90)
- Methylviologen resistance (Escherichia coli G3/10):**
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 91)
- Small Multidrug Resistance protein (Escherichia coli TW10509):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 92)
- 15 **Multidrug transporter EmrE (Escherichia coli 4.0522):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 93)
- Integral membrane drug resistance protein EmrE (Escherichia coli O111:H- (strain 11128/EHEC)):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 94)
- Multidrug transporter EmrE (Escherichia coli KTE20):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 95)
- Multidrug transporter EmrE (Escherichia coli 2-005-03_S4_C2):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 96)
- Multidrug transporter EmrE (Escherichia coli M605):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 97)
- 30 **Multidrug transporter EmrE (Escherichia coli TA447):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 98)
- Multidrug SMR transporter (Escherichia coli O104:H4):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 99)
- Multidrug transporter EmrE (Escherichia coli UMEA 3212-1):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSAHP (SEQ ID NO: 100)
- Multidrug transporter EmrE (Escherichia coli 2-177-06_S3_C2):**

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 101)
- Multidrug transporter EmrE (Escherichia coli 99.0741):**
- 5 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 102)
- Multidrug transporter EmrE (Escherichia coli UMEA 3323-1):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 103)
- Multidrug transporter EmrE (Escherichia coli KTE10):**
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 104)
- Multidrug transporter EmrE (Escherichia coli KTE182):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 105)
- 15 **Multidrug transporter EmrE (Escherichia coli H386):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 106)
- Multidrug efflux protein (Escherichia coli O83:H1 (strain NRG 857C/AIEC)):**
- 20 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 107)
- Multidrug transporter EmrE (Escherichia coli 1-392-07_S4_C3):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 108)
- Multidrug transporter EmrE (Escherichia coli 1-392-07_S4_C1):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 109)
- Multidrug transporter EmrE (Escherichia coli 1-176-05_S3_C2):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 110)
- 30 **Multidrug transporter (Escherichia coli O25b:H4-ST131):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 111)
- Multidrug transporter EmrE (Shigella flexneri VA-6):**
- 35 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 112)
- Multidrug transporter EmrE (Escherichia coli H736):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 113)
- Multidrug SMR transporter (Shigella flexneri 4c):**

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 114)
- Multidrug SMR transporter (*Shigella flexneri*):**
- 5 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 115)
- Multidrug SMR transporter (*Escherichia coli*):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 116)
- Multidrug SMR transporter (*Shigella sonnei*):**
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 117)
- Multidrug transporter EmrE (*Escherichia coli* H605):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 118)
- 15 **Quaternary ammonium transporter (*Escherichia coli* APEC O18):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 119)
- Multidrug transporter (*Escherichia coli* N40513):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 120)
- Multidrug transporter (*Escherichia coli* N40607):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 121)
- Multidrug resistance protein DLP12 prophage (*Escherichia coli* NCCP15648):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 122)
- Multidrug transporter (*Escherichia coli* N36254PS):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 123)
- 30 **Multidrug SMR transporter (*Shigella boydii*):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 124)
- Multidrug SMR transporter (*Shigella flexneri* 1a):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 125)
- Multidrug transporter EmrE (*Escherichia coli* MS 84-1):**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 126)
- Multidrug transporter EmrE (*Escherichia coli* MS 124-1):**

- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 127)
- Multidrug transporter EmrE (Escherichia coli 110957):**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
5 VGIVLISLLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 128)
- Multidrug transporter EmrE (Escherichia coli MS 85-1):**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 129)
- Multidrug transporter EmrE (Escherichia coli MS 117-3):**
- 10 MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 130)
- Multidrug transporter EmrE (Escherichia coli 909945-2):**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 131)
- Multidrug transporter EmrE (Escherichia coli 113290):**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 132)
- Multidrug transporter EmrE (Escherichia coli MS 115-1):**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
20 VGIVLISLLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 133)
- Multidrug transporter EmrE (Escherichia coli (strain MS 21-1)):**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 134)
- Multidrug transporter EmrE (Escherichia sp. KTE52):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
LLSWGLFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 135)
- Uncharacterized protein (Escherichia fergusonii ECD227):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
LLSWGLFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 136)
- EmrE SMR transporter (Escherichia coli O55:H7 (strain CB9615/EPEC)):**
- 30 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
LLSWGLFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 137)
- SMR family multidrug resistance protein (Klebsiella oxytoca):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
35 LLSWGLFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 138)
- Multidrug transporter (Escherichia coli O128:H2 str. 2011C-3317):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
LLSWGLFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 139)
- Multidrug efflux protein (Escherichia coli O157:H7 str. SS52):**

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 140)
- Multidrug transporter EmrE (Escherichia coli 97.0259):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 141)
- Multidrug transporter EmrE (Escherichia coli 9.0111):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 142)
- Multidrug SMR transporter (Escherichia coli):**
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 143)
- Multidrug transporter (Escherichia coli N37139PS):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 144)
- 15 **Multidrug transporter (Escherichia coli N36410PS):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 145)
- Multidrug transporter (Escherichia coli N37122PS):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 146)
- Multidrug transporter EmrE (Escherichia sp. KTE31):**
- MNPYIYLGGAILAEVIGTTLMKYSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 147)
- Multidrug SMR transporter (Escherichia coli):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 148)
- Multidrug transporter EmrE (Escherichia coli KTE33):**
- MNPYIYLGGAILAEVIGTTLMKYSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 149)
- 30 **Multidrug transporter EmrE (Shigella flexneri 2850-71):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICTGVLVINLLSRSTPH (SEQ ID NO: 150)
- Multidrug transporter EmrE (Escherichia sp. KTE11):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCTSEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 151)
- Multidrug transporter EmrE (Escherichia sp. KTE52):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCTSEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 152)
- Multidrug transporter EmrE (Escherichia sp. KTE96):**

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 153)
- Multidrug transporter EmrE (Escherichia sp. KTE159):**
- 5 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 154)
- QacE family quaternary ammonium compound efflux SMR transporter (Escherichia coli):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSAGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 155)
- Multidrug SMR transporter (Escherichia coli):**
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 156)
- Multidrug SMR transporter (Shigella sonnei):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 157)
- 15 **Multidrug SMR transporter (Shigella sonnei):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 158)
- Multidrug transporter EmrE (Escherichia coli E1118):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 159)
- Multidrug transporter EmrE (Escherichia coli KTE108):**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFVQRLDLPAAIGMMLICAGVLVINLLRSSTPH (SEQ ID NO: 160)
- Multidrug transporter (Shigella sp. PAMC 28760):**
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYGIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSSTPH (SEQ ID NO: 161)
- Multidrug SMR transporter (Escherichia coli BL21-DE3)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYGIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSSTPH (SEQ ID NO: 162)
- 30 **Multidrug transporter (Escherichia coli SE11)**
- MNSFVSLGFLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
TTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLDLPAAI
GMMLICAGVLVINLLRSAPH (SEQ ID NO: 163)
- Methylviologen transporter EmrE (Shigella flexneri strain 8401)**
- 35 MNSFVSLGFLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
TTLMKFSEGFTRLWPSVGTTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLDLPAAI
GMMLICAGVLVINLLRSAPH (SEQ ID NO: 164)
- Multidrug transporter EmrE (Escherichia coli O1:K1)**

MNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
 TTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLDLPAT
 GMMLICAGVLVINLLSRSAPH (SEQ ID NO: 165)

Multidrug transporter EmrE (Shigella flexneri strain 2002017)

5 MNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
 TTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLDLPAT
 GMMLICAGVLVINLLSRSAPH (SEQ ID NO: 166)

Multidrug transporter EmrE (Shigella sonnei)

10 MNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
 TTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLDLPAT
 GMMLICAGVLVINLLSRSAPH (SEQ ID NO: 167)

Multidrug transporter EmrE (Escherichia coli O45:K1)

15 MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLSRSAPH (SEQ ID NO: 168)

Multidrug transporter EmrE (Escherichia coli strain 55989)

MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLSRSAPH (SEQ ID NO: 169)

20 **Multidrug transporter EmrE (Escherichia coli O8 strain ED1a)**

MLIGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLSRSAPH (SEQ ID NO: 170)

Multidrug transporter EmrE (Escherichia coli strain UTI89/UPEC)

25 MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLSRSAPH (SEQ ID NO: 171)

Multidrug transporter EmrE (Escherichia coli O6:H1 strain CFT073)

30 MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLSRSAPH (SEQ ID NO: 172)

Multidrug transporter EmrE (Escherichia coli O25b:H4)

35 MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENSELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLSRSAPH (SEQ ID NO: 173)

Multidrug transporter EmrE (Escherichia coli O25b:H4-ST131)

MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENSELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLSRSAPH (SEQ ID NO: 174)

40 **Multidrug transporter EmrE (Escherichia coli TW10598)**

- MLIGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
AEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 175)
- Multidrug transporter EmrE (Escherichia coli 1.2741)**
- 5 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFSQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 176)
- Multidrug SMR transporter (Escherichia coli M863)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFSQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 177)
- 10 **Multidrug SMR transporter (Escherichia coli)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFSQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 178)
- Multidrug SMR transporter (Shigella sonnei)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPKGIAYAIWSGVGIVLIS
15 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 179)
- Multidrug SMR transporter (Escherichia coli)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPKGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 180)
- Multidrug transporter EmrE (Escherichia coli DORA_B_14)**
- 20 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPN (SEQ ID NO: 181)
- Multidrug transporter EmrE (Escherichia coli)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPN (SEQ ID NO: 182)
- 25 **Multidrug transporter EmrE (Escherichia coli 908573)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLDQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 183)
- Multidrug SMR transporter (Shigella sp. FC2928)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
30 LLSWGFFGQRLDLSAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 184)
- Multidrug transporter EmrE (Escherichia coli HVH 41)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLDQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 185)
- QacE quaternary ammonium compound efflux SMR transporter (Escherichia coli)**
- 35 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLDQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 186)
- Multidrug SMR transporter (Shigella boydii)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLDQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 187)
- 40 **Multidrug SMR transporter (Shigella dysenteriae)**

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYYASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 188)
Multidrug transporter EmrE (Shigella dysenteriae)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYYASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 189)
Multidrug transporter EmrE (Escherichia sp. KTE11)
- MNPYIYLGGAIFAEVIGTTLMKYSDGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMILICAGVLVINLLRSAPH (SEQ ID NO: 190)
Multidrug transporter EmrE (Escherichia albertii B156)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGIFGQRLDLPAAIGMMLICAGVLVINLLRSATH (SEQ ID NO: 191)
Multidrug transporter EmrE (Escherichia sp. KTE96)
- MNPYIYLGGAIFAEVIGTTLMKYSDGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMILICAGVLVINLLRSAPH (SEQ ID NO: 192)
Multidrug transporter EmrE (Escherichia sp. KTE159)
- 15 MNPYIYLGGAIFAEVIGTTLMKYSDGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMILICAGVLVINLLRSAPH (SEQ ID NO: 193)
Multidrug SMR transporter (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSRGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 194)
Multidrug transporter EmrE (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGIFGQRLDLPAAIGMMLICAGVLVINLLRSATH (SEQ ID NO: 195)
Multidrug transporter EmrE (Escherichia albertii)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGIFGQRLDLPAAIGMMLICAGVLVINLLRSATH (SEQ ID NO: 196)
Multidrug transporter EmrE (Escherichia coli E1118)
- MNPYIYLGGAIFAEVIGTTLMKYSDGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMILICAGVLVINLLRSAPH (SEQ ID NO: 197)
Ethidium bromide-methyl viologen transporter EmrE (Escherichia albertii KF1)
- 30 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGIFGQRLDLPAAIGMMLICAGVLVINLFSRSATH (SEQ ID NO: 198)
Multidrug transporter EmrE (Escherichia albertii)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGIFGQRLDLPAAIGMMLICAGVLVINLLRSATH (SEQ ID NO: 199)
Multidrug transporter EmrE (Escherichia sp. KTE52)
- MNPYIYLGGAIFAEVIGTTLMKYSDGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLFWGFFGQRLDLPAAIGMILICAGVLVINLLRSAPH (SEQ ID NO: 200)
Multidrug transporter EmrE (Escherichia albertii strain TW07627)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIANAIWSGVGIVLIS
LLSWGIFGQRLDLPAAIGMMLICAGVLVINLLRSATH (SEQ ID NO: 201)
- Multidrug transporter EmrE (Shigella sonnei)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLGDAAANLLI (SEQ ID NO: 202)
- Multidrug transporter EmrE (Shigella flexneri 5a strain M90T)**
- MNSFVSLGFLLIIVPAFISCHARAPWIIHQDENGELCSNCSSTILSSMNRKEYAMNPYIYLGGAILAEVIG
TTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLDLPAAI
GMMLICAYYG (SEQ ID NO: 203)
- 10 **Multidrug transporter EmrE (Citrobacter sp. MGH106)**
- MNTYIYLGAAILAEVIGTTLMKFDTGFTRLWPSVGTTIICYCASFWLLSQTLAHIPTGIAYAIWSGVGIVLIS
LLAWVIHQRLDLPAAIGMALICAGVLIINLLRSASVH (SEQ ID NO: 204)
- Multidrug SMR transporter (Escherichia coli)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSAGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
15 LLSWGFFGQRLDLPAAIDTVMACKFFPGPVSR (SEQ ID NO: 205)
- Multidrug SMR transporter (Paenibacillus sp. VT-16-81)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQR (SEQ ID NO: 206)
- Ethidium bromide-methyl viologen EmrE transporter (Klebsiella pneumoniae)**
- 20 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYGIWSGVGIVLIS
LLSWGFFLPTAGPASHYRHDVLDLCRCVGY (SEQ ID NO: 207)
- Multidrug SMR transporter (Shigella sonnei)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVRYCPD
(SEQ ID NO: 208)
- 25 **Multidrug transporter EmrE (Escherichia coli)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWYMRTFISCK
R (SEQ ID NO: 209)
- Futher exemplary polypeptides which include an α -helix include polypeptides which
include a sequence at least 80% identical to PAIIGMMLICAG (SEQ ID NO: 210):
- 30 **Multidrug transporter EmrE (Escherichia coli O104:H4 strain 2011C-3493)**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWYM
RTFISCKR (SEQ ID NO: 211)
- Membrane transporters of cations (Fundulus heteroclitus)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 212)
- Multidrug transporter EmrE (Escherichia coli 2.3916)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 213)
- Multidrug transporter EmrE (Escherichia coli UMN18)**

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 214)
- QacE family quaternary ammonium compound efflux SMR transporter (Escherichia coli)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 215)
- Multidrug transporter EmrE (Escherichia coli strain K12)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLIINLLSRSTPH (SEQ ID NO: 216)
- Multidrug SMR transporter (Shigella sonnei)**
- 10 MLSGQESGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 217)
- Multidrug transporter EmrE (Escherichia coli strain UMEA 3162-1)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 218)
- Multidrug transporter EmrE (Escherichia sp. KTE11)**
- 15 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 219)
- Multidrug transporter EmrE (Escherichia sp. KTE52)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 220)
- 20 **Multidrug transporter EmrE (Escherichia sp. KTE52)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 221)
- Multidrug SMR transporter (Escherichia coli strain SE11)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
25 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 222)
- Multidrug transporter EmrE (Escherichia coli 2-005-03_S4_C3)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 223)
- Multidrug transporter EmrE (Escherichia coli H420)**
- 30 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 224)
- Multidrug transporter EmrE (Escherichia coli DEC6A)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 225)
- 35 **Multidrug transporter EmrE (Escherichia coli 97.0246)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 226)
- Multidrug transporter EmrE (Escherichia coli O104:H4 strain 2011C-3493)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
40 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 227)

- Multidrug transporter EmrE (*Escherichia coli* H591)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 228)
- Multidrug SMR transporter (*Escherichia fergusonii* ECD227)
 5 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 229)
- Multidrug transporter EmrE (*Escherichia coli* O111:H8 str. CVM9634)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 230)
- 10 Multidrug transporter EmrE (*Escherichia coli* O55:H7 strain CB9615/EPEC)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 231)
- Multidrug transporter EmrE (*Escherichia coli* KTE73)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 15 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 232)
- Multidrug transporter EmrE (*Escherichia coli* KTE75)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 233)
- Multidrug transporter EmrE (*Escherichia coli* HVH 70 4-2963531)
 20 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 234)
- Multidrug transporter EmrE (*Klebsiella oxytoca*)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 235)
- 25 Multidrug transporter EmrE (*Escherichia coli* HVH 70 4-2963531)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 236)
- Multidrug transporter EmrE (*Escherichia coli* 1.2741)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 30 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 237)
- Multidrug transporter EmrE (*Escherichia coli* UMNK88)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 238)
- Multidrug SMR transporter (*Escherichia fergusonii*)
 35 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 239)
- Multidrug transporter EmrE (*Escherichia coli* B088)
 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 240)
- 40 Multidrug transporter EmrE (*Escherichia coli* B088)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 241)
Multidrug transporter EmrE (Escherichia coli strain 55989/EAEC)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 242)
Ethidium bromide-methyl viologen transporter EmrE (Escherichia coli ISC7)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 243)
Multidrug transporter EmrE (Escherichia coli TA054)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 244)
Multidrug transporter EmrE (Escherichia coli ATCC BAA-2209)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 245)
15 **Multidrug transporter EmrE (Escherichia albertii B156)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGIFGQRLDLPAAIGMMLICAGVLVINLLSR SATH (SEQ ID NO: 246)
Multidrug transporter EmrE (Escherichia sp. KTE96)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 247)
Multidrug transporter EmrE (Escherichia sp. KTE114)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 248)
Multidrug transporter EmrE (Escherichia coli HVH 25 4-5851939)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 249)
Multidrug transporter EmrE (Escherichia coli H461)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 250)
30 **Multidrug transporter EmrE (Escherichia coli M718)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 251)
Methyl viologen transporter EmrE (Achromobacter sp.)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 252)
Multidrug transporter EmrE (Escherichia coli 2-427-07_S4_C3)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 253)
Multidrug transporter EmrE (Escherichia coli KOEGE 71 186a)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 254)
Multidrug transporter EmrE (Escherichia coli 2-427-07_S4_C3)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 255)
Multidrug SMR transporter (Escherichia coli O111:NM strain K6722)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 256)
Quaternary ammonium transporter (Escherichia coli APEC O2-211)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 257)
Multidrug transporter EmrE (Escherichia coli KTE21)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 258)
15 **Multidrug SMR transporter (Escherichia coli O128:H2 strain 2011C-3317)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 259)
Multidrug SMR transporter (Shigella dysenteriae)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 260)
Multidrug transporter EmrE (Escherichia coli 4.0967)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 261)
Multidrug transporter EmrE (Escherichia sp. KTE159)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 262)
Multidrug transporter EmrE (Escherichia coli strain ATCC 9637)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 263)
30 **Multidrug transporter EmrE (Escherichia coli 3-267-03_S4_C1)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 264)
Multidrug transporter EmrE (Escherichia coli 2-177-06_S3_C3)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 265)
Multidrug transporter EmrE (Escherichia coli 3-267-03_S4_C1)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 266)
Multidrug transporter EmrE (Escherichia coli HVH 50 4-2593475)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 267)
Multidrug transporter EmrE (Escherichia coli 1.2264)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 268)
Multidrug transporter EmrE (Shigella flexneri K-227)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 269)
Multidrug SMR transporter (Escherichia coli O146:H21 strain 2010C-3325)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 270)
Multidrug transporter EmrE (Shigella flexneri 2a strain 301)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 271)
- 15 **Methylviologen resistance transporter EmrE (Shigella sonnei strain Ss046)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 272)
Multidrug SMR transporter (Escherichia coli O174:H8 strain 04-3038)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 273)
Multidrug transporter EmrE (Escherichia coli KTE108)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 274)
Multidrug transporter EmrE (Escherichia coli O157:H7 strain SS52)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 275)
Multidrug transporter EmrE (Escherichia coli MS 145-7)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 276)
- 30 **Multidrug transporter EmrE (Shigella dysenteriae 225-75)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYYASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 277)
Multidrug transporter EmrE (Escherichia coli 908573)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFLFDQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 278)
Methylviologen transporter (Escherichia coli G3/10)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 279)
Multidrug transporter EmrE (Escherichia coli HVH 41 4-2677849)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLDQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 280)
Multidrug SMR transporter (Escherichia coli M863)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFSQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 281)
Multidrug SMR transporter (Escherichia coli TW10509)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 282)
Multidrug transporter EmrE (Escherichia coli 4.0522)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 283)
Multidrug transporter EmrE (Escherichia coli O111:H- strain 11128/EHEC)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 284)
Multidrug transporter EmrE (Escherichia coli KTE20)
- 15 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 285)
Multidrug transporter EmrE (Escherichia coli 2-005-03_S4_C2)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 286)
Multidrug transporter EmrE (Escherichia sp. KTE31)
- MNPYIYLGGAILAEVIGTTLMKYSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 287)
Multidrug transporter EmrE (Escherichia coli M605)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 288)
Multidrug transporter EmrE (Escherichia coli TA447)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 289)
Multidrug SMR transporter (Escherichia coli O104:H4)
- 30 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 290)
Multidrug transporter EmrE (Escherichia albertii strain TW07627)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIANAIWSGVGIVLIS
35 LLSWGIFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 291)
Multidrug SMR transporter (Shigella sp. PAMC 28760)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCSFWLLAQTLAYIPTGIAYGIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 292)
Multidrug transporter EmrE (Escherichia coli 2-011-08_S1_C1)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 293)
Multidrug transporter EmrE (Escherichia coli UMEA 3212-1)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 294)
Multidrug transporter EmrE (Escherichia coli 2-177-06_S3_C2)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 295)
Multidrug transporter EmrE (Escherichia coli 97.0259)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 296)
Multidrug transporter EmrE (Escherichia coli 99.0741)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 297)
Multidrug transporter EmrE (Escherichia coli KTE66)
- 15 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 298)
Multidrug transporter EmrE (Escherichia coli B185)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 299)
Multidrug transporter EmrE (Escherichia coli O139:H28 strain E24377A/ETEC)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 300)
Multidrug transporter EmrE (Escherichia coli UMEA 3323-1)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 301)
Multidrug transporter EmrE (Escherichia coli KTE10)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 302)
Multidrug transporter EmrE (Escherichia coli 9.0111)
- 30 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 303)
Multidrug transporter EmrE (Escherichia coli KTE182)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 304)
Multidrug transporter EmrE (Escherichia coli H386)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 305)
Multidrug transporter EmrE (Escherichia coli O83:H1 strain NRG 857C/AIEC)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 306)
Multidrug transporter EmrE (Escherichia coli 1-392-07_S4_C3)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 307)
Multidrug transporter EmrE (Escherichia coli 1-392-07_S4_C1)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 308)
Multidrug transporter EmrE (Escherichia coli 1-392-07_S4_C3)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 309)
Multidrug transporter EmrE (Escherichia coli 1-392-07_S4_C1)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 310)
Multidrug transporter EmrE (Escherichia coli 1-176-05_S3_C2)
- 15 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 311)
Multidrug transporter EmrE (Escherichia coli UMEA 3718-1)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 312)
Multidrug SMR transporter (Escherichia coli strain B/BL21-DE3)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYGIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 313)
Multidrug SMR transporter (Escherichia coli)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSRGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 314)
QacE family quaternary ammonium compound efflux SMR transporter (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSAGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 315)
Multidrug transporter EmrE (Escherichia coli)
- 30 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGIFGQRLDLPAAIGMMLICAGVLVINLLRSATH (SEQ ID NO: 316)
QacE family quaternary ammonium compound efflux SMR transporter (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFLFDQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 317)
Multidrug SMR transporter (Escherichia coli O25b:H4-ST131)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSRAPH (SEQ ID NO: 318)
Multidrug SMR transporter (Escherichia coli)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFSQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 319)
Multidrug SMR transporter (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCTSFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 320)
Multidrug transporter EmrE (Escherichia coli KTE33)
- MNPYIYLGGAILAEVIGTTLMKYSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 321)
Multidrug transporter EmrE (Shigella flexneri VA-6)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 322)
Multidrug transporter EmrE (Escherichia coli H736)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 323)
Multidrug SMR transporter (Shigella flexneri 4c)
- 15 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 324)
Multidrug SMR transporter (Shigella flexneri)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 325)
Multidrug SMR transporter (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 326)
Multidrug transporter EmrE (Escherichia coli)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 327)
Multidrug transporter EmrE (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 328)
Multidrug transporter EmrE (Shigella sonnei)
- 30 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 329)
Multidrug transporter EmrE (Escherichia coli DORA_B_14)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPATIGMMLICAGVLVINLLRSAPN (SEQ ID NO: 330)
Multidrug SMR transporter (Escherichia coli N37139PS)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 331)
Multidrug transporter EmrE (Escherichia coli N36410PS)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 332)
Multidrug transporter EmrE (Escherichia coli H605)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 333)
Quaternary ammonium transporter (Escherichia coli APEC O18)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 334)
Multidrug transporter EmrE (Escherichia coli N40513)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 335)
Multidrug transporter EmrE (Escherichia albertii)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCTSEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGIFGQRLDLPATIGMMLICAGVLVINLLSR SATH (SEQ ID NO: 336)
15 **Multidrug transporter EmrE (Escherichia albertii)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGIFGQRLDLPATIGMMLICAGVLVINLLSR SATH (SEQ ID NO: 337)
Multidrug transporter EmrE (Escherichia coli N40607)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 338)
Multidrug SMR transporter (Escherichia coli NCCP15648)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 339)
Multidrug SMR transporter (Escherichia coli NCCP15648)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 340)
Multidrug transporter EmrE (Escherichia coli N36254PS)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 341)
30 **Multidrug SMR transporter (Shigella sonnei)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIG
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 342)
Multidrug SMR transporter (Shigella sonnei)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASFWLLAQTLAYIPKGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 343)
Multidrug SMR transporter (Shigella sonnei)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCTSEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPATIGMMLICAGVLVINLLSR SAPH (SEQ ID NO: 344)
Multidrug transporter EmrE (Escherichia coli N37122PS)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLFGQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 345)
Multidrug transporter EmrE (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 346)
Multidrug SMR transporter (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPKGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 347)
Multidrug transporter EmrE (Escherichia coli E1118)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCTSEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 348)
Multidrug SMR transporter (Shigella boydii)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFLFDQRLDLPAAIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 349)
- 15 **Multidrug SMR transporter (Shigella boydii)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 350)
Multidrug SMR transporter (Shigella flexneri 1a)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 351)
Multidrug transporter EmrE (Escherichia coli MS 84-1)
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 352)
Multidrug transporter EmrE (Escherichia coli MS 124-1)
- 25 MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 353)
Multidrug transporter EmrE (Escherichia coli 110957)
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 354)
- 30 **Multidrug transporter EmrE (Escherichia coli MS 85-1)**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 355)
Multidrug transporter EmrE (Escherichia coli MS 117-3)
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSG
35 VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 356)
Multidrug transporter EmrE (Escherichia coli 909945-2)
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLSRAPN (SEQ ID NO: 357)
Multidrug transporter EmrE (Escherichia coli 113290)

- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 358)
- Multidrug transporter EmrE (Escherichia coli O83:H1 strain NRG 857C/AIEC)**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
5 VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSSTPH (SEQ ID NO: 359)
- Multidrug transporter EmrE (Escherichia coli MS 115-1)**
- MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 360)
- Multidrug transporter EmrE (Escherichia coli strain MS 21-1)**
- 10 MNRKEYAMNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSG
VGIVLISLLSWGFFGQRLDLPAAIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 361)
- Multidrug SMR transporter (Escherichia coli strain SE11)**
- MNSFVSLGFLLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
TTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGVIVLISLLSWGFFGQRLDLPAAI
15 GMLICAGVLVINLLRSAPH (SEQ ID NO: 362)
- Methylviologen resistance transporter EmrE (Shigella flexneri serotype 5b strain 8401)**
- MNSFVSLGFLLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
TTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGVIVLISLLSWGFFGQRLDLPAAI
GMLICAGVLVINLLRSAPH (SEQ ID NO: 363)
- 20 **Multidrug transporter EmrE (Escherichia coli O1:K1/APEC)**
- MNSFVSLGFLLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
TTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGVIVLISLLSWGFFGQRLDLPAAI
GMLICAGVLVINLLRSAPH (SEQ ID NO: 364)
- Multidrug transporter EmrE (Shigella flexneri serotype X strain 2002017)**
- 25 MNSFVSLGFLLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
TTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGVIVLISLLSWGFFGQRLDLPAAI
GMLICAGVLVINLLRSAPH (SEQ ID NO: 365)
- Multidrug transporter EmrE (Shigella sonnei)**
- MNSFVSLGFLLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAILAEVIG
30 TTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGVIVLISLLSWGFFGQRLDLPAAI
GMLICAGVLVINLLRSAPH (SEQ ID NO: 366)
- Multidrug transporter EmrE (Escherichia coli O45:K1 strain S88/ExPEC)**
- MLPGRVNSFVSLGFLLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGVIVLISLLSWGFFGQRLD
35 LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 367)
- Multidrug transporter EmrE (Escherichia coli strain 55989/EAEC)**
- MLPGRVNSFVSLGFLLLIIVPAFISCHARAPWIIHQDENGELCSNCSTILSSMNRKEYAMNPYIYLGGAIL
AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGVIVLISLLSWGFFGQRLD
LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 368)
- 40 **Multidrug transporter EmrE (Escherichia coli O81 strain ED1a)**

MLIGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGE LCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 369)

Multidrug transporter EmrE (Escherichia coli strain UTI89/UPEC)

5 MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGE LCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 370)

Multidrug transporter EmrE (Escherichia coli O6:H1 strain CFT073)

10 MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGE LCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 371)

Multidrug transporter EmrE (Escherichia coli O25b:H4)

15 MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGE LCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 372)

Multidrug transporter EmrE (Escherichia coli O25b:H4-ST131)

20 MLPGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGE LCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 373)

Multidrug transporter EmrE (Escherichia coli TW10598)

25 MLIGRVNSFVSLGFLLLIIIVPAFISCHARAPWIIHQDENGE LCSNCSTILSSMNRKEYAMNPYIYLGGAIL
 AEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLISLLSWGFFGQRLD
 LPAIIGMMLICAGVLVINLLRSAPH (SEQ ID NO: 374)

Multidrug SMR transporter (Escherichia coli O157)

30 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLD LPAVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 375)

Multidrug transporter EmrE (Escherichia coli KTE100)

35 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLD LPAVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 376)

Multidrug transporter EmrE (Escherichia sp. KTE159)

40 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLD LPAVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 377)

Multidrug transporter EmrE (Escherichia coli Xuzhou21)

45 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFGQRLD LPAVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 378)

Multidrug transporter EmrE (Escherichia coli KTE108)

50 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
 LLSWGFFVQRLD LPAVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 379)

Ethidium bromide-methyl viologen transporter EmrE (Escherichia coli O157:H7 strain SS52)

- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 380)
Multidrug transporter EmrE (Escherichia coli O157:H7 strain EC869)
- 5 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 381)
Multidrug SMR transporter (Escherichia coli)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 382)
Multidrug SMR transporter (Escherichia coli)
- 10 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 383)
Multidrug transporter EmrE (Escherichia coli O157:H7)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 384)
- 15 **Multidrug transporter EmrE (Escherichia coli)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDMPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 385)
Multidrug transporter EmrE (Shigella flexneri 2850-71)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
20 LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 386)
Ethidium bromide-methyl viologen transporter EmrE (Escherichia albertii KF1)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 387)
Multidrug SMR transporter (Shigella sp. FC2928)
- 25 MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 388)
Multidrug transporter EmrE (Citrobacter sp. MGH106)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 389)
- 30 **Multidrug transporter EmrE (Escherichia sp. KTE11)**
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 390)
Multidrug transporter EmrE (Escherichia sp. KTE52)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
35 LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 391)
Multidrug transporter EmrE (Escherichia sp. KTE96)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTTICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPVIGMMLICAGVLVINLLSRSTPH (SEQ ID NO: 392)
Multidrug transporter EmrE (Escherichia sp. KTE159)

- MNPYIYLGGAIFAEVIGTTLMKYSDGFTRLWPSVGTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMILICAGVLVINLLSRSAPH (SEQ ID NO: 393)
Multidrug transporter EmrE (Escherichia coli E1118)
- MNPYIYLGGAIFAEVIGTTLMKYSDGFTRLWPSVGTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
5 LLSWGFFGQRLDLPAAIGMILICAGVLVINLLSRSAPH (SEQ ID NO: 394)
Multidrug transporter EmrE (Shigella sonnei)
- MNPYIYLGGAILAEVIGTTLMKFSEGFTRLWPSVGTIICYCASEFWLLAQTLAYIPTGIAYAIWSGVGIVLIS
LLSWGFFGQRLDLPAAIGMMLICAGVLVINLGDAAANLLI (SEQ ID NO: 395)
Multidrug DMT transporter (Shigella sp. FC1967)
- 10 MVFSRLYPSIVVVIGYCLSEFWALSQVVRVMPGLIAYAIWSGLGIVLVSVAAVFLYQQKLDLPAAIGMSLIIA
GVLVINLLSKSASH (SEQ ID NO: 396)
Multidrug DMT transporter (Shigella sp. FC130)
- MNGLTYLMLAIISEVIATTMLKASDGFSLYPSIVVVIGYCLSEFWALSQVVRVMPGLIAYAIWSGLGIVLVSV
VAAVFLYQQKLDLPAAIGMSLIAGVLVINLLSKSASH (SEQ ID NO: 397)
Multidrug DMT transporter (Shigella sp. FC1655)
- 15 MNGLTYLMLAIISEVIATTMLKASDGFSLYPSIVVVIGYCLSEFWALSQVVRVMPGLIAYAIWSGLGIVLVSV
VAAVFLYQQKLDLPAAIGMSLIAGVLVINLLSKSASH (SEQ ID NO: 398)
Multidrug transporter EmrE (Serratia plymuthica 4Rx13)
- MSGFIYLTMAIVAIEVIATTMLKASEGFTRLWPSLVVVVGYYAVAFWGLSMVVKTMPLGIVYAIWSGMGIVLVSV
20 IAAVFVYQQKLDLPAVIGMVLIAGVLVINLLSKTAAH (SEQ ID NO: 399)
Multidrug DMT transporter (Serratia plymuthica S13)
- MSGFIYLTMAIVAIEVIATTMLKASEGFTRLWPSLVVVVGYYAVAFWGLSMVVKTMPLGIVYAIWSGMGIVLVSV
IAAVFVYQQKLDLPAVIGMVLIAGVLVINLLSKTAAH (SEQ ID NO: 400)
Multidrug transporter EmrE (Proteus vulgaris)
- 25 MNGLTYLMLAIISEVIATTMLKASEGFSLYPSIVVVIGYCFSEFWALSQVVRVMPGLIAYAIWSGLGIVLVSV
VAAVFIYQQKLDLPAAIGMGLIAGVLVINLLSKSASH (SEQ ID NO: 401)
Multidrug transporter EmrE (Proteus vulgaris)
- MNGLTYLILAIIESEVIATTMLKASEGFSLYPSIIVVIGYCFSEFWALSQVVKVMPGLIAYAIWSGLGIVSVSV
VAAVFIYQQKLDLPAAIGMGLIAGVLVINLLSKSASH (SEQ ID NO: 402)
Multidrug transporter EmrE (Proteus vulgaris)
- 30 MLAIIESEVIATTMLKASDGFSLYPSIVVVIGYCFSEFWALSQVVKVMPGLIAYAIWSGLGIVLVSVAAVFLY
QQKLDLPAIVGMTLIIAGVLVINLLSKSASH (SEQ ID NO: 403)
Multidrug transporter EmrE (Proteus mirabilis ATCC 29906)
- MNGLTYLILAIIESEVIATTMLKASDGFSLYPSIVVVVGYYCFSEFWALSQVVKVMPGLIAYAIWSGLGIVLVSV
35 VAAVFVYQQKLDLPAIVGMTLIIAGVLVINLLSNSTSH (SEQ ID NO: 404)
Multidrug DMT transporter (Proteus sp. HMSC14B05)
- MNGLTYLILAIIESEVIATTMLKASDGFSLYPSIVVVVGYYCFSEFWALSQVVKVMPGLIAYAIWSGLGIVLVSV
VAAVFVYQQKLDLPAIVGMTLIIAGVLVINLLSNSTSH (SEQ ID NO: 405)
Methyl viologen transporter EmrE (Proteus hauseri ZMd44)

- MNGLTYLMLAIISEVIATTMLKASDGFSLYPSIVVVIGYCLSFWALSQVVRVMPLGIAYAIWSGLGIVLVS
VAAVFLYQQKLDLPAIVGMTLIIAGVLVINLLSKSASH (SEQ ID NO: 406)
Methyl viologen transporter EmrE (Proteus mirabilis strain HI4320)
- MNGLTYLMLAIISEVIATTMLKASDGFSLYPSIVVVIGYCFSEFWALSQVVKVMPLGIAYAIWSGLGIVLVS
5 VAAVFVYQQKLDLPAIVGMTLIIAGVLVINLLSNSTSH (SEQ ID NO: 407)
Multidrug SMR transporter (Proteus penneri ATCC 35198)
- MNGLTYLMLAIISEVIATTMLKASDGFSLYPSIVVVIGYCFSEFWALSQVVKVMPLGIAYAIWSGLGIVLVS
VAAVFLYQQKLDLPAIVGMTLIIAGVLVINLLSKSASH (SEQ ID NO: 408)
Multidrug DMT transporter (Proteus mirabilis)
- 10 MNGLTYLMLAIISEVIATTMLKASDGFSLYPSIVVVIGYCFSEFWALSQVVKVMPLGIAYAIWSGLGIVLVS
VAAVFVYQQKLDLPAIVGMTLIIAGVLVINLLSNSTAH (SEQ ID NO: 409)
Multidrug transporter EmrE (Providencia rettgeri)
- MKGLSFLFISIIAEVIATTLKASDGFSLYPSIVVVIGYAVSEFWALSQVVKVMPLGIAYAIWSGLGIVLVS
IAAIYIYNQKLDLPAIIGMLFIIVGVLIINLLSKSGTH (SEQ ID NO: 410)
15 **Multidrug SMR transporter (Providencia rustigianii DSM 4541)**
- MKGLGFLLSIVAIEVIATTLKASDGFSLYPSIVVVIGYAVSEFWALSQVVKVMPLGIAYAIWSGLGIVLVS
VAAIYIYNQKLDLPAIIGMLFIIVGVLIINLLSKSGTH (SEQ ID NO: 411)
Multidrug SMR transporter (Xenorhabdus thuongxuanensis)
- MKFALSYNFGLVSNMNVWGYLFIAILSEVIATTMLKSADGFTRLVPSIIVVTGYCLSFWALSQVVKVMPLGI
20 AYAVWSCLGIVLVSIAIGIFLYQQKLDLPAIIGILLIAGVLVINLLSKSAGH (SEQ ID NO: 412)
Multidrug transporter EmrE (Xenorhabdus doucetiae)
- MVNWAVFWKFGLSYHLGLVSNMNVWGYLFIAILSEVIATTMLKTADGFTRLVPSIVVVLGYCLSFWALSQV
KTMPLGIAYAVWSCLGIVLVSIAIGIFLYQQKLDLPAIIGILLIAGVLVINLLSKSAGH (SEQ ID NO:
413)
25 **Multidrug SMR transporter (Enterobacter cancerogenus)**
- MNTYLFLGIAIVAIEVIGTTFMKYSEGFTRLWPSLATLICFYFAAFYMLSQTLAHIPTGVAYAIWSGAGIVLIS
LVGWLVSQKLDLPAIIGMAFICIGVLIINVLKSGAH (SEQ ID NO: 414)
Multidrug transporter EmrE (Serratia plymuthica PRI-2C)
- MSGFIYLTMAIVAIEVIATTMLKASEGFTRLWPSLAVIVGYAVAFWGLSMVVKTMPLGIVYAIWSGMGIVLVS
30 IAAVFVYQQKLDLPAVIGMGLIAGVLVINLLSKTAAH (SEQ ID NO: 415)
Ethidium bromide-methyl viologen transporter EmrE (Serratia fonticola AU-P3(3))
- MTAFIYLAMAIIEVIATTLKASEGFTRLWPSVVFVVLGYAVAFWGLSMVVKTMPLGIVYAIWSGLGIVLVS
IAAVFIYQQKLDLPAVIGMGLIAGVLVINLLSKSAGH (SEQ ID NO: 416)
Multidrug transporter EmrE (Escherichia vulneris NBRC 102420)
- 35 MHAYVHLGIAIVAIEVIGTTLRYSEGFTKLWPTVATLGCYAVAFWFLSQTLQYIPTGIAYAIWSGVGIVLIS
AAGWIFSGQKLDLPAIGGMALICAGVLVINLFSKSAH (SEQ ID NO: 417)
Ethidium bromide-methyl viologen transporter EmrE (Serratia rubidaea)
- MYLTMAIIAEVIATTMLKASEGFTRLWPSLVVVLGYGVAFWGLSMVVKSMPLGIVYAIWSGMGVVLVSIAAV
FIYNQKLDWPAIIGMLIVAGVLVINLLSKTSAH (SEQ ID NO: 418)
40 **Cation/cationic drug transporter (Serratia marcescens FG194)**

MTGLMYLTMAIIAEVIATTMLKASEGFTRLWPSLVVVLGYGVAFWGLSMVVKSMPLGIVYAIWSGMGVVLVS
IAAVFIYNQKLDWPAIIGMGLIVAGVLVINLLSKTSAH (SEQ ID NO: 419)

Multidrug DMT transporter (*Serratia marcescens*)

MSGFMYLTMAIIAEVIATTMLKASEGFTRLWPSLLVVLGYGVAFWGLSMVVKSMPLGIVYAIWSGMGIVLVS
5 VAAVFVYQQKLDWPAIIGMGLIAGVLVINLLSKASVH (SEQ ID NO: 420)

Multidrug transporter EmrE (*Serratia odorifera* DSM 4582)

MNGFIYLTMAIIAEVIATTMLKASEGFTRLWPSLVVVVGYGVAFWGLSMVVKTMPLGIVYAIWSGMGIVLVS
IAAVFVYNQKLDWPAIIGMGLIAGVLVINLLSKTSAH (SEQ ID NO: 421)

Methods of Treatment

10 This invention describes peptides and methods of use for the treatment of bacterial infections. Pathogenic bacterial strains may become resistant to various treatments by developing a resistance to certain pharmaceutical agents. The resistance is conferred by small multidrug resistance (SMR) membrane-bound transporters. SMRs are a family of ubiquitous transporters in bacteria (e.g., *M. tuberculosis*, *P. aeruginosa*, *B. pertussis*, *N. meningitis*, *B. anthracis*, and *S.*
15 *aureus*) that efflux a wide range of cytotoxic compounds through transmembrane pumps. SMRs include, for example, EmrE transporters and various quaternary ammonium compound (QAC) transporters. In an attempt to treat a bacterial infection, one might administer an antibiotic agent to combat the infection. However, an SMR transporter effluxes the antibiotic agent before it can kill the infection, thus conferring resistance to the antibiotic. Therefore, to effectively treat a drug
20 resistant bacterial infection, one may need to inhibit one or more SMRs.

The peptides of the invention described herein include a C-terminal polypeptide of any one of an SMR transporter. SMRs exist as obligate dimers in their active form, with each monomer a ~110 residue four helix-bundle. The C-terminal polypeptide inhibits the dimerization of the SMR, thus preventing it from oligomerizing into its active state and reducing (e.g., by about 1%, 2%, 3%,
25 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 97%, 99%, or about 100%) or completely eliminating its ability to efflux the antibiotic. Following administration of the peptide, one could then administer an antibiotic agent, to which the bacteria is now sensitive, in order to effectively treat the infection. Following treatment with a peptide of the invention with or without an antibiotic agent, the size of the bacterial infection, the bacterial load, or the total number
30 of bacterial cells is reduced (e.g., by about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 97%, 99%, or about 100%) or completely eliminated relative to its initial size.

The polypeptides of the invention may be able to treat bacterial infections by preventing efflux of antibacterial agents administered in combination with a polypeptide of the invention. In
35 some embodiments, the bacterial infection includes bacteria which express one or more small molecule resistance membrane-bound transporters.

"Antibacterial agents," also known as antibiotics, as used herein refer to agents used in the treatment and prevention of bacterial infections. Antibacterial agents include agents which kill the bacteria, known as "bactericidal agents" and agents which inhibit bacterial growth, known as
40 "bacteriostatic agents." Antibacterial agents are generally classed based on their mechanism of

action, chemical structure, or spectrum of activity. Some antibacterial agents useful in combination with the polypeptides of the invention include (i) agents which target the bacterial cell wall (e.g., β -lactam antibiotics, cephalosporin antibiotics, carbapenem antibiotics), (ii) agents which target the cell membrane (e.g., polymyxin antibiotics), (iii) agents that interfere with bacterial enzymes (e.g., rifamycin antibiotics, lipiarmycin antibiotics, quinolone antibiotics, sulfonamide antibiotics), or (iv) agents which inhibit protein synthesis (e.g., macrolide antibiotics, lincosamide antibiotics, tetracycline antibiotics, aminoglycoside antibiotics).

In some embodiments, the method further includes administering one or more antibacterial agents (e.g., ampicillin, erythromycin, or tetracycline). In some embodiments, the one or more antibacterial agents is a β -lactam antibiotic such as a penicillin antibiotic (e.g., amoxicillin, ampicillin, bacampicillin, carbenicillin, cloxacillin, dicloxacillin, flucloxacillin, mexlocillin, nafcillin, oxacillin, penicillin G, penicillin V, piperacillin, pivampicillin, pivmecillinam, ticarcillin), a cephalosporin antibiotic (e.g., cefacetile, cefadroxil, cephalixin, cefaloglycin, cefalonium, cefaloridine, cefalotin, cefapirin, cefatrizine, cefazaflur, cefazedone, cefazolin, cefradine, cefroxadine, ceftazole, cefaclor, cefamandole, cefmetazole, cefonicid, cefotetan, cefoxitin, cefprozil, cefuroxime, cefuzonam, cefcapene, cefdaloxime, cefdininir, cefditoren, cefetamet, cefixime, cefmenoxime, cefodizime, cefotaxime, cefpimizole, cefpodoxime, cefteteram, ceftibuten, ceftiofur, ceftiolene, ceftizoxime, ceftriaxone, cefoperazone, ceftazidime, cefclidine, cefepime, cefluprenam, cefoselis, cefozopran, ceftiprome, ceftquinome, ceftobiprole, ceftaroline, cefaclomezine, cefaloram, cefaparole, cefcanel, cefedrolor, cefempidon, cefetrizole, cefivitril, cefmatilen, cefmepidium, cefovecin, cefoxazole, cefrotil, cefsumide, cefuracetim, ceftioxide), a monobactam antibiotic (e.g., aztreonam), or a carbapenem antibiotic (e.g., imipenem, doripenem, ertapenem, meropenem), a polymyxin antibiotic (e.g., polymyxin B), a rifamycin antibiotic (e.g., rifampin, rifabutin, rifapentine, rifalazil), a lipiarycin antibiotic, a quinolone antibiotic (e.g., flumequine, nalidixic acid, oxolinic acid, piromidic acid, pipemidic acid, rosoxacin, ciprofloxacin, enoxacin, lomefloxacin, nadifloxacin, norfloxacin, ofloxacin, pefloxacin, rufloxacin, balofloxacin, gatifloxacin, grepafloxacin, levofloxacin, moxifloxacin, pazufloxacin, sparfloxacin, temafloxacin, tosufloxacin, besifloxacin, delafloxacin, clinafloxacin, gemifloxacin, prulifloxacin, sitafloxacin, trovafloxacin), a fluoroquinolone antibiotic (e.g., delafloxacin), a sulfonamide antibiotic (e.g., sulfamethizole, sulfamethoxazole, trimethoprim-sulfamethoxazole), a macrolide antibiotic (e.g., fidaxomicin, azithromycin, erythromycin, clarithromycin, roxithromycin, dirithromycin, telithromycin), a lincosamide antibiotic (e.g., clindamycin, lincomycin), a tetracycline antibiotic (e.g., demeclocycline, doxycycline, minocycline, oxytetracycline, tetracycline, tigecycline), a streptogramin antibiotic (e.g., pristnamycin, quiupristin/dalfoprstin), an aminoglycoside antibiotic (e.g., amikacin, gentamicin, kanamycin, neomycin, netilmicin, paromomycin, streptomycin, tobramycin), a cyclic lipopeptide antibiotic (e.g., daptomycin), a lipoglycopeptide antibiotic (e.g., telavancin), a glycopeptide antibiotic (e.g., vancomycin, teicoplanin), a glycylcycline antibiotic, an oxazolidinone antibiotic (e.g., linezolid, cycloserine), a tuberactinomycin antibiotic (e.g., viomycin, capreomycin), chloramphenicol, metronidazole, tinidazole, nitrofurantoin, or combinations thereof.

In some embodiments, the one or more antibacterial agent and any of the foregoing polypeptides or pharmaceutical compositions are administered within 28 days of each other (e.g., within 21, 14, 10, 7, 5, 4, 3, 2, or 1 days) or within 24 hours (e.g., 12, 6, 3, 2, or 1 hours; or concomitantly) each in an amount that together are effective to treat the subject.

5 Administration and dosage

The present invention also features pharmaceutical compositions that contain a therapeutically effective amount of a polypeptide of the invention. The composition can be formulated for use in a variety of drug delivery systems. One or more physiologically acceptable excipients or carriers can also be included in the composition for proper formulation. Suitable
10 formulations for use in the present invention are found in *Remington's Pharmaceutical Sciences*, Mack Publishing Company, Philadelphia, PA, 17th ed., 1985. For a brief review of methods for drug delivery, see, e.g., Langer (*Science* 249:1527-1533, 1990).

The pharmaceutical compositions are intended for parenteral, intranasal, topical, oral, or local administration, such as by a transdermal means, for prophylactic and/or therapeutic
15 treatment. The pharmaceutical compositions can be administered parenterally (e.g., by intravenous, intramuscular, or subcutaneous injection), or by oral ingestion, or by topical application or intraarticular injection at areas affected by the vascular or cancer condition. Additional routes of administration include intravascular, intra-arterial, intratumor, intraperitoneal, intraventricular, intraepidural, as well as nasal, ophthalmic, intrascleral, intraorbital, rectal, topical,
20 or aerosol inhalation administration. Sustained release administration is also specifically included in the invention, by such means as depot injections or erodible implants or components. Thus, the invention provides compositions for parenteral administration that include the above mention agents dissolved or suspended in an acceptable carrier, preferably an aqueous carrier, e.g., water, buffered water, saline, PBS, and the like. The compositions may contain pharmaceutically
25 acceptable auxiliary substances as required to approximate physiological conditions, such as pH adjusting and buffering agents, tonicity adjusting agents, wetting agents, detergents and the like. The invention also provides compositions for oral delivery, which may contain inert ingredients such as binders or fillers for the formulation of a tablet, a capsule, and the like. Furthermore, this invention provides compositions for local administration, which may contain inert ingredients such
30 as solvents or emulsifiers for the formulation of a cream, an ointment, and the like.

These compositions may be sterilized by conventional sterilization techniques, or may be sterile filtered. The resulting aqueous solutions may be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile aqueous carrier prior to administration. The pH of the preparations typically will be between 3 and 11, more preferably between 5 and 9 or
35 between 6 and 8, and most preferably between 7 and 8, such as 7 to 7.5. The resulting compositions in solid form may be packaged in multiple single dose units, each containing a fixed amount of the above-mentioned agent or agents, such as in a sealed package of tablets or capsules. The composition in solid form can also be packaged in a container for a flexible quantity, such as in a squeezable tube designed for a topically applicable cream or ointment.

The compositions containing an effective amount can be administered for prophylactic or therapeutic treatments. In therapeutic applications, compositions are administered to a subject (e.g., a human) already suffering from a bacterial infection in an amount sufficient to cure or at least partially arrest the symptoms of the infection and its complications. An amount adequate to
5 accomplish this purpose is defined as a "therapeutically effective amount," an amount of a polypeptide sufficient to substantially improve at least one symptom associated with the disease or a medical condition. For example, in the treatment of an infection, an agent or polypeptide that decreases, prevents, delays, suppresses, or arrests any symptom of the disease or condition would be therapeutically effective. A therapeutically effective amount of an agent or polypeptide is
10 not required to cure a disease or condition but will provide a treatment for a disease or condition such that the onset of the disease or condition is delayed, hindered, or prevented, or the disease or condition symptoms are ameliorated, or the term of the disease or condition is changed or, for example, is less severe or recovery is accelerated in an individual.

Amounts effective for this use may depend on the severity of the disease or condition and
15 the weight and general state of the subject. The therapeutically effective amount of the compositions of the invention and used in the methods of this invention applied to mammals (e.g., humans) can be determined by the ordinarily-skilled artisan with consideration of individual differences in age, weight, and the condition of the mammal. The agents of the invention are administered to a subject (e.g., a mammal, such as a human) in an effective amount, which is an
20 amount that produces a desirable result in a treated subject. Therapeutically effective amounts can also be determined empirically by those of skill in the art.

Single or multiple administrations of the compositions of the invention including an effective amount can be carried out with dose levels and pattern being selected by the treating physician. The dose and administration schedule can be determined and adjusted based on the
25 severity of the disease or condition in the subject, which may be monitored throughout the course of treatment according to the methods commonly practiced by clinicians or those described herein.

The polypeptides of the present invention may be used in combination with either conventional methods of treatment or therapy or may be used separately from conventional methods of treatment or therapy.

30 When the polypeptides of this invention are administered in combination therapies with other agents, they may be administered sequentially or concurrently to an individual. Alternatively, pharmaceutical compositions according to the present invention may be comprised of a combination of a polypeptide of the present invention in association with a pharmaceutically acceptable excipient, as described herein, and another therapeutic or prophylactic agent known in
35 the art.

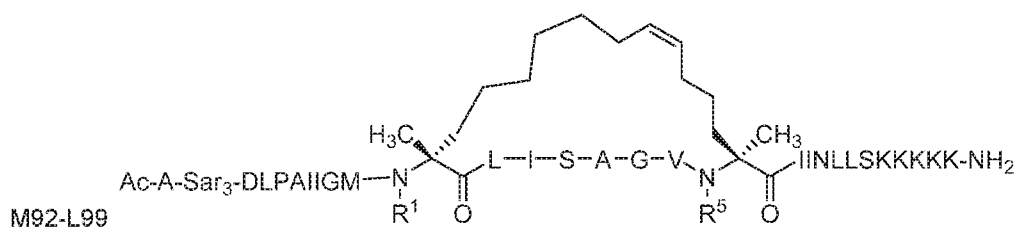
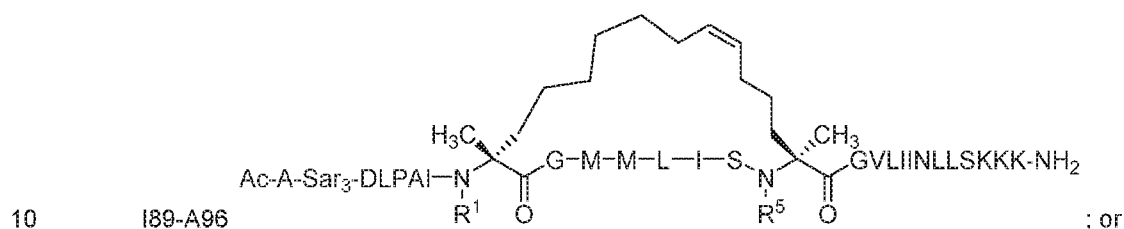
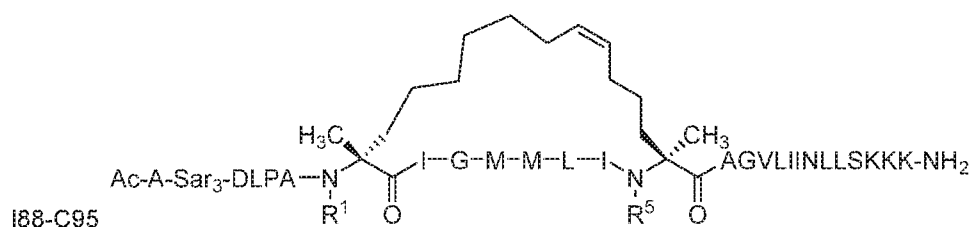
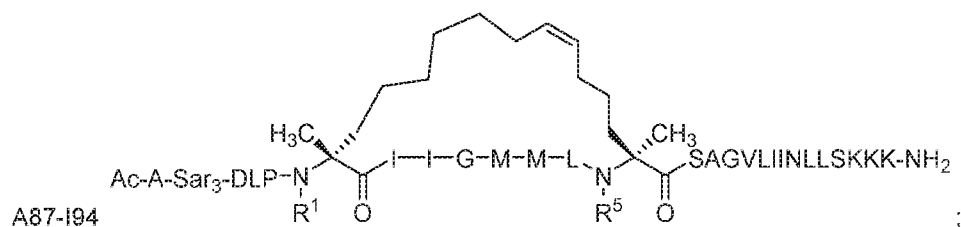
EXAMPLES

Example 1. Liposome Preparation

1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) and 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-(1'-rac-glycerol) (POPG) in chloroform (Avanti Polar Lipids Inc., AL, USA) were
40 mixed in a 3:1 mol ratio (POPC:POPG) and dried into thin films. Lipid films were lyophilized

overnight and brought up in 1 mL water, vortexed, frozen and lyophilized again. Lipids were then resuspended in 10 mM Tris buffer 10 mM NaCl pH 7.4 (5 mM) and freeze thawed 5X over dry ice and a water bath (50 ° C). Lipids were then extruded using a 0.2 micron sized filter and left to equilibrate overnight. Samples were diluted further with buffer (2.5 mM) prior to addition to lyophilized peptide.

The lyophilized peptides added were:



Example 2. Determination of Helicity of Stapled Polypeptides by Circular Dichromism

The helicity of the polypeptides described in Example 1 were tested by circular dichromism (CD) spectroscopy. The helicity of the polypeptides was determined in SDS micelles and in lipid bilayers.

The conditions in which the helicity in micelles were tested was stapled peptides (20 μM) in buffer (10 mM Tris HCl; 10 mM NaCl pH 7.4) and 140 mM SDS. The conditions in which the helicity in lipid bilayers were tested was 10 μM peptides in 2.5 mM POPC:POPG (3:1 mol ratio) (bacterial membrane mimetic lipid mixture).

As shown in FIGs. 1A and 1B, all of the tested polypeptides were found to be helical in both micelles and lipid bilayers.

Example 3. Determination of Cell Toxicity of Stapled Polypeptides

E. coli K12 cells were grown overnight to saturation in LB (Luria broth). Cells were harvested and resuspended in fresh media to a final OD600 of 0.1. Cells were then grown in the presence of DMSO (dimethyl sulfoxide) alone or in DMSO-solubilized peptide (4 μ M) over 1 hour, while OD600 was recorded in 15-minute intervals. *E. coli* growth curves were normalized to the starting OD600. Growth in the presence of peptide was normalized to the growth of cells with DMSO alone, using:

$$Growth = \frac{OD_{600}^{+peptide}}{OD_{600}^{-peptide}}$$

As shown in FIG. 2, none of the four hydrocarbon-stapled peptides severely impact cell growth over the time tested. A dashed line at 1.0 represents the starting conditions of the cells. S-CAP-2G (sequence: KKKKKK-AGFAAWAAFGA, hydrocarbon staple indicated by underlined A) is a positive control for cell death. Data shown represents the average of at least 2 independent experiments. Error is indicated as SD.

Example 4. Inhibition of Efflux by Stapled Polypeptides

E. coli K12 cells were harvested by centrifugation, re-suspended and diluted to an OD600 = 0.1 in Minimal Medium A. Cells were then treated with 80 μ M carbonyl cyanide m-chlorophenyl hydrazine (CCCP) for 5 min at room temperature, before adding 1 μ g/mL EtBr and either DMSO (8 μ l) or peptide (4 μ M) from a concentrated DMSO stock (1000 μ M peptide). Cells were incubated at 37 °C with shaking (250 rpm) for 30 min, centrifuged for 10 min, resuspended in fresh Minimal Medium A supplemented with 1 μ g/mL EtBr (without CCCP). Fluorescence decay was immediately measured using a spectropolarimeter (Photon Technology International, NJ, USA) over 2200s with stirring (λ_{ex} = 530 nm, slit width 2 nm, λ_{em} = 600nm, slit width 4 nm, 1s intervals). Background fluorescence intensity (ethidium alone, as well as final plateau values for *E. coli* cells alone) was subtracted from fluorescence values. Efflux experiments were repeated three times.

As shown in FIG. 3, M92-L99 inhibits efflux activity by 68%, A87-I94 by 60%, I89-A96 by 26%. I88-C95 does show any inhibition of efflux activity. A dashed line at 1.0 represents 100% inhibition.

Other Embodiments

It is to be understood that while the present disclosure has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the present disclosure, which is defined by the scope of the appended claims. Other aspects, advantages, and alterations are within the scope of the following claims.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments in accordance with the invention described herein. The scope of the present invention is not intended to be limited to the above Description, but rather is as set forth in the appended claims.

In the claims, articles such as "a," "an," and "the" may mean one or more than one unless indicated to the contrary or otherwise evident from the context. Claims or descriptions that include "or" between one or more members of a group are considered satisfied if one, more than one, or all of the group members are present in, employed in, or otherwise relevant to a given product or process unless indicated to the contrary or otherwise evident from the context. The invention includes embodiments in which exactly one member of the group is present in, employed in, or otherwise relevant to a given product or process. The invention includes embodiments in which more than one, or all of the group members are present in, employed in, or otherwise relevant to a given product or process.

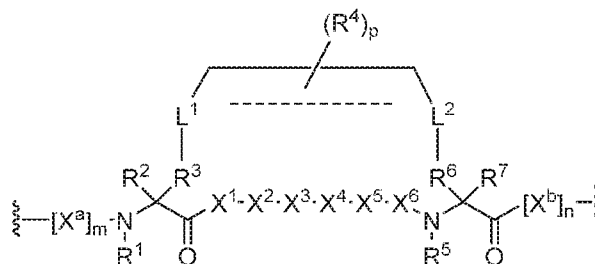
It is also noted that the term "comprising" is intended to be open and permits but does not require the inclusion of additional elements or steps. When the term "comprising" is used herein, the term "consisting of" is thus also encompassed and disclosed.

Where ranges are given, endpoints are included. Furthermore, it is to be understood that unless otherwise indicated or otherwise evident from the context and understanding of one of ordinary skill in the art, values that are expressed as ranges can assume any specific value or subrange within the stated ranges in different embodiments of the invention, to the tenth of the unit of the lower limit of the range, unless the context clearly dictates otherwise.

In addition, it is to be understood that any particular embodiment of the present invention that falls within the prior art may be explicitly excluded from any one or more of the claims. Since such embodiments are deemed to be known to one of ordinary skill in the art, they may be excluded even if the exclusion is not set forth explicitly herein. Any particular embodiment of the compositions of the invention (e.g., any polynucleotide or protein encoded thereby; any method of production; any method of use) can be excluded from any one or more claims, for any reason, whether or not related to the existence of prior art.

CLAIMS

1. A polypeptide, or a pharmaceutically acceptable salt thereof, comprising a stabilized α -helix, wherein the polypeptide comprises the structure of Formula I:



Formula I

wherein the dotted line represents an optional double bond;

m is 1, 2, 3, 4, 5, or 6;

n is 6-m;

p is 0, 1, or 2;

each of $[X^a]_m$, $[X^b]_n$, and X^1 - X^6 consist of consecutive amino acids of an α -helix of a monomer of a small multidrug resistance transporter, or conservative substitutions thereof;

R^1 and R^5 are, independently, hydrogen, optionally substituted acyl, or optionally substituted C_1 - C_8 alkyl;

R^2 and R^7 are, independently, optionally substituted C_1 - C_8 alkyl, optionally substituted C_1 - C_8 alkenyl, optionally substituted C_1 - C_8 alkynyl, optionally substituted C_1 - C_8 heteroalkyl, optionally substituted C_3 - C_8 carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl;

R^3 and R^6 are, independently, optionally substituted C_1 - C_8 alkylene, optionally substituted C_1 - C_8 heteroalkylene, optionally substituted C_3 - C_8 carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl, or R^1 and R^3 or R^5 and R^6 combine with the atoms to which they are attached to form an optionally substituted C_5 - C_8 heterocyclyl;

L^1 and L^2 are, independently, absent, optionally substituted C_1 - C_8 alkylene, or $-C(=O)OR^{L1}-$, wherein each R^{L1} is, independently, an optionally substituted C_1 - C_8 alkyl; and

each R^4 is, independently, optionally substituted C_1 - C_8 alkyl, optionally substituted C_1 - C_8 heteroalkyl, optionally substituted C_6 - C_{10} alkyl,

wherein the polypeptide binds to the monomer of a small multidrug resistance transporter.

2. The polypeptide of claim 1, wherein the structure of Formula I comprises the sequence of an α -helix of a monomer of a small multidrug resistance transporter in which two of the amino acids are replaced with a cross-link.

3. The polypeptide of any one of claims 1 or 2, wherein R^2 is optionally substituted C_1 - C_8 alkyl.

4. The polypeptide of claim 3, wherein the optionally substituted C_1 - C_8 alkyl is methyl.

5. The polypeptide of any one of claims 1 to 4, wherein R^7 is optionally substituted C_1 - C_8 alkyl.

6. The polypeptide of claim 5, wherein the optionally substituted C_1 - C_8 alkyl is methyl.

7. The polypeptide of any one of claims 1 to 6, wherein R¹ is hydrogen.
8. The polypeptide of any one of claims 1 to 7, wherein R⁵ is hydrogen.
9. The polypeptide of any one of claims 1 to 8, wherein p is 0.
10. The polypeptide of any one of claims 1 to 9, wherein R⁸ is optionally substituted C₁-C₈ alkylene.
11. The polypeptide of claim 10, wherein the optionally substituted C₁-C₈ alkylene is methylene.
12. The polypeptide of any one of claims 1 to 11, wherein R³ is optionally substituted C₁-C₈ alkylene.
13. The polypeptide of claim 12, wherein the optionally substituted C₁-C₈ alkylene is methylene.
14. The polypeptide of any one of claims 1 to 13, wherein L¹ is optionally substituted C₁-C₈ alkylene.
15. The polypeptide of claim 14, wherein optionally substituted C₁-C₈ alkylene is pentylene.
16. The polypeptide of any one of claims 1 to 15, wherein L² is optionally substituted C₁-C₈ alkylene.
17. The polypeptide of claim 16, wherein optionally substituted C₁-C₈ alkylene is ethylene.
18. The polypeptide of any one of claims 1 to 17, wherein the dotted line represents a double bond.
19. The polypeptide of any one of claims 1 to 18, wherein X¹ is glycine, alanine, valine, leucine, or isoleucine.
20. The polypeptide of claim 19, wherein X¹ is glycine.
21. The polypeptide of claim 19, wherein X¹ is alanine.
22. The polypeptide of claim 19, wherein X¹ is valine.
23. The polypeptide of claim 19, wherein X¹ is leucine.
24. The polypeptide of claim 19, wherein X¹ is isoleucine.
25. The polypeptide of any one of claims 1 to 24, wherein X² is glycine, alanine, valine, leucine, or isoleucine.
26. The polypeptide of claim 25, wherein X² is glycine.
27. The polypeptide of claim 25, wherein X² is alanine.
28. The polypeptide of claim 25, wherein X² is valine.
29. The polypeptide of claim 25, wherein X² is leucine.
30. The polypeptide of claim 25, wherein X² is isoleucine.
31. The polypeptide of any one of claims 1 to 30, wherein X³ is glycine, alanine, valine, leucine, or isoleucine.
32. The polypeptide of claim 31, wherein X³ is glycine.
33. The polypeptide of claim 31, wherein X³ is alanine.
34. The polypeptide of claim 31, wherein X³ is valine.
35. The polypeptide of claim 31, wherein X³ is leucine.

36. The polypeptide of claim 31, wherein X³ is isoleucine.
37. The polypeptide of any one of claims 1 to 36, wherein X⁴ is serine, cysteine, selenocysteine, threonine, or methionine.
38. The polypeptide of claim 37, wherein X⁴ is serine.
39. The polypeptide of claim 37, wherein X⁴ is cysteine.
40. The polypeptide of claim 37, wherein X⁴ is selenocysteine.
41. The polypeptide of claim 37, wherein X⁴ is threonine.
42. The polypeptide of claim 37, wherein X⁴ is methionine.
43. The polypeptide of any one of claims 1 to 42, wherein X⁵ is serine, cysteine, selenocysteine, threonine, or methionine.
44. The polypeptide of claim 43, wherein X⁵ is serine.
45. The polypeptide of claim 43, wherein X⁵ is cysteine.
46. The polypeptide of claim 43, wherein X⁵ is selenocysteine.
47. The polypeptide of claim 43, wherein X⁵ is threonine.
48. The polypeptide of claim 43, wherein X⁵ is methionine.
49. The polypeptide of any one of claims 1 to 48, wherein X⁶ is histidine, lysine, or arginine.
50. The polypeptide of claim 49, wherein X⁶ is histidine.
51. The polypeptide of claim 49, wherein X⁶ is lysine.
52. The polypeptide of claim 49, wherein X⁶ is arginine.
53. The polypeptide of any one of claims 1 to 30, wherein X³ is serine, cysteine, selenocysteine, threonine, or methionine.
54. The polypeptide of claim 53, wherein X³ is serine.
55. The polypeptide of claim 53, wherein X³ is cysteine.
56. The polypeptide of claim 53, wherein X³ is selenocysteine.
57. The polypeptide of claim 53, wherein X³ is threonine.
58. The polypeptide of claim 53, wherein X³ is methionine.
59. The polypeptide of any one of claims 1 to 30 or 53 to 58, wherein X⁴ is serine, cysteine, selenocysteine, threonine, or methionine.
60. The polypeptide of claim 59, wherein X⁴ is serine.
61. The polypeptide of claim 59, wherein X⁴ is cysteine.
62. The polypeptide of claim 59, wherein X⁴ is selenocysteine.
63. The polypeptide of claim 59, wherein X⁴ is threonine.
64. The polypeptide of claim 59, wherein X⁴ is methionine.
65. The polypeptide of any one of claims 1 to 30 or 53 to 64, wherein X⁵ is histidine, lysine, or arginine,
66. The polypeptide of claim 65, wherein X⁵ is histidine.
67. The polypeptide of claim 66, wherein X⁵ is lysine.
68. The polypeptide of claim 66, wherein X⁵ is arginine.

69. The polypeptide of any one of claims 1 to 30 or 53 to 69, wherein X⁶ is glycine, alanine, valine, leucine, or isoleucine.
70. The polypeptide of claim 69, wherein X⁶ is glycine.
71. The polypeptide of claim 69, wherein X⁶ is alanine.
72. The polypeptide of claim 69, wherein X⁶ is valine.
73. The polypeptide of claim 69, wherein X⁶ is leucine.
74. The polypeptide of claim 69, wherein X⁶ is isoleucine.
75. The polypeptide of any one of claims 1 to 24, wherein X² is serine, cysteine, selenocysteine, threonine, or methionine.
76. The polypeptide of claim 75, wherein X² is serine.
77. The polypeptide of claim 75, wherein X² is cysteine.
78. The polypeptide of claim 75, wherein X² is selenocysteine.
79. The polypeptide of claim 75, wherein X² is threonine.
80. The polypeptide of claim 75, wherein X² is methionine.
81. The polypeptide of any one of claims 1 to 24 or 75 to 80, wherein X³ is serine, cysteine, selenocysteine, threonine, or methionine.
82. The polypeptide of claim 81, wherein X³ is serine.
83. The polypeptide of claim 81, wherein X³ is cysteine.
84. The polypeptide of claim 81, wherein X³ is selenocysteine.
85. The polypeptide of claim 81, wherein X³ is threonine.
86. The polypeptide of claim 81, wherein X³ is methionine.
87. The polypeptide of any one of claims 1 to 24 or 75 to 86, wherein X⁴ is histidine, lysine, or arginine.
88. The polypeptide of claim 87, wherein X⁴ is histidine.
89. The polypeptide of claim 87, wherein X⁴ is lysine.
90. The polypeptide of claim 87, wherein X⁴ is arginine.
91. The polypeptide of any one of claims 1 to 24 or 75 to 90, wherein X⁵ is glycine, alanine, valine, leucine, or isoleucine.
92. The polypeptide of claim 91, wherein X⁵ is glycine.
93. The polypeptide of claim 91, wherein X⁵ is alanine.
94. The polypeptide of claim 91, wherein X⁵ is valine.
95. The polypeptide of claim 91, wherein X⁵ is leucine.
96. The polypeptide of claim 91, wherein X⁵ is isoleucine.
97. The polypeptide of any one of claims 1 to 24 and 75 to 96, wherein X⁶ is serine, cysteine, selenocysteine, threonine, or methionine.
98. The polypeptide of claim 97, wherein X⁶ is serine.
99. The polypeptide of claim 97, wherein X⁶ is cysteine.
100. The polypeptide of claim 97, wherein X⁶ is selenocysteine.
101. The polypeptide of claim 97, wherein X⁶ is threonine.
102. The polypeptide of claim 97, wherein X⁶ is methionine.

103. The polypeptide of any one of claims 1 to 18, wherein X¹ is histidine, lysine, or arginine.
104. The polypeptide of claim 103, wherein X¹ is histidine.
105. The polypeptide of claim 103, wherein X¹ is lysine.
106. The polypeptide of claim 103, wherein X¹ is arginine.
107. The polypeptide of any one of claims 1 to 18 or 103 to 106, wherein X² is glycine, alanine, valine, leucine, or isoleucine.
108. The polypeptide of claim 107, wherein X² is glycine.
109. The polypeptide of claim 107, wherein X² is alanine.
110. The polypeptide of claim 107, wherein X² is valine.
111. The polypeptide of claim 107, wherein X² is leucine.
112. The polypeptide of claim 107, wherein X² is isoleucine.
113. The polypeptide of any one of claims 1 to 18 or 103 to 112, wherein X³ is serine, cysteine, selenocysteine, threonine, or methionine.
114. The polypeptide of claim 113, wherein X³ is serine.
115. The polypeptide of claim 113, wherein X³ is cysteine.
116. The polypeptide of claim 113, wherein X³ is selenocysteine.
117. The polypeptide of claim 113, wherein X³ is threonine.
118. The polypeptide of claim 113, wherein X³ is methionine.
119. The polypeptide of any one of claims 1 to 18 or 103 to 118, wherein X⁴ is glycine, alanine, valine, leucine, or isoleucine.
120. The polypeptide of claim 119, wherein X⁴ is glycine.
121. The polypeptide of claim 119, wherein X⁴ is alanine.
122. The polypeptide of claim 119, wherein X⁴ is valine.
123. The polypeptide of claim 119, wherein X⁴ is leucine.
124. The polypeptide of claim 119, wherein X⁴ is isoleucine.
125. The polypeptide of any one of claims 1 to 18 or 103 to 124, wherein X⁵ is glycine, alanine, valine, leucine, or isoleucine.
126. The polypeptide of claim 125, wherein X⁵ is glycine.
127. The polypeptide of claim 125, wherein X⁵ is alanine.
128. The polypeptide of claim 125, wherein X⁵ is valine.
129. The polypeptide of claim 125, wherein X⁵ is leucine.
130. The polypeptide of claim 125, wherein X⁵ is isoleucine.
131. The polypeptide of any one of claims 1 to 18 or 103 to 130, wherein X⁶ is glycine, alanine, valine, leucine, or isoleucine.
132. The polypeptide of claim 131, wherein X⁶ is glycine.
133. The polypeptide of claim 131, wherein X⁶ is alanine.
134. The polypeptide of claim 131, wherein X⁶ is valine.
135. The polypeptide of claim 131, wherein X⁶ is leucine.
136. The polypeptide of claim 131, wherein X⁶ is isoleucine.

137. The polypeptide of any one of claims 1 to 136, wherein $[X^b]_n$ comprises the sequence lysine-lysine-serine, or conservative substitutions thereof.

138. The polypeptide of any one of claims 1 to 137, wherein $[X^b]_n$ comprises the sequence isoleucine-isoleucine-asparagine-lysine-lysine-serine, or conservative substitutions thereof.

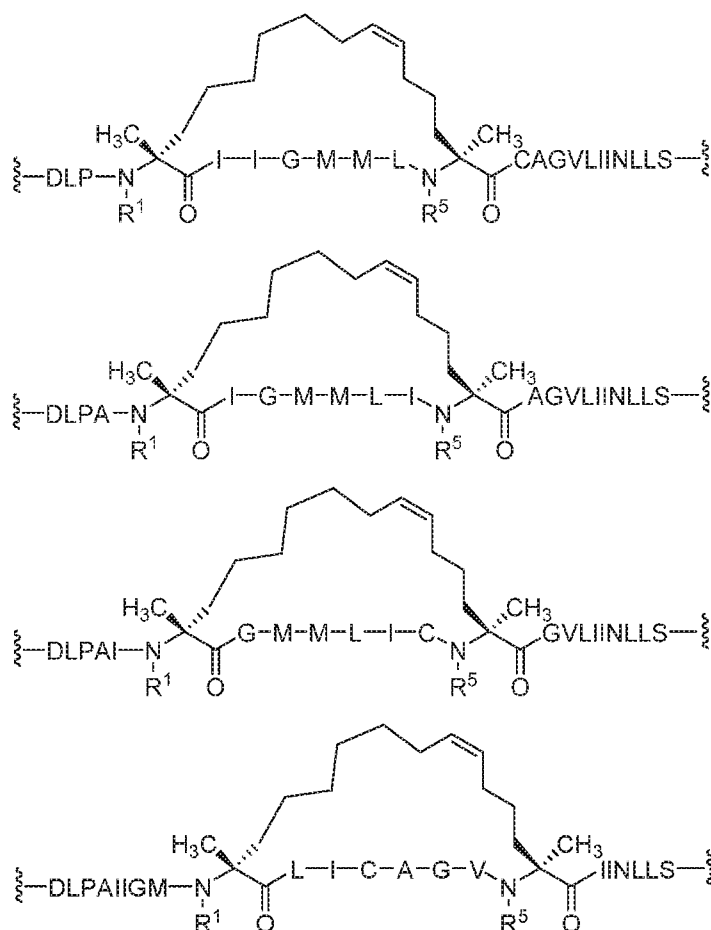
139. The polypeptide of any one of claims 1 to 138, wherein X^1 - X^6 or $[X^b]_n$ comprises the sequence cysteine-alanine-glycine, or conservative substitutions thereof.

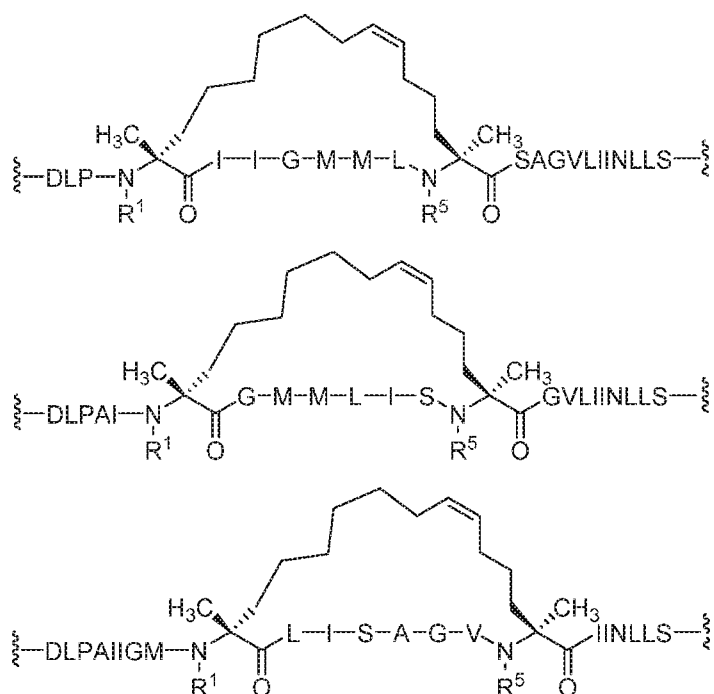
140. The polypeptide of any one of claims 1 to 139, wherein $[X^b]_n$ comprises the sequence cysteine-alanine-glycine-valine-leucine-isoleucine-isoleucine-asparagine-lysine-lysine-serine, or conservative substitutions thereof.

141. The polypeptide of any one of claims 1 to 140, wherein $[X^a]_m$ comprises the sequence Aspartic acid-leucine-proline, or conservative substitutions thereof.

142. The polypeptide of any one of claims 1 to 141, wherein $[X^a]_m$ comprises the sequence Aspartic acid-leucine-proline-alanine-isoleucine-isoleucine-glycine-methionine, or conservative substitutions thereof.

143. The polypeptide of any one of claims 1 to 142, wherein the polypeptide comprises the structure:



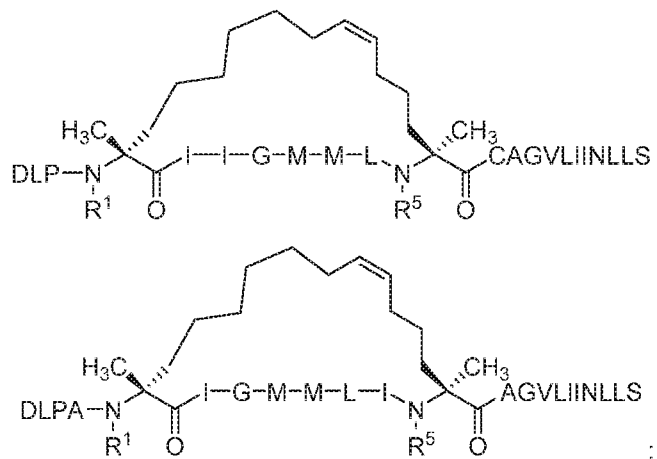


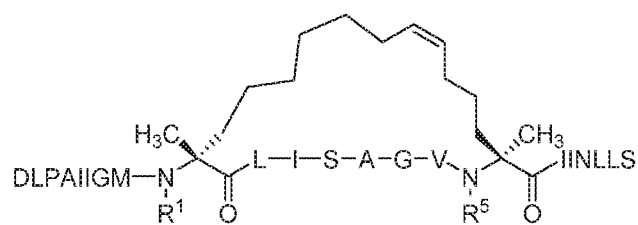
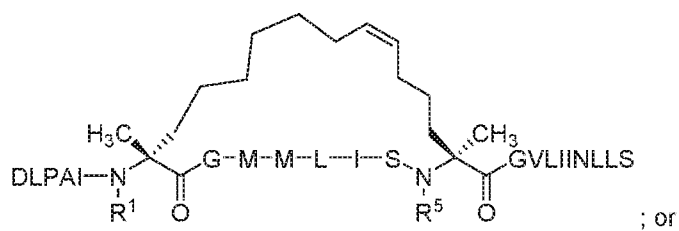
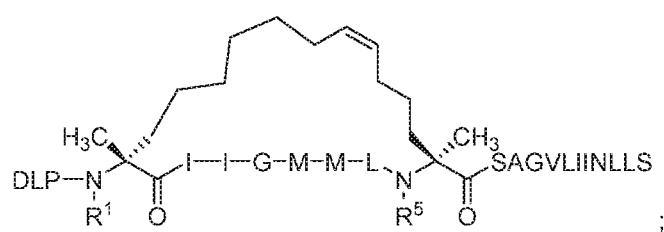
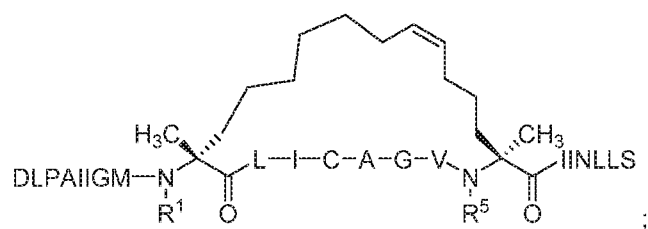
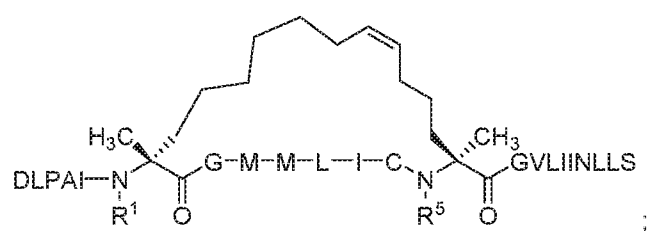
144. The polypeptide of any one of claims 1 to 143, wherein the polypeptide is acetylated at the N-terminus.

145. The polypeptide of any one of claims 1 to 144, wherein the polypeptide is amidated at the C-terminus.

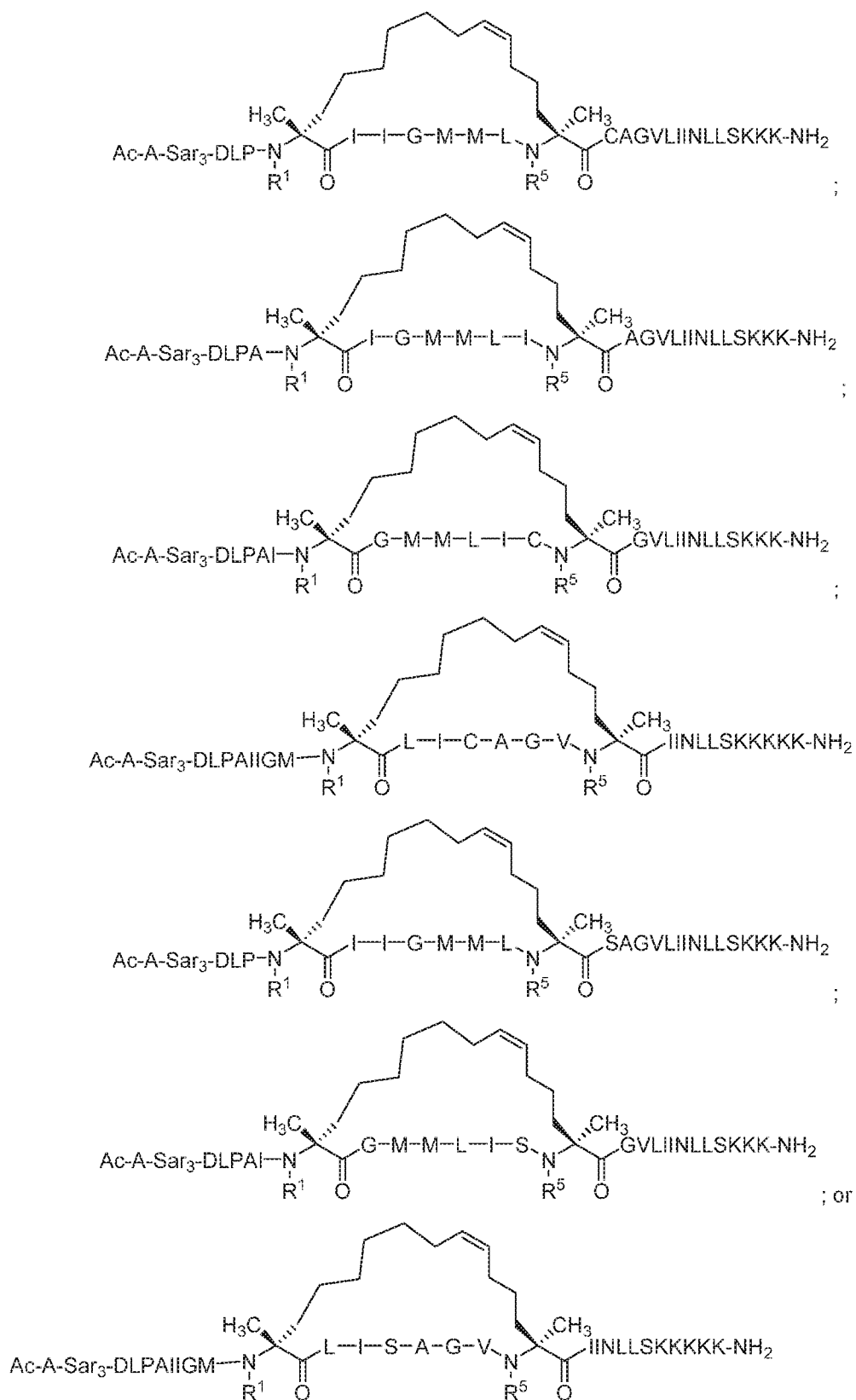
146. The polypeptide of any one of claims 1 to 145, wherein the polypeptide comprises a solubility tag at the N- and/or C-terminus.

147. The polypeptide of any one of claims 1 to 146, wherein the polypeptide consists of the structure:





148. The polypeptide of any one of claims 1 to 146, wherein the polypeptide consists of the structure:



149. A pharmaceutical composition comprising a polypeptide of any one of claims 1 to 148 and a pharmaceutically acceptable carrier.

150. A method of reducing efflux in a bacterial cell, the method comprising contacting the cell with a polypeptide of any one of claims 1 to 148 or a pharmaceutical composition of claim 149.

151. The method of claim 150, wherein the bacterial cell is a gram-negative bacteria.

152. The method of claim 150 or 151, wherein the bacterial cell is *E. coli*, *P. aeruginosa*, *B. pertussis*, or *N. meningitidis*.

153. The method of claim 150, wherein the bacterial cell is a gram-positive bacteria.

154. The method of claim 150 or 153, wherein the bacteria cell is *S. Aureus* or *B. anthracis*.

155. A method of treating a bacterial infection in a subject in need thereof, the method comprising administering an effective amount of a polypeptide of any one of claims 1 to 148 or a pharmaceutical composition of claim 149 and one or more antibacterial agents to the subject.

156. The method of claim 155, wherein the bacterial infection comprises bacteria which are resistant to one or more antibacterial agents or the bacterial infection has failed to respond to treatment with one or more antibacterial agents.

157. The method of claim 155 or 156, wherein the bacterial infection comprises bacteria which express one or more small molecule resistance membrane-bound transporters.

158. The method of any one of claims 155 to 157, wherein the polypeptide of any one of claims 1 to 148 or pharmaceutical composition of claim 149 and the one or more antibacterial agents are administered within 28 days of each other.

159. The method of any one of claims 155 to 158, wherein the one or more antibacterial agents comprise ampicillin, erythromycin, or tetracycline.

FIG. 1A

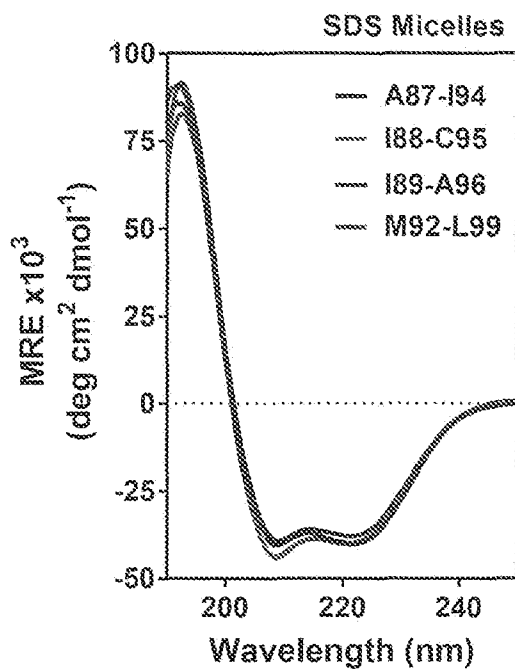


FIG. 1B

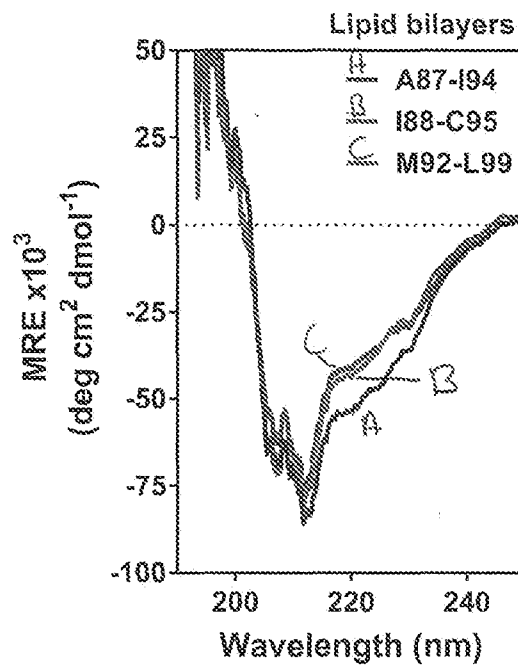


FIG. 1

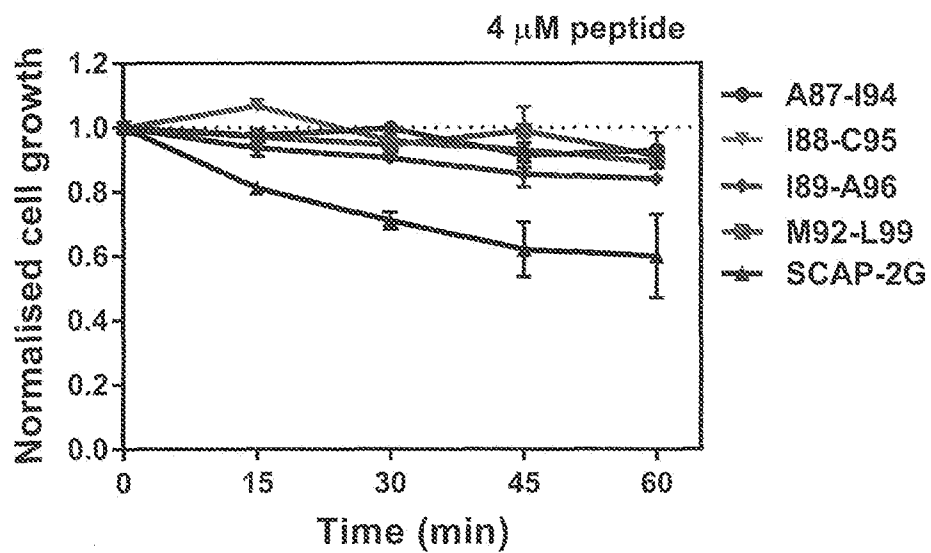


FIG. 2

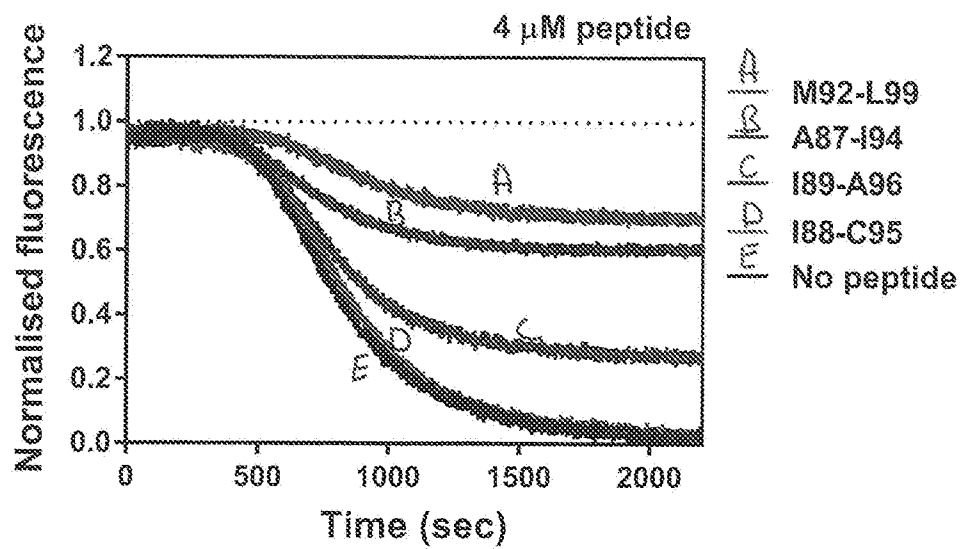


FIG. 3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/012291

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/00; A61K 38/02; A61K 38/08; A61K 38/10; A61K 38/12; A61K 49/00 (2019.01)

CPC - A61K 38/08; A61K 38/10; A61K 38/12; C07K 1/113; C07K 7/06 (2019.02)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

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

USPC - 514/9; 514/21.1; 530/326; 530/333 (keyword delimited)

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2017/0008930 A1 (WALENSKY et al) 12 January 2017 (12.01.2017) entire document	1-4
Y	—BELLMANN-SICKERT et al. "Efflux by Small Multidrug Resistance Proteins Is Inhibited by Membrane-interactive Helix-stapled Peptides," The Journal of Biological Chemistry, 25 November 2014 (25.11.2014), Vol. 290, No. 3, Pgs. 1752-1759. entire document	1-4
P, X	—OVCHINNIKOV et al. "Structure of the EmrE multidrug transporter and its use for inhibitor peptide design," PNAS, 06 August 2018 (06.08.2018), Vol. 115, No. 34, PGs. E7932-E7941. entire document	1-4
A	US 2014/0256912 A1 (MOELLERING et al) 11 September 2014 (11.09.2014) entire document	1-4
A	US 2016/0244494 A1 (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 25 August 2016 (25.08.2016) entire document	1-4
A	—WANG et al. "Functional response of the small multidrug resistance protein EmrE to mutations in transmembrane helix 2," FEBS Letters, 16 October 2014 (16.10.2014), Vol. 588, Iss. 20, Pgs. 3720-3725. entire document	1-4

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

04 March 2019

Date of mailing of the international search report

29 MAR 2019

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
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PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/012291

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 5-159
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.