CLAIMS

WHAT IS CLAIMED IS:

1. A composition comprising

a carrier derived from a bacterial toxin capable of entering a polarized epithelial cell or transcytosing across a polarized epithelial cell; and

a transition metal cation or a polycation, wherein the polycation is a molecule or chemical complex having more than 2 positive charges.

2. The composition of claim 1, wherein the composition comprises the transition metal cation.

3. The composition of claim 2, wherein the transition metal cation is selected from the group consisting of Fe^{2+}, Mn^{2+}, Zn^{2+}, Co^{2+}, Ni^{2+}, and Cu^{2+}.

4. The composition of claim 3, wherein the transition metal cation comprises Zn^{2+}.

5. The composition of claim 1, wherein the composition comprises the polycation.

6. The composition of claim 5, wherein the polycation comprises protamine, poly-lysine, poly-ornithine, poly-ethylene-imine (PEI), prolamin, protamine, polyvinyl pyrrolidone (PVP), polyarginine, polyvinylamine, or a combination thereof.

7. The composition of claim 5, wherein the polycation comprises a protamine salt.

8. The composition of claim 7, wherein the protamine salt comprises protamine sulfate, protamine acetate, protamine bromide, protamine chloride, protamine caproate, protamine trifluoroacetate, protamine HCO_3, protamine propionate, protamine lactate, protamine formate, protamine nitrate, protamine citrate, protamine monohydrogenphosphate, protamine dihydrogenphosphate, protamine tartrate, or protamine perchlorate.

9. The composition of claim 7, wherein the protamine salt comprises protamine sulfate.

10. The composition of claim 1, further comprising a heterologous payload.

11. The composition of claim 10, wherein the heterologous payload comprises insulin or human growth hormone.

12. The composition of claim 1, wherein the carrier comprises Pseudomonas exotoxin A or a portion of the Pseudomonas exotoxin A.

13. The composition of claim 12, wherein the carrier comprises the sequence set forth in SEQ ID NO: 69 or a portion of the sequence set forth in SEQ ID NO: 69.

14. The composition of claim 1, wherein the carrier comprises a Cholix polypeptide.

15. The composition of claim 14, wherein the Cholix polypeptide consists of an amino acid sequence with a C-terminus at any one of amino acid positions 206 to 425, wherein the amino acid positions are based on alignment of the Cholix polypeptide to the sequence set forth in SEQ ID NO: 7, starting with position 1 at the N-terminus.

16. The composition of claim 14, wherein the Cholix polypeptide consists of an amino acid sequence with a C-terminus at any one of amino acid positions 150 to 205, wherein the amino acid positions are based on alignment of the Cholix polypeptide to the sequence set forth in SEQ ID NO: 7, starting with position 1 at the N-terminus.

17. The composition of claim 14, wherein the Cholix polypeptide consists of an amino acid sequence with a C-terminus at any one of amino acids 150 to 195, wherein the amino acid positions are based on alignment of the Cholix polypeptide to the sequence set forth in SEQ ID NO: 7, starting with position 1 at the N-terminus.

18. The composition of claim 14, wherein the Cholix polypeptide consists of an amino acid sequence with an N-terminus at any one of amino acid positions 1 to 41, wherein the amino acid positions are based on alignment of the Cholix polypeptide to the sequence set forth in SEQ ID NO: 7, starting with position 1 at the N-terminus.

19. The composition of claim 14, wherein the Cholix polypeptide consists of an amino acid sequence with an N-terminus at any one of amino acid positions 35 to 40, wherein the amino acid positions are based on alignment of the Cholix polypeptide to the sequence set forth in SEQ ID NO: 7, starting with position 1 at the N-terminus.

20. The composition of claim 14, wherein the Cholix polypeptide consists of an amino acid sequence from amino acid position 40 to any one of amino acid positions 150 to 205, wherein the amino acid positions are based on alignment of the Cholix polypeptide to the sequence set forth in SEQ ID NO: 7, starting with position 1 at the N-terminus.

21. The composition of claim 14, wherein the Cholix polypeptide has a C-terminus at any one of amino acid positions 150 to 187, wherein the amino acid positions are based on alignment of the Cholix polypeptide to the sequence set forth in SEQ ID NO: 7, starting with position 1 at the N-terminus.

22. The composition of claim 14, wherein the Cholix polypeptide consists of the amino acid sequence set forth in SEQ ID NO: 66, and the carrier further comprises a methionine N-terminal to the sequence set forth in SEQ ID NO: 66.

23. The composition of claim 14, wherein the Cholix polypeptide consists of the amino acid sequence set forth in SEQ ID NO: 2, and the carrier further comprises a methionine N-terminal to the sequence set forth in SEQ ID NO: 2.

24. The composition of claim 10, wherein the heterologous payload comprises an incretin.

25. The composition of claim 24, wherein the incretin comprises glucagon-like peptide-1 (GLP-1) or gastric inhibitory peptide (GIP).

26. The composition of claim 10, wherein the heterologous payload comprises an incretin mimetic peptide.

27. The composition of claim 26, wherein the incretin mimetic peptide comprises liraglutide, dulaglutide, semaglutide, exenatide, albiglutide, or lixisenatide.

28. The composition of claim 10, wherein the heterologous payload comprises tirzepatide.

29. The composition of claim 10, wherein the heterologous payload comprises glucagon-like peptide 2 (GLP-2) or a GLP-2 analog.

30. The composition of claim 29, wherein the heterologous payload comprises the GLP-2 analog, wherein the GLP-2 analog is teduglutide.