WHAT IS CLAIMED IS:

1. A conjugate, comprising:
a knottin peptide comprising an engineered loop that binds to a cell surface molecule; and
an immunostimulant conjugated to the knottin peptide via a linker.

2. The conjugate of claim 1, wherein the immunostimulant activates a pathogen recognition receptor (PRR).

3. The conjugate of claim 2, wherein the PRR is selected from the group consisting of: a Toll-like receptor (TLR), a RIG-I-like receptor (RLR), a NOD-like receptor (NLR), a C-type lectin receptor (CLR), a cytosolic dsDNA sensor (CDS), a stimulator of interferon genes (STING), and any combination thereof.

4. The conjugate of claim 2, wherein the immunostimulant is a Toll-Like Receptor (TLR) agonist.

5. The conjugate of claim 4, wherein the TLR agonist is a TLR 9 agonist.

6. The conjugate of claim 4 or claim 5, wherein the TLR agonist is an oligonucleotide-based TLR agonist.

7. The conjugate of claim 6, wherein the oligonucleotide-based TLR agonist comprises one or more CpG dinucleotides.

8. The conjugate of claim 7, wherein the oligonucleotide-based TLR agonist is a CpG oligodeoxynucleotide (ODN).

9. The conjugate of claim 8, wherein the CpG ODN is from a class selected from the group consisting of: class A (type D), class B (type K), and class C.

10. The conjugate of claim 4, wherein the TLR agonist is an agonist of TLR 7, TLR8, or both.

11. The conjugate of claim 10, wherein the TLR agonist comprises an imidazoquinoline (IMZQ) compound.

12. The conjugate of claim 11, wherein the TLR agonist is selected from the group consisting of: T78a, Hybrid-2, Para-amine, Meta-amine, XG1-236, DS802, CL075, CL097, and R848.

13. The conjugate of claim 12, wherein the TLR agonist is T78a.

14. The conjugate of any one of claims 1 to 13, wherein the knottin peptide is conjugated to two or more immunostimulants.

15. The conjugate of claim 14, wherein two of the two or more immunostimulants are the same.

16. The conjugate of claim 14 or claim 15, wherein two of the two or more immunostimulants are different.

17. The conjugate of any one of claims 14 to 16, wherein the two or more immunostimulants are independently selected from an immunostimulant as defined in any one of claims 2 to 13.

18. The conjugate of any one of claims 1 to 17, wherein the knottin peptide is further conjugated to a detectable label.

19. The conjugate of claim 18, wherein the detectable label is an *in vivo* imaging agent.

20. The conjugate of any one of claims 1 to 19, wherein the knottin peptide is fused to one or more heterologous polypeptides.

21. The conjugate of claim 20, wherein the one or more heterologous polypeptides comprises an Fc domain, an albumin, a transferrin, XTEN, a homo-amino acid polymer, a proline-alanine-serine polymer, an elastin-like peptide, or any combination thereof.

22. The conjugate of claim 21, wherein the one or more heterologous polypeptides comprises an Fc domain.

23. The conjugate of claim 22, wherein the Fc domain is a human Fc domain.

24. The conjugate of any one of claims 20 to 23, wherein the one or more heterologous polypeptides comprises a polypeptide detectable *in vivo*.

25. The conjugate of any one of claims 1 to 24, wherein the knottin peptide is selected from the group consisting of: an EETI-II peptide, an AgRP peptide, a ω-conotoxin peptide, a Kalata B1 peptide, an MCoTI-II peptide, an agatoxin peptide, and a chlorotoxin peptide.

26. The conjugate of claim 25, wherein the knottin peptide is an EETI-II peptide.

27. The conjugate of claim 26, wherein the knottin peptide comprises an amino acid sequence having 70% or greater, 80% or greater, 90% or greater, 95% or greater, or 100% identity to the amino acid sequence set forth in SEQ ID NO:8.

28. The conjugate of claim 26, wherein the knottin peptide comprises an amino acid sequence having 70% or greater, 80% or greater, 90% or greater, 95% or greater, or 100% identity to the amino acid sequence set forth in SEQ ID NO:9.

29. The conjugate of claim 26, wherein the knottin peptide comprises an amino acid sequence having 70% or greater, 80% or greater, 90% or greater, 95% or greater, or 100% identity to the amino acid sequence set forth in SEQ ID NO:10.

30. The conjugate of any one of claims 1 to 29, wherein the cell surface molecule is a cancer cell surface molecule.

31. The conjugate of claim 30, wherein the cancer cell surface molecule is present on cancer cells of a solid tumor.

32. The conjugate of claim 30, wherein the cancer cell surface molecule is present on cancer cells of a liquid tumor.

33. The conjugate of any one of claims 1 to 32, wherein the cell surface molecule is a cell surface receptor.

34. The conjugate of claim 33, wherein the cell surface receptor is a cell adhesion receptor.

35. The conjugate of claim 34, wherein the cell adhesion receptor is an integrin.

36. The conjugate of claim 35, wherein the integrin is selected from the group consisting of: αvβ1 integrin, αvβ3 integrin, αvβ5 integrin, αvβ6 integrin, α5β1 integrin, and any combination thereof.

37. The conjugate of any one of claims 34 to 36, wherein the cell adhesion receptor is present on tumor vasculature cells.

38. The conjugate of claim 33, wherein the cell surface receptor is selected from the group consisting of: a growth factor receptor, a chemokine receptor, an immune cell receptor, and combinations thereof.

39. The conjugate of any one of claims 1 to 32, wherein the cell surface molecule is a membrane protease.

40. A composition comprising the conjugate of any one of claims 1 to 39.

41. The composition of claim 40, wherein the composition is a pharmaceutical composition comprising:

the conjugate; and

a pharmaceutically acceptable carrier.

42. The composition of claim 41, wherein the pharmaceutical composition is formulated for parenteral administration.

43. The composition of claim 41, wherein the pharmaceutical composition is formulated for oral administration.

44. A kit comprising:

a therapeutically effective amount of the pharmaceutical composition of any one of claims 41 to 43; and

instructions for administering the pharmaceutical composition to an individual in need thereof.

45. The kit of claim 44, wherein the pharmaceutical composition is present in one or more unit dosages.

46. A method comprising administering a therapeutically effective amount of the pharmaceutical composition of any one of claims 41 to 43 to an individual in need thereof.

47. The method according to claim 46, wherein the administering is by systemic administration.

48. The method according to claim 47, wherein the systemic administration is by parenteral administration.

49. The method according to claim 48, wherein the parenteral administration is by intravenous administration.

50. The method according to claim 47, wherein the systemic administration is by oral administration.

51. The method according to any one of claims 46 to 50, wherein the individual has cancer, the engineered loop binds to a cell surface molecule on cancer cells present in the individual, and the method is a method of treating the cancer of the individual.

52. The method according to claim 51, wherein the cell surface molecule is a cell surface receptor.

53. The method according to claim 52, wherein the cell surface receptor is a cell adhesion receptor.

54. The method according to claim 53, wherein the cell adhesion receptor is an integrin.

55. The method according to claim 54, wherein the integrin is selected from the group consisting of: αvβ1 integrin, αvβ3 integrin, αvβ5 integrin, αvβ6 integrin, α5β1 integrin, and any combination thereof.

56. The method according to any one of claims 51 to 55, wherein the individual has a solid tumor comprising the cancer cells.

57. The method according to claim 56, wherein the administering is by systemic administration, and wherein the immune cell microenvironment of the solid tumor is characterized by one or any combination of increased percentage of CD8+ T cells, increased percentage of CD4+ T cells, increased percentage of B cells, and/or decreased percentage of myeloid-derived suppressor cells (MDSCs), as compared to the immune cell microenvironment of the tumor when the immunostimulant alone is administered systemically to the individual.

58. The method according to claim 56, wherein the administering is by systemic administration, and wherein the immune cell microenvironment of the solid tumor as assessed by one or any combination of the percentage of CD8+ T cells, the percentage of CD4+ T cells, the percentage of B cells, and/or the percentage of myeloid-derived suppressor cells (MDSCs), is not statistically significantly different as compared to the immune cell microenvironment of the tumor when the immunostimulant alone is administered intratumorally to the individual.

59. The method according to any one of claims 51 to 55, wherein the individual has a liquid tumor comprising the cancer cells.

60. A method of making a knottin-immunostimulant conjugate, comprising conjugating an immunostimulant to a knottin peptide via a linker.

61. The method according to claim 60, wherein the conjugating comprises:
functionalizing the immunostimulant; and
conjugating the functionalized immunostimulant to the knottin peptide.

62. The method according to claim 61, wherein the immunostimulant comprises a primary amine, and wherein functionalizing the immunostimulant comprises reacting the primary amine with an amine-reactive linker.

63. The method according to claim 62, wherein the amine-reactive linker is an amine-reactive NHS ester linker.

64. The method according to claim 62 or claim 63, wherein the amine-reactive linker comprises a moiety selected from the group consisting of: bicyclo[6.1.0]nonyne (BCN), dibenzocyclooctyne (DBCO), and an azide moiety.

65. The method according to claim 64, wherein conjugating the functionalized immunostimulant to the knottin peptide comprises reacting the moiety of the amine-reactive linker with a moiety of the knottin peptide.

66. The method according to claim 65, wherein the knottin peptide comprises a non-natural amino acid comprising the moiety of the knottin peptide.

67. The method according to claim 66, wherein the non-natural amino acid is 5-azido-L-norvaline.

68. The method according to claim 65, wherein the moiety of the knottin peptide is an N-terminal amine group.

69. The method according to any one of claims 60 to 68, wherein the immunostimulant is an immunostimulant as defined in any one of claims 2 to 13.

70. The method according to any one of claims 60 to 69, wherein the knottin peptide is a knottin peptide as defined in any one of claims 20 to 39.