

CLAIMS

1. — A fusion polypeptide comprising:
 - (a) a first polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) a transmembrane domain; and
 - (iii) an immune receptor intracellular signaling domain;
 - (b) a polypeptide cleavage signal; and
 - (c) a second polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) a transmembrane domain; and
 - (iii) an immune receptor intracellular signaling domain.
2. — The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is isolated from a cytokine receptor, an interleukin receptor, a pattern recognition receptor, or a toll-like receptor.
3. — The fusion polypeptide of claim 1 or claim 2, wherein the immune receptor intracellular signaling domain of the second polypeptide is isolated from a cytokine receptor, an interleukin receptor, a pattern recognition receptor, or a toll-like receptor.
4. — The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-12R β 2 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-12R β 1 intracellular signaling domain.
5. — The fusion polypeptide of claim 4, wherein the transmembrane domain of the first polypeptide comprises an IL-12R β 2 transmembrane domain.

6. — The fusion polypeptide of claim 4 or claim 5, wherein the transmembrane domain of the second polypeptide comprises an IL-12R β 1 transmembrane domain.

7. — The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-12R β 1 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-12R β 2 intracellular signaling domain.

8. — The fusion polypeptide of claim 7, wherein the transmembrane domain of the first polypeptide comprises an IL-12R β 1 transmembrane domain.

9. — The fusion polypeptide of claim 7 or claim 8, wherein the transmembrane domain of the second polypeptide comprises an IL-12R β 2 transmembrane domain.

10. — The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-7R α intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-2R γ intracellular signaling domain.

11. — The fusion polypeptide of claim 10, wherein the transmembrane domain of the first polypeptide comprises an IL-7R α transmembrane domain.

12. — The fusion polypeptide of claim 10 or claim 11, wherein the transmembrane domain of the second polypeptide comprises an IL-2R γ transmembrane domain.

13. — The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-2R γ intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-7R α intracellular signaling domain.

14. — ~~The fusion polypeptide of claim 13, wherein the transmembrane domain of the first polypeptide comprises an IL-2R γ transmembrane domain.~~

15. — ~~The fusion polypeptide of claim 13 or claim 14, wherein the transmembrane domain of the second polypeptide comprises an IL-7R α transmembrane domain.~~

16. — ~~The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-2R β intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-2R γ intracellular signaling domain.~~

17. — ~~The fusion polypeptide of claim 16, wherein the transmembrane domain of the first polypeptide comprises an IL-2R β transmembrane domain.~~

18. — ~~The fusion polypeptide of claim 16 or claim 17, wherein the transmembrane domain of the second polypeptide comprises an IL-2R γ transmembrane domain.~~

19. — ~~The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-2R γ intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-2R β intracellular signaling domain.~~

20. — ~~The fusion polypeptide of claim 19, wherein the transmembrane domain of the first polypeptide comprises an IL-2R γ transmembrane domain.~~

21. — ~~The fusion polypeptide of claim 19 or claim 20, wherein the transmembrane domain of the second polypeptide comprises an IL-2R β transmembrane domain.~~

22. — The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-21R intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-2R γ intracellular signaling domain.

23. — The fusion polypeptide of claim 22, wherein the transmembrane domain of the first polypeptide comprises an IL-21R transmembrane domain.

24. — The fusion polypeptide of claim 22 or claim 23, wherein the transmembrane domain of the second polypeptide comprises an IL-2R γ transmembrane domain.

25. — The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-2R γ intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-21R intracellular signaling domain.

26. — The fusion polypeptide of claim 25, wherein the transmembrane domain of the first polypeptide comprises an IL-2R γ transmembrane domain.

27. — The fusion polypeptide of claim 25 or claim 26, wherein the transmembrane domain of the second polypeptide comprises an IL-21R transmembrane domain.

28. — The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-18R1 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-18RAP intracellular signaling domain.

29. — The fusion polypeptide of claim 28, wherein the transmembrane domain of the first polypeptide comprises an IL-18R1 transmembrane domain.

30. — ~~The fusion polypeptide of claim 28 or claim 29, wherein the transmembrane domain of the second polypeptide comprises an IL-18RAP transmembrane domain.~~

31. — ~~The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-18RAP intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-18R1 intracellular signaling domain.~~

32. — ~~The fusion polypeptide of claim 31, wherein the transmembrane domain of the first polypeptide comprises an IL-18RAP transmembrane domain.~~

33. — ~~The fusion polypeptide of claim 31 or claim 32, wherein the transmembrane domain of the second polypeptide comprises an IL-18R1 transmembrane domain.~~

34. — ~~The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-1R1 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-1RAP intracellular signaling domain.~~

35. — ~~The fusion polypeptide of claim 34, wherein the transmembrane domain of the first polypeptide comprises an IL-1R1 transmembrane domain.~~

36. — ~~The fusion polypeptide of claim 34 or claim 35, wherein the transmembrane domain of the second polypeptide comprises an IL-1RAP transmembrane domain.~~

37. — ~~The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-1RAP intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-1R1 intracellular signaling domain.~~

38.——The fusion polypeptide of claim 37, wherein the transmembrane domain of the first polypeptide comprises an IL-1RAP transmembrane domain.

39.——The fusion polypeptide of claim 37 or claim 38, wherein the transmembrane domain of the second polypeptide comprises an IL-1R1 transmembrane domain.

40.——The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-1RAP intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-1RL2 intracellular signaling domain.

41.——The fusion polypeptide of claim 22, wherein the transmembrane domain of the first polypeptide comprises an IL-1RAP transmembrane domain.

42.——The fusion polypeptide of claim 40 or claim 41, wherein the transmembrane domain of the second polypeptide comprises an IL-1RL2 transmembrane domain.

43.——The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IL-1RL2 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IL-1RAP intracellular signaling domain.

44.——The fusion polypeptide of claim 43, wherein the transmembrane domain of the first polypeptide comprises an IL-1RL2 transmembrane domain.

45.——The fusion polypeptide of claim 43 or claim 44, wherein the transmembrane domain of the second polypeptide comprises an IL-1RAP transmembrane domain.

46.——The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IFNAR1 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IFNAR2 intracellular signaling domain.

47.——The fusion polypeptide of claim 46, wherein the transmembrane domain of the first polypeptide comprises an IFNAR1 transmembrane domain.

48.——The fusion polypeptide of claim 46 or claim 47, wherein the transmembrane domain of the second polypeptide comprises an IFNAR2 transmembrane domain.

49.——The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is an IFNAR2 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is an IFNAR1 intracellular signaling domain.

50.——The fusion polypeptide of claim 49, wherein the transmembrane domain of the first polypeptide comprises an IFNAR2 transmembrane domain.

51.——The fusion polypeptide of claim 49 or claim 50, wherein the transmembrane domain of the second polypeptide comprises an IFNAR1 transmembrane domain.

52.——The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR1 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR1 intracellular signaling domain.

53.——The fusion polypeptide of claim 52, wherein the transmembrane domain of the first polypeptide comprises a TLR1 transmembrane domain.

54. —The fusion polypeptide of claim 52 or claim 53, wherein the transmembrane domain of the second polypeptide comprises a TLR1 transmembrane domain.

55. —The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR2 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR2 intracellular signaling domain.

56. —The fusion polypeptide of claim 55, wherein the transmembrane domain of the first polypeptide comprises a TLR2 transmembrane domain.

57. —The fusion polypeptide of claim 55 or claim 56, wherein the transmembrane domain of the second polypeptide comprises a TLR2 transmembrane domain.

58. —The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR3 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR3 intracellular signaling domain.

59. —The fusion polypeptide of claim 58, wherein the transmembrane domain of the first polypeptide comprises a TLR3 transmembrane domain.

60. —The fusion polypeptide of claim 58 or claim 59, wherein the transmembrane domain of the second polypeptide comprises a TLR3 transmembrane domain.

61. —The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR4 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR4 intracellular signaling domain.

62. — ~~The fusion polypeptide of claim 61, wherein the transmembrane domain of the first polypeptide comprises a TLR4 transmembrane domain.~~

63. — ~~The fusion polypeptide of claim 61 or claim 62, wherein the transmembrane domain of the second polypeptide comprises a TLR4 transmembrane domain.~~

64. — ~~The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR5 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR5 intracellular signaling domain.~~

65. — ~~The fusion polypeptide of claim 64, wherein the transmembrane domain of the first polypeptide comprises a TLR5 transmembrane domain.~~

66. — ~~The fusion polypeptide of claim 64 or claim 65, wherein the transmembrane domain of the second polypeptide comprises a TLR5 transmembrane domain.~~

67. — ~~The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR6 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR6 intracellular signaling domain.~~

68. — ~~The fusion polypeptide of claim 67, wherein the transmembrane domain of the first polypeptide comprises a TLR6 transmembrane domain.~~

69. — ~~The fusion polypeptide of claim 67 or claim 68, wherein the transmembrane domain of the second polypeptide comprises a TLR6 transmembrane domain.~~

70.——The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR7 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR7 intracellular signaling domain.

71.——The fusion polypeptide of claim 70, wherein the transmembrane domain of the first polypeptide comprises a TLR7 transmembrane domain.

72.——The fusion polypeptide of claim 70 or claim 71, wherein the transmembrane domain of the second polypeptide comprises a TLR7 transmembrane domain.

73.——The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR8 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR8 intracellular signaling domain.

74.——The fusion polypeptide of claim 73, wherein the transmembrane domain of the first polypeptide comprises a TLR8 transmembrane domain.

75.——The fusion polypeptide of claim 73 or claim 74, wherein the transmembrane domain of the second polypeptide comprises a TLR8 transmembrane domain.

76.——The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR9 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR9 intracellular signaling domain.

77.——The fusion polypeptide of claim 76, wherein the transmembrane domain of the first polypeptide comprises a TLR9 transmembrane domain.

78. — ~~The fusion polypeptide of claim 76 or claim 77, wherein the transmembrane domain of the second polypeptide comprises a TLR9 transmembrane domain.~~

79. — ~~The fusion polypeptide of claim 1, wherein the immune receptor intracellular signaling domain of the first polypeptide is a TLR10 intracellular signaling domain and the immune receptor intracellular signaling domain of the second polypeptide is a TLR10 intracellular signaling domain.~~

80. — ~~The fusion polypeptide of claim 79, wherein the transmembrane domain of the first polypeptide comprises a TLR10 transmembrane domain.~~

81. — ~~The fusion polypeptide of claim 79 or claim 80, wherein the transmembrane domain of the second polypeptide comprises a TLR10 transmembrane domain.~~

82. — ~~The fusion polypeptide of any one of claims 1 to 81, wherein the polypeptide cleavage signal is a viral self-cleaving polypeptide.~~

83. — ~~The fusion polypeptide of any one of claims 1 to 82, wherein the polypeptide cleavage signal is a viral self-cleaving 2A polypeptide.~~

84. — ~~The fusion polypeptide of any one of claims 1 to 83, wherein the polypeptide cleavage signal is a viral self-cleaving polypeptide selected from the group consisting of: a foot-and-mouth disease virus (FMDV) (F2A) peptide, an equine rhinitis A virus (ERAV) (E2A) peptide, a Thosela asina virus (TaV) (T2A) peptide, a porcine teschovirus-1 (PTV-1) (P2A) peptide, a Theilovirus 2A peptide, and an encephalomyocarditis virus 2A peptide.~~

85. — ~~A fusion polypeptide comprising:~~

~~(a) a TGF β R2 polypeptide comprising:~~

~~(i) an extracellular TGF β 1 binding domain of TGF β R2;~~

- (ii) an IL-12R β 2 transmembrane domain; and
- (iii) an IL-12R β 2 intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) an IL-12R β 1 transmembrane domain; and
 - (iii) an IL-12R β 1 intracellular signaling domain.

86. — A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) an IL-12R β 1 transmembrane domain; and
 - (iii) an IL-12R β 1 intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) an IL-12R β 2 transmembrane domain; and
 - (iii) an IL-12R β 2 intracellular signaling domain.

87. — A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) an IL-7R α transmembrane domain; and
 - (iii) an IL-7R α intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) an IL-2R γ transmembrane domain; and
 - (iii) an IL-2R γ intracellular signaling domain.

88. — A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;
- (ii) an IL-2R γ transmembrane domain; and
- (iii) an IL-2R γ intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R1;
- (ii) an IL-7R α transmembrane domain; and
- (iii) an IL-7R α intracellular signaling domain.

89. — A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;
- (ii) an IL-2R β transmembrane domain; and
- (iii) an IL-2R β intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R1;
- (ii) an IL-2R γ transmembrane domain; and
- (iii) an IL-2R γ intracellular signaling domain.

90. — A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;
- (ii) an IL-2R γ transmembrane domain; and
- (iii) an IL-2R γ intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R1;
- (ii) an IL-2R β transmembrane domain; and
- (iii) an IL-2R β intracellular signaling domain.

91. — A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;
- (ii) an IL-21R transmembrane domain; and
- (iii) an IL-21R intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R1;
- (ii) an IL-2R γ transmembrane domain; and
- (iii) an IL-2R γ intracellular signaling domain.

92. — A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;
- (ii) an IL-2R γ transmembrane domain; and
- (iii) an IL-2R γ intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R1;
- (ii) an IL-21R transmembrane domain; and
- (iii) an IL-21R intracellular signaling domain.

93. — A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;

- (ii) ~~an IL-18R1 transmembrane domain; and~~
 - (iii) ~~an IL-18R1 intracellular signaling domain;~~
- (b) ~~a viral self-cleaving 2A peptide; and~~
- (c) ~~a TGF β R1 polypeptide comprising:~~
 - (i) ~~an extracellular TGF β 1 binding domain of TGF β R1;~~
 - (ii) ~~an IL-18RAP transmembrane domain; and~~
 - (iii) ~~an IL-18RAP intracellular signaling domain.~~

94. — ~~A fusion polypeptide comprising:~~

- (a) ~~a TGF β R2 polypeptide comprising:~~
 - (i) ~~an extracellular TGF β 1 binding domain of TGF β R2;~~
 - (ii) ~~an IL-18RAP transmembrane domain; and~~
 - (iii) ~~an IL-18RAP intracellular signaling domain;~~
- (b) ~~a viral self-cleaving 2A peptide; and~~
- (c) ~~a TGF β R1 polypeptide comprising:~~
 - (i) ~~an extracellular TGF β 1 binding domain of TGF β R1;~~
 - (ii) ~~an IL-18R1 transmembrane domain; and~~
 - (iii) ~~an IL-18R1 intracellular signaling domain.~~

95. — ~~A fusion polypeptide comprising:~~

- (a) ~~a TGF β R2 polypeptide comprising:~~
 - (i) ~~an extracellular TGF β 1 binding domain of TGF β R2;~~
 - (ii) ~~an IL-1R1 transmembrane domain; and~~
 - (iii) ~~an IL-1R1 intracellular signaling domain;~~
- (b) ~~a viral self-cleaving 2A peptide; and~~
- (c) ~~a TGF β R1 polypeptide comprising:~~
 - (i) ~~an extracellular TGF β 1 binding domain of TGF β R1;~~
 - (ii) ~~an IL-1RAP transmembrane domain; and~~
 - (iii) ~~an IL-1RAP intracellular signaling domain.~~

96. — A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) an IL-1RAP transmembrane domain; and
 - (iii) an IL-1RAP intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) an IL-1R1 transmembrane domain; and
 - (iii) an IL-1R1 intracellular signaling domain.

97. — A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) an IFNAR1 transmembrane domain; and
 - (iii) an IFNAR1 intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) an IFNAR2 transmembrane domain; and
 - (iii) an IFNAR2 intracellular signaling domain.

98. — A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) an IFNAR2 transmembrane domain; and
 - (iii) an IFNAR2 intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:

- (i) ~~an extracellular TGF β 1 binding domain of TGF β R1;~~
- (ii) ~~an IFNAR1 transmembrane domain; and~~
- (iii) ~~an IFNAR1 intracellular signaling domain.~~

99. — ~~A fusion polypeptide comprising:~~

~~(a) a TGF β R2 polypeptide comprising:~~

- ~~(i) an extracellular TGF β 1 binding domain of TGF β R2;~~
- ~~(ii) a TLR1 transmembrane domain; and~~
- ~~(iii) a TLR1 intracellular signaling domain;~~

~~(b) a viral self cleaving 2A peptide; and~~

~~(c) a TGF β R1 polypeptide comprising:~~

- ~~(i) an extracellular TGF β 1 binding domain of TGF β R1;~~
- ~~(ii) a TLR1 transmembrane domain; and~~
- ~~(iii) a TLR1 intracellular signaling domain.~~

100. — ~~A fusion polypeptide comprising:~~

~~(a) a TGF β R2 polypeptide comprising:~~

- ~~(i) an extracellular TGF β 1 binding domain of TGF β R2;~~
- ~~(ii) a TLR2 transmembrane domain; and~~
- ~~(iii) a TLR2 intracellular signaling domain;~~

~~(b) a viral self cleaving 2A peptide; and~~

~~(c) a TGF β R1 polypeptide comprising:~~

- ~~(i) an extracellular TGF β 1 binding domain of TGF β R1;~~
- ~~(ii) a TLR2 transmembrane domain; and~~
- ~~(iii) a TLR2 intracellular signaling domain.~~

101. — ~~A fusion polypeptide comprising:~~

~~(a) a TGF β R2 polypeptide comprising:~~

- ~~(i) an extracellular TGF β 1 binding domain of TGF β R2;~~

- (ii) a TLR3 transmembrane domain; and
 - (iii) a TLR3 intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) a TLR3 transmembrane domain; and
 - (iii) a TLR3 intracellular signaling domain.

102. —A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) a TLR4 transmembrane domain; and
 - (iii) a TLR4 intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) a TLR4 transmembrane domain; and
 - (iii) a TLR4 intracellular signaling domain.

103. —A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) a TLR5 transmembrane domain; and
 - (iii) a TLR5 intracellular signaling domain;
- (b) a viral self-cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) a TLR5 transmembrane domain; and
 - (iii) a TLR5 intracellular signaling domain.

104. —A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;
- (ii) a TLR6 transmembrane domain; and
- (iii) a TLR6 intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R1;
- (ii) a TLR6 transmembrane domain; and
- (iii) a TLR6 intracellular signaling domain.

105. —A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;
- (ii) a TLR7 transmembrane domain; and
- (iii) a TLR7 intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R1;
- (ii) a TLR7 transmembrane domain; and
- (iii) a TLR7 intracellular signaling domain.

106. —A fusion polypeptide comprising:

(a) a TGF β R2 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R2;
- (ii) a TLR8 transmembrane domain; and
- (iii) a TLR8 intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

- (i) an extracellular TGF β 1 binding domain of TGF β R1;
- (ii) a TLR8 transmembrane domain; and
- (iii) a TLR8 intracellular signaling domain.

107. — A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) a TLR9 transmembrane domain; and
 - (iii) a TLR9 intracellular signaling domain;
- (b) a viral self cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) a TLR9 transmembrane domain; and
 - (iii) a TLR9 intracellular signaling domain.

108. — A fusion polypeptide comprising:

- (a) a TGF β R2 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R2;
 - (ii) a TLR10 transmembrane domain; and
 - (iii) a TLR10 intracellular signaling domain;
- (b) a viral self cleaving 2A peptide; and
- (c) a TGF β R1 polypeptide comprising:
 - (i) an extracellular TGF β 1 binding domain of TGF β R1;
 - (ii) a TLR10 transmembrane domain; and
 - (iii) a TLR10 intracellular signaling domain.

109. — The fusion polypeptide of any one of claims 85 to 108, wherein the viral self cleaving 2A polypeptide is selected from the group consisting of: a foot and mouth disease virus (FMDV) (F2A) peptide, an equine rhinitis A virus (ERAV) (E2A) peptide, a Thossea asigna virus

~~(TaV) (T2A) peptide, a porcine teschovirus 1 (PTV 1) (P2A) peptide, a Theilovirus 2A peptide, and an encephalomyocarditis virus 2A peptide.~~

110.—The fusion polypeptide of any one of claims 1 to 109, further comprising an engineered antigen receptor and a second viral self-cleaving 2A polypeptide.

111.—The fusion polypeptide of claim 110, wherein the second viral self-cleaving 2A polypeptide is selected from the group consisting of: ~~a foot and mouth disease virus (FMDV) (F2A) peptide, an equine rhinitis A virus (ERAV) (E2A) peptide, a Thosa asigna virus (TaV) (T2A) peptide, a porcine teschovirus 1 (PTV 1) (P2A) peptide, a Theilovirus 2A peptide, and an encephalomyocarditis virus 2A peptide.~~

112.—The polypeptide of claim 110 or claim 111, wherein the engineered antigen receptor is selected from the group consisting of: ~~an engineered T cell receptor (TCR), a chimeric antigen receptor (CAR), a DARIC receptor or components thereof, and a chimeric cytokine receptor; optionally, wherein the engineered antigen receptor recognizes an antigen selected from the group consisting of: alpha folate receptor, 5T4, $\alpha\beta6$ integrin, BCMA, B7-H3, B7-H6, CAIX, CD16, CD19, CD20, CD22, CD30, CD33, CD44, CD44v6, CD44v7/8, CD70, CD79a, CD79b, CD123, CD138, CD171, CEA, CSPG4, EGFR, EGFR family including ErbB2 (HER2), EGFRvIII, EGP2, EGP40, EPCAM, EphA2, EpCAM, FAP, fetal AchR, FR α , GD2, GD3, Glypican-3 (GPC3), HLA-A1+MAGE1, HLA-A2+MAGE1, HLA-A3+MAGE1, HLA-A1+NY-ESO-1, HLA-A2+NY-ESO-1, HLA-A3+NY-ESO-1, IL-11R α , IL-13R $\alpha2$, Lambda, Lewis-Y, Kappa, Mesothelin, Muc1, Muc16, NCAM, NKG2D Ligands, NY-ESO-1, PRAME, PSCA, PSMA, ROR1, SSX, Survivin, TAG72, TEMs, VEGFR2, and WT-1.~~

113.—A polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 26 to 35.

114. — A polypeptide complex comprising the TGF β R2 polypeptide and the TGF β R1 polypeptide of any one of claims 1-113.

115. — A polynucleotide encoding the polypeptide set forth in any one of claims 1 to 113.

116. — A vector comprising the polynucleotide encoding a polypeptide of any one of claims 1 to 113, or the polynucleotide of claim 114.

117. — A cell comprising the polypeptide of any one of claims 1 to 113, the polypeptide complex of claim 113, the polynucleotide of claim 114, or the vector of claim 115.

118. — The cell of claim 117, wherein the cell is a hematopoietic cell.

119. — The cell of claim 117 or 118, wherein the cell is a T cell.

120. — The cell of any one of claims 117 to 119, wherein the cell is a CD3⁺, CD4⁺, and/or CD8⁺ cell.

121. — The cell of any one of claims 117 to 120, wherein the cell is an immune effector cell.

122. — The cell of any one of claims 117 to 121, wherein the cell is a cytotoxic T lymphocytes (CTLs), a tumor infiltrating lymphocytes (TILs), or a helper T cells.

123. — The cell of any one of claims 117 to 122, wherein the cell is a natural killer (NK) cell or natural killer T (NKT) cell.

124.—The cell of any one of claims 117 to 123, wherein the source of the cell is peripheral blood mononuclear cells, bone marrow, lymph nodes tissue, cord blood, thymus issue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, or tumors.

125.—The cell of any one of claims 117 to 124, further comprising an engineered antigen receptor.

126.—The cell of claim 125, wherein the engineered antigen receptor is selected from the group consisting of: an engineered T cell receptor (TCR), a chimeric antigen receptor (CAR), a DARIC receptor or components thereof, and a chimeric cytokine receptor.

127.—A composition comprising the polypeptide of any one of claims 1 to 113, the polypeptide complex of claim 114, the polynucleotide of claim 115, the vector of claim 116, or the cell of any one of claims 117 to 126.

128.—A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polypeptide of any one of claims 1 to 113, the polypeptide complex of claim 113, the polynucleotide of claim 114, the vector of claim 115, or the cell of any one of claims 117 to 126.

129.—A method of treating a subject in need thereof comprising administering the subject an effective amount of the composition of claim 128.

130.—A method of treating, preventing, or ameliorating at least one symptom of a cancer, infectious disease, autoimmune disease, inflammatory disease, and immunodeficiency, or condition associated therewith, comprising administering to the subject an effective amount of the composition of claim 128.

131.—A method of treating a solid cancer comprising administering to the subject an effective amount of the composition of claim 128.

~~132. The method of claim 131, wherein the solid cancer comprises liver cancer, pancreatic cancer, lung cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, bladder cancer, brain cancer, sarcoma, head and neck cancer, bone cancer, thyroid cancer, kidney cancer, or skin cancer.~~

~~133. The method of claim 131 or 132, wherein the solid cancer is a pancreatic cancer, a lung cancer, or a breast cancer.~~

~~134. A method of treating a hematological malignancy comprising administering to the subject an effective amount of the composition of claim 128.~~

~~135. The method of claim 134, wherein the hematological malignancy is a leukemia, lymphoma, or multiple myeloma.~~

1. A lentiviral vector comprising a polynucleotide encoding a fusion polypeptide comprising:

I) (a) a TGF β R2 polypeptide comprising:

(i) an extracellular TGF β 1-binding domain of TGF β R2;

(ii) an IL-12R β 2 transmembrane domain; and

(iii) an IL-12R β 2 intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

(i) an extracellular TGF β 1-binding domain of TGF β R1;

(ii) an IL-12R β 1 transmembrane domain; and

(iii) an IL-12R β 1 intracellular signaling domain; or

II) (a) a TGF β R2 polypeptide comprising:

(i) an extracellular TGF β 1-binding domain of TGF β R2;

(ii) an IL-12R β 1 transmembrane domain; and

(iii) an IL-12R β 1 intracellular signaling domain;

(b) a viral self-cleaving 2A peptide; and

(c) a TGF β R1 polypeptide comprising:

(i) an extracellular TGF β 1-binding domain of TGF β R1;

(ii) an IL-12R β 2 transmembrane domain; and

(iii) an IL-12R β 2 intracellular signaling domain.

2. The lentiviral vector of claim 1, further comprising an engineered antigen receptor and a second viral self-cleaving 2A polypeptide.

3. The lentiviral vector of claim 2, wherein the engineered antigen receptor is selected from the group consisting of: an engineered T cell receptor (TCR), a chimeric antigen receptor (CAR), a DARIC receptor or components thereof, and a chimeric cytokine receptor; optionally, wherein the engineered antigen receptor recognizes an antigen selected from the group consisting of: alpha folate receptor, 5T4, α v β 6 integrin, BCMA, B7-H3, B7-H6, CAIX, CD16, CD19, CD20, CD22, CD30, CD33, CD44, CD44v6, CD44v7/8, CD70, CD79a, CD79b, CD123, CD138, CD171, CEA, CSPG4, EGFR, EGFR family including ErbB2 (HER2), EGFRvIII, EGP2, EGP40, EphA2, EpCAM, FAP, fetal AchR, GD2, GD3, Glypican-3 (GPC3), HLA-A1+MAGE1, HLA-A2+MAGE1, HLA-A3+MAGE1, HLA-A1+NY-ESO-1, HLA-A2+NY-ESO-1, HLA-A3+NY-ESO-1, IL-11R α , IL-13R α 2, Lambda, Lewis-Y, Kappa, Mesothelin, Muc1, Muc16, NCAM, NKG2D Ligands, NY-ESO-1, PRAME, PSCA, PSMA, ROR1, SSX, Survivin, TAG72, TEMs, VEGFR2, and WT-1.

4. A cell comprising the lentiviral vector of any one of claims 1 to 3.

5. The cell of claim 4, wherein the cell is:

(a) a hematopoietic cell;

(b) a T cell;

(c) a CD3⁺, CD4⁺, and/or CD8⁺ cell;

(d) an immune effector cell;

(e) a cytotoxic T lymphocyte (CTL), a tumor infiltrating lymphocyte (TIL), or a helper T cell; or

(f) a natural killer (NK) cell or natural killer T (NKT) cell.

6. A composition comprising the lentiviral vector of any one of claims 1 to 3, or the cell of claim 4 or claim 5.

7. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the lentiviral vector of any one of claims 1 to 3, or the cell of claim 4 or claim 5.

8. Use of the composition of claim 7 in the manufacture of a medicament for treating, preventing, or ameliorating at least one symptom of a cancer, solid cancer, or hematological malignancy.

9. Use of the lentiviral vector of any one of claims 1 to 3, or the cell of claim 4 or claim 5 in the manufacture of a medicament for treating, preventing, or ameliorating at least one symptom of a cancer, solid cancer, or hematological malignancy.