WHAT IS CLAIMED IS:

1. An isolated fusion protein comprising:

(i) a first portion of an extracellular domain, transmembrane domain, or intracellular domain of a cytokine, cytokine receptor, or immunomodulatory protein;

(ii) an amino acid linker; and at least one of,

(iii) a second portion of an extracellular domain, transmembrane domain, or intracellular domain of a cytokine, cytokine receptor, or immunomodulatory protein;

(iv) an immunoglobulin (Ig) hinge region; and

(v) an immunoglobulin (Ig) Fc domain.

2. The isolated fusion protein of claim 1, wherein the linker comprises from about 5 to about 40 amino acid residues.

3. An isolated fusion protein comprising, in an N- to C- terminal orientation:

(i) a soluble portion of an extracellular domain of a cytokine receptor;

(ii) an amino acid linker;

(iii) an immunoglobulin (Ig) hinge region; and

(iv) an immunoglobulin (Ig) Fc domain;

wherein the linker comprises from about 5 to about 40 amino acid residues.

4. The isolated fusion protein of any one of claims 1-3, wherein the linker comprises from about 5 to about 30 amino acid residues.

5. The isolated fusion protein of any one of claims 1-3, wherein the linker comprises from about 5 to about 20 amino acid residues.

6. The isolated fusion protein of any one of claims 1-3, wherein the linker comprises from about 5 to about 15 amino acid residues.

7. The isolated fusion protein of any one of claims 1-3, wherein the linker comprises from about 10 to about 40 amino acid residues.

8. The isolated fusion protein of any one of claims 1-3, wherein the linker comprises from about 10 to about 30 amino acid residues.

9. The isolated fusion protein of any one of claims 1-3, wherein the linker comprises from about 10 to about 20 amino acid residues.

10. The isolated fusion protein of any one of claims 1-3, wherein the linker comprises from about 10 to about 15 amino acid residues.

11. The isolated fusion protein of any one of claims 1-10, wherein the linker comprises a sequence derived from an endogenous human protein.

12. The isolated fusion protein of any one of claims 1-11, wherein the linker comprises a C-terminal portion of an immunoglobulin (Ig) CH1 domain.

13. The isolated fusion protein of claim 12, wherein the Ig CH1domain is selected from an IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, IgD, IgE, and IgM CH1domain.

14. The isolated fusion protein of claim 13, wherein the linker comprises an amino acid sequence selected from SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 60, and SEQ ID NO: 61.

15. The isolated fusion protein of claim 13, wherein the linker comprises an amino acid sequence selected from SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9.

16. The isolated fusion protein of claim 14 or 15, wherein the Ig CH1domain is an IgG1 CH1 domain.

17. The isolated fusion protein of claim 16, wherein the linker comprises an amino acid sequence selected from SEQ ID NO: 1, SEQ ID NO: 60, and SEQ ID NO: 61.

18. The isolated fusion protein of claim 16, wherein the linker comprises the amino acid sequence of SEQ ID NO: 1.

19. The isolated fusion protein of any one of claims 1-11, wherein the linker comprises a sequence derived from a human protein selected from albumin and casein.

20. The isolated fusion protein of claim 19, wherein the linker comprises an amino acid sequence selected from SEQ ID NO: 10 and SEQ ID NO: 11.

21. The isolated fusion protein of any one of claims 1-11, wherein the linker comprises a sequence derived from a cytokine, signaling molecule, immunomodulatory protein or a peptide.

22. The isolated fusion protein of any one of claims 1-21, wherein the linker comprises a cleavage site.

23. The isolated fusion protein of claim 22, wherein the cleavage site is a proteolytic cleavage site.

24. The isolated fusion protein of claim 23, wherein the proteolytic cleavage site is cleaved by a protease that is present in the endoplasmic reticulum or golgi of a eukaryotic cell.

25. The isolated fusion protein of claims 23 or 24, wherein the proteolytic cleavage site is a furin cleavage site.

26. The isolated fusion protein of claim 25, wherein the furin cleavage site comprises RX_1X_2R (SEQ ID NO: 50), wherein X_1 is any amino acid, and X_2 is Lys or Arg.

27. The isolated fusion protein of claim 26, wherein the furin cleavage site comprises RAKR (SEQ ID NO: 51).

28. The isolated fusion protein of any one of claims 1-21, wherein the linker comprises an amino acid sequence which is proteolytically stable in a mammal or plant.

29. The isolated fusion protein of any one of claims 1-28, wherein the cytokine receptor is a human TGFβ type II receptor.

30. The isolated fusion protein of claim 29, wherein the soluble portion of an extracellular domain of a cytokine receptor comprises the amino acid sequence of SEQ ID NO: 12.

31. The isolated fusion protein of claim 29, wherein the soluble portion of an extracellular domain of a cytokine receptor comprises amino acid residues 23-159 of SEQ ID NO: 12.

32. The isolated fusion protein of any one of claims 1-31, wherein the fusion protein comprises one or more of TGF-β, CD80, CD19, CD20, IL-1, IL-3, IL-4, IL-5, IL-6, IL-8, IL-9, IL-12B/p40, IL-23A/p19, IL27A/p28, IL-27B/EBI3, CD154, CD86, CD137, CD137L, IFN-α, IFN-β, BORIS/CTCFL, FGF, ICAM, IL-24, MAGE, NY-ESO-1, angiostatin, endostatin, acetylcholine, interferon-gamma, DKK1/Wnt, p53, thymidine kinase, an anti-PD-1 antibody heavy chain or light chain, and an anti-PD-L1 antibody heavy chain or light chain, or a functional fragment thereof.

33. The isolated fusion protein of any one of claims 1-32, wherein the Ig Fc domain and hinge region are selected from a human IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, IgD, IgE, and IgM Fc domain and hinge region.

34. The isolated fusion protein of claim 33, wherein the Ig Fc domain and hinge region comprise an amino acid sequence selected from SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20 and SEQ ID NO: 21.

35. The isolated fusion protein of claim 34, wherein the Ig Fc domain and hinge region are a human IgG1 Fc domain and hinge region.

36. The isolated fusion protein of claim 35, wherein the Ig Fc domain and hinge region comprise the amino acid sequence of SEQ ID NO: 13.

37. The isolated fusion protein of any one of claims 1-36, wherein the Ig Fc, Ig hinge region, and Ig CH1 domain are derived from a single immunoglobulin.

38. The isolated fusion protein of any one of claims 1-37, wherein the fusion protein comprises an amino acid sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 62, and SEQ ID NO: 63.

39. The isolated fusion protein of any one of claims 1-37, wherein the fusion protein comprises an amino acid sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, and SEQ ID NO: 33.

40. The isolated fusion protein of claim 38 or 39, wherein the fusion protein comprises an amino acid sequence selected from SEQ ID NO: 22, SEQ ID NO: 62, and SEQ ID NO: 63.

41. The isolated fusion protein of claim 38 or 39, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 22.

42. A cytokine binding protein comprising two fusion proteins of any one of claims 1-41, wherein each fusion protein comprises an extracellular domain of a cytokine receptor, wherein

the two fusion proteins are covalently linked together, and wherein the two extracellular domains together define a binding site for binding a cytokine.

43. An isolated nucleic acid comprising a nucleotide sequence encoding the fusion protein of any one of claims 1-42.

44. An expression vector comprising the nucleic acid of claim 43.

45. The expression vector of claim 44, wherein the expression vector is an oncolytic virus.

46. The expression vector of claim 45, wherein the oncolytic virus is an adenovirus.

47. The expression vector of claim 46, wherein the adenovirus is a type 2 or 5 adenovirus.

48. The expression vector of claim 47, wherein the adenovirus is a type 5 adenovirus .

49. The expression vector of any one of claims 46-48, wherein the nucleotide sequence encoding the fusion protein is inserted into an E1b-19K insertion site located between the start site of E1b-19K and the start site of E1b-55K.

50. The expression vector of claim 49, wherein the E1b-19K insertion site comprises a deletion of about 200 nucleotides adjacent the start site of E1b-19K.

51. The expression vector of claim 49 or 50, wherein the E1b-19K insertion site comprises a deletion of 203 nucleotides adjacent the start site of E1b-19K.

52. The expression vector of any one of claims 49-51, wherein the E1b-19K insertion site comprises a deletion corresponding to nucleotides 1714-1916 of the Ad5 genome (SEQ ID NO: 52).

53. The expression vector of any one of claims 49-52, wherein the nucleotide sequence encoding the fusion protein is inserted between nucleotides corresponding to 1714 and 1916 of the Ad5 genome (SEQ ID NO: 52).

54. The expression vector of any one of claims 49-53, wherein the nucleotide sequence encoding the fusion protein is inserted between CTGACCTC (SEQ ID NO: 53) and TCACCAGG (SEQ ID NO: 54).

55. The expression vector of any one of claims 49-54, wherein the adenovirus comprises, in a 5' to 3' orientation, CTGACCTC (SEQ ID NO: 53), the nucleotide sequence encoding the fusion protein, and TCACCAGG (SEQ ID NO: 54).

56. The expression vector of any one of claims 46-55, wherein the adenovirus comprises a deletion of a Pea3 binding site, or a functional fragment thereof.

57. The expression vector of claim 56, wherein the adenovirus comprises a deletion of nucleotides corresponding to about -300 to about -250 upstream of the initiation site of E1a.

58. The expression vector of claim 56 or 57, wherein the adenovirus comprises a deletion of nucleotides corresponding to -305 to -255 upstream of the initiation site of E1a.

59. The expression vector of any one of claims 56-58, wherein the adenovirus comprises a deletion of nucleotides corresponding to 195-244 of the Ad5 genome (SEQ ID NO: 52).

60. The expression vector of any one of claims 56-59, wherein the adenovirus comprises the sequence GGTGTTTTGG (SEQ ID NO: 55).

61. The expression vector of any one of claims 46-60, wherein the adenovirus comprises an E3 deletion, wherein the E3 deletion is located between the stop site of pVIII and the start site of Fiber.

62. The expression vector of claim 61, wherein the E3 deletion is located between the stop site of E3-10.5K and the stop site of E3-14.7K.

63. The expression vector of claim 61 or 62, wherein the E3 deletion comprises a deletion of from about 500 to about 3185, from about 500 to about 3000, from about 500 to about 2500, from about 500 to about 2000, from about 500 to about 1500, from about 500 to about 1000, from about 1000 to about 3185, from about 1000 to about 3000, from about 1000 to about 2500, from about 1000 to about 2000, from about 1000 to about 1500, from about 1500 to about 3185, from about 1500 to about 3000, from about 1500 to about 2000, from about 2000 to about 3185, from about 2000 to about 3000, from about 2000 to about 2500, from about 2500 to about 3185, from about 2500 to about 3000, or from about 3000 to about 3185 nucleotides.

64. The expression vector of any one of claims 61-63, wherein the E3 deletion comprises a deletion of from about 500 to about 1551, from about 500 to about 1500, from about 500 to about 1000, from about 1000 to about 1551, from about 1000 to about 1500, or from about 1500 to about 1551 nucleotides adjacent the stop site of E3-10.5K.

65. The expression vector of any one of claims 61-64, wherein the E3 deletion comprises a deletion of about 1050 nucleotides adjacent the stop site of E3-10.5K.

66. The expression vector of any one of claims 61-65, wherein the E3 deletion comprises a deletion of 1064 nucleotides adjacent the stop site of E3-10.5K.

67. The expression vector of any one of claims 61-66, wherein the E3 deletion comprises a deletion corresponding to the Ad5 dl309 E3 deletion.

68. The expression vector of any one of claims 61-67, wherein the E3 deletion comprises a deletion corresponding to nucleotides 29773-30836 of the Ad5 genome (SEQ ID NO: 52).

69. The expression vector of any one of claims 61-68, wherein the nucleotide sequence encoding the fusion protein is inserted into the E3 deletion.

70. The expression vector of claim 69, wherein the nucleotide sequence encoding the fusion protein is inserted between nucleotides corresponding to 29773 and 30836 of the Ad5 genome (SEQ ID NO: 52).

71. The expression vector of claim 69 or 70, wherein the nucleotide sequence encoding the fusion protein is inserted between CAGTATGA (SEQ ID NO: 56) and TAATAAAAAA (SEQ ID NO: 57).

72. The expression vector of any one of claims 69-71, wherein the adenovirus comprises, in a 5' to 3' orientation, CAGTATGA (SEQ ID NO: 56), the nucleotide sequence encoding the fusion protein, and TAATAAAAAA (SEQ ID NO: 57).

73. The expression vector of any one of claims 46-72, wherein the adenovirus does not comprise a deletion of a functional E2F binding site.

74. The expression vector of any one of claims 46-73, wherein the adenovirus comprises a deletion of a functional E2F binding site.

75. The expression vector of any one of claim 46-74, wherein the adenovirus comprises:

(i) an E1b-19K and an E1b-55K start site;

(ii) a nucleotide sequence encoding the fusion protein of any one of claims 1-42 inserted into an E1b-19K insertion site, wherein the insertion site is located between the start site of E1b-19K and the start site of E1b-55K; and

(iii) a modified E1a regulatory sequence, wherein at least one Pea3 binding site, or a functional portion thereof, is deleted.

76. The expression vector of any of claims 45-75, wherein the oncolytic virus selectively replicates in a hyperproliferative cell.

77. The expression vector of any of claims 45-76, wherein the oncolytic virus selectively expresses the fusion protein in a hyperproliferative cell.

78. A host cell comprising the expression vector of any one of claims 44-77.

79. A method of producing a fusion protein comprising:

(a) growing the host cell of claim 78 under conditions to express the fusion protein; and

(b) purifying the fusion protein.

80. A pharmaceutical composition comprising: (i) the fusion protein of any one of claims 1-42 or the expression vector of any one of claims 44-77; and (ii) at least one pharmaceutically acceptable carrier or diluent.

81. A method of expressing a fusion protein in a target cell comprising exposing the cell to an effective amount of the expression vector of any one of claims 44-77 to express the fusion protein.

82. The method of claim 81, wherein the fusion protein is cleaved posttranslationally into two polypeptide chains.

83. A method of inhibiting proliferation of a tumor cell comprising exposing the cell to an effective amount of the dimeric fusion protein of claim 42 to inhibit proliferation of the tumor cell.

84. A method of inhibiting proliferation of a tumor cell comprising exposing the cell to an effective amount of the fusion protein of any one of claims 1-41 to inhibit proliferation of the tumor cell.

85. A method of inhibiting tumor growth in a subject in need thereof, the method comprising administering to the subject to an effective amount of the dimeric fusion protein of claim 42 to inhibit growth of the tumor.

86. A method of inhibiting tumor growth in a subject in need thereof, the method comprising administering to the subject to an effective amount of the fusion protein of any one of claims 1-41 to inhibit growth of the tumor.

87. A method of treating cancer in a subject in need thereof, the method comprising administering an effective amount of the dimeric fusion protein of claim 42 to the subject.

88. A method of treating cancer in a subject in need thereof, the method comprising administering an effective amount of the fusion protein of any one of claims 1-41 to the subject.

89. A method of reducing TGFβ activity in a cell comprising exposing the cell to an effective amount of the dimeric fusion protein of claim 42 to reduce TGFβ activity.

90. A method of reducing TGFβ activity in a cell comprising exposing the cell to an effective amount of the fusion protein of any one of claims 1-41 to reduce TGFβ activity.

91. A method of treating an inflammatory condition in a subject in need thereof, the method comprising administering an effective amount of the dimeric fusion protein of claim 42 to the subject.

92. A method of treating an inflammatory condition in a subject in need thereof, the method comprising administering an effective amount of the fusion protein of any one of claims 1-41 to the subject.

93. A method of inhibiting proliferation of a tumor cell comprising exposing the cell to an effective amount of the expression vector of any one of claims 44-77 to inhibit proliferation of the tumor cell.

94. A method of inhibiting tumor growth in a subject in need thereof, the method comprising administering to the subject an effective amount of the expression vector of any one of claims 44-77 to inhibit growth of the tumor.

95. A method of treating cancer in a subject in need thereof, the method comprising administering an effective amount of the expression vector of any one of claims 44-77 to the subject.

96. A method of reducing TGFβ activity in a cell comprising exposing the cell to an effective amount of the expression vector of any one of claims 44-77 to reduce TGFβ activity.

97. A method of treating an inflammatory condition in a subject in need thereof, the method comprising administering an effective amount of the expression vector of any one of claims 44-77 to the subject.

98. A method of treating an infection in a subject in need thereof, the method comprising administering an effective amount of the expression vector of any one of claims 44-77 to the subject.

99. The method of any one of claims 87, 88 or 95, wherein the cancer is selected from melanoma, squamous cell carcinoma of the skin, basal cell carcinoma, head and neck cancer, breast cancer, anal cancer, cervical cancer, non-small cell lung cancer, mesothelioma, small cell lung cancer, renal cell carcinoma, prostate cancer, gastroesophageal cancer, colorectal cancer, testicular cancer, bladder cancer, ovarian cancer, liver cancer, hepatocellular carcinoma, cholangiocarcinoma, brain and central nervous system cancer, thyroid cancer, parathyroid cancer (*e.g.,* parathyroid carcinoma), endometrial cancer, neuroendocrine cancer, lymphoma (*e.g.*, Hodgkin and non-Hodgkin), leukemia, merkel cell carcinoma, gastrointestinal stromal tumors, multiple myeloma, uterine cancer, a sarcoma, kidney cancer, ocular cancer, pancreatic cancer, and a germ cell cancer (*e.g.,* ovarian germ cell cancer).

100. The method of any one of claims 87, 88 or 95, wherein the cancer is selected from leukemia, breast cancer, lung cancer, pancreatic cancer, endometrial cancer, ovarian cancer, prostate cancer, cervical cancer, brain cancer, skin cancer, colorectal cancer, gastric cancer, head and neck cancer, and leukemia.

101. The method of claim 100, wherein the cancer is selected from skin cancer, head and neck cancer, and lung cancer.

102. The method of any one of claims 85-88, 91, 92, 94, 95 or 97-101, wherein the expression vector is administered in combination with one or more therapies selected from surgery, radiation, chemotherapy, immunotherapy, hormone therapy, and virotherapy.

103. The method of any one of claims 85-88, 91, 92, 94, 95 or 97-101, wherein the expression vector is administered in combination with lymphocytes, *e.g.,* T-cells, *e.g.,* CAR T-cells.

104. The method of claim 103, wherein the lymphocytes are T-cells.

105. The method of claim 104, wherein the T-cells are CAR T-cells.

106. The method of any one of claims 85-88, 91, 92, 94, 95 or 97-101, wherein the subject is a human or animal.

107. The method of claim 106, wherein the subject is a pediatric human.