CLAIMS

What is claimed is:

1. A composition, wherein the composition comprises:
    a vector; and
    a nucleic acid encoding for a fusion protein, wherein the fusion protein comprises:
        a TNF-superfamily ligand (TNFSF-L) or functional variant thereof; and
        a plurality of domains from a collectin family protein, wherein the plurality of domains from the collectin family protein comprises:
            an oligomerization domain or functional variant thereof; and
            a neck domain or functional variant thereof,
    wherein the oligomerization domain or functional variant thereof and the neck domain or functional variant thereof are closer in sequence proximity compared to their location in the collectin family protein.

2. The composition of claim 1, wherein the vector is a viral vector or non-viral vector.

3. The composition of claim 2, wherein the non-viral vector comprises a nanoparticle carrier.

4. The composition of claim 2, wherein the non-viral vector comprises a lipid nanoparticle carrier.

5. The composition of claim 3, wherein the nanoparticle carrier comprises gold, silica, carbon nanotubes, water soluble fullerenes, silicon nanowires, quantum dots, or any combination thereof.

6. The composition of claim 1, wherein the vector comprises a bacteriophage, virus-like particles (VLP), erythrocyte ghosts, bactofection, exosomes, or any combination thereof.

7. The composition of claim 1, wherein the fusion protein comprises, in N-terminal to C-terminal order:
    the oligomerization domain or functional variant thereof;
    the neck domain or functional variant thereof;
    optionally, a linker sequence; and
    the TNFSF-L or functional variant thereof.

8. The composition of claim 1, wherein the TNFSF-L comprises Lymphotoxin alpha, OX40 ligand, CD40 ligand, Fas ligand, CD27 ligand, CD30 ligand, 4-1BBL, TNF-related apoptosis-inducing ligand (TRAIL), Receptor activator of nuclear factor kappa-B ligand (RANKL), TNF-related weak inducer of apoptosis, A proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), LIGHT, Vascular endothelial growth inhibitor (VEGI), TNF superfamily member 18 ligand (GITRL), Ectodysplasin A, or any combination thereof.

9. The composition of claim 8, wherein the TNFSF-L is a CD40 ligand.

10. The composition of claim 9, wherein the CD40 ligand comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 1.

11. The composition of claim 8, wherein the TNFSF-L is an OX40 ligand.

12. The composition of claim 11, wherein the OX40 ligand comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 2 or SEQ ID NO: 3.

13. The composition of claim 8, wherein the TNFSF-L is a 4-1BBL.

14. The composition of claim 13, wherein the 4-1BBL comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 4 or SEQ ID NO: 5.

15. The composition of claim 8, wherein the TNFSF-L is a LIGHT.

16. The composition of claim 15, wherein the LIGHT comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 6.

17. The composition of claim 8, wherein the TNFSF-L is a TNF superfamily member 18 ligand (GITRL).

18. The composition of claim 17, wherein the GITRL comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 7 or SEQ ID NO: 8.

19. The composition of claim 1, wherein the collectin family protein comprises SP-A, SP-D, mannose binding lectin (MBL), conglutinin, CL-43, CL-L1, CL-K1, CL-P1, or CL-46.

20. The composition of claim 19, wherein the collectin family protein is SP-D.

21. The composition of claim 1, wherein the oligomerization domain comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 9.

22. The composition of claim 1, wherein the oligomerization domain and the neck domain together comprise a sequence comprising at least 85% sequence identity to SEQ ID NO: 10.

23. The composition of claim 1, wherein the oligomerization domain and the neck domain together comprise SEQ ID NO: 10.

24. The composition of claim 7, wherein the fusion protein comprises the linker sequence, and wherein the linker sequence comprises GSG (glycine-serine-glycine) (SEQ ID NO: 12).

25. The composition of any one of claims 1 to 24, wherein the nucleic acid comprises an RNA.

26. The composition of any one of claims 1 to 24, wherein the nucleic acid comprises a DNA.

27. A fusion protein, wherein the fusion protein comprises:

    a TNF-superfamily ligand (TNFSF-L) or functional variant thereof; and

    a plurality of domains from a collectin family protein, wherein the plurality of domains from the collectin family protein comprises:

        an oligomerization domain or functional variant thereof; and

        a neck domain or functional variant thereof,

wherein the oligomerization domain or functional variant thereof and the neck domain or functional variant thereof are closer in sequence proximity compared to their location in the collectin family protein.

28. The fusion protein of claim 27, wherein the fusion protein comprises the following, in N-terminal to C-terminal order:

    the oligomerization domain or functional variant thereof;

    the neck domain or functional variant thereof;

    optionally, a linker sequence; and

    the TNFSF-L or functional variant thereof.

29. The fusion protein of claim 27, wherein the TNFSF-L comprises Lymphotoxin alpha, OX40 ligand, CD40 ligand, Fas ligand, CD27 ligand, CD30 ligand, 4-1BBL, TNF-related apoptosis-inducing ligand (TRAIL), Receptor activator of nuclear factor kappa-B ligand (RANKL), TNF-related weak inducer of apoptosis, A proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), LIGHT, Vascular endothelial growth inhibitor (VEGI), TNF superfamily member 18 ligand (GITRL), Ectodysplasin A, or any combination thereof.

30. The fusion protein of claim 29, wherein the TNFSF-L is a CD40 ligand.

31. The fusion protein of claim 30, wherein the CD40 ligand comprises at least 85% sequence identity to SEQ ID NO: 1.

32. The fusion protein of claim 29, wherein the TNFSF-L is an OX40 ligand.

33. The fusion protein of claim 32, wherein the OX40 ligand comprises at least 85% sequence identity to SEQ ID NO: 2 or SEQ ID NO: 3.

34. The fusion protein of claim 29, wherein the TNFSF-L is a 4-1BBL.

35. The fusion protein of claim 34, wherein the 4-1BBL comprises at least 85% sequence identity to SEQ ID NO: 4 or SEQ ID NO: 5.

36. The fusion protein of claim 29, wherein the TNFSF-L is a LIGHT.

37. The fusion protein of claim 36, wherein the LIGHT comprises at least 85% sequence identity to SEQ ID NO: 6.

38. The fusion protein of claim 29, wherein the TNFSF-L is a TNF superfamily member 18 ligand (GITRL).

39. The fusion protein of claim 38, wherein the GITRL comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 7 or SEQ ID NO: 8.

40. The fusion protein of claim 27, wherein the collectin family protein comprises SP-A, SP-D, mannose binding lectin (MBL), conglutinin, CL-43, CL-L1, CL-K1, CL-P1, CL-46, or any combination thereof.

41. The fusion protein of claim 27, wherein the collectin family protein is SP-D.

42. The fusion protein of claim 27, wherein the oligomerization domain comprises at least 85% sequence identity to SEQ ID NO: 9.

43. The fusion protein of claim 27, wherein the oligomerization domain and neck domain together comprise at least 85% sequence identity to SEQ ID NO: 10.

44. The fusion protein of claim 27, wherein the oligomerization domain and neck domain together comprise SEQ ID NO: 10.

45. The fusion protein of claim 28, wherein the fusion protein comprises the linker sequence, and wherein the linker sequence comprises GSG (glycine-serine-glycine) (SEQ ID NO: 12).

46. An oncolytic virus, wherein the oncolytic virus comprises:

an exogenous nucleic acid encoding for a TNF-superfamily ligand (TNFSF-L) or functional variant thereof, wherein the TNFSF-L or functional variant thereof is fused to an oligomerization domain.

47. The oncolytic virus of claim 46, wherein the oncolytic virus is Newcastle disease virus (NDV), Reovirus (RV), Myxoma virus (MYXV), Measles virus (MV), Herpes Simplex virus (HSV), Vaccinia virus (VV), Vesicular Somatitis virus (VSV), Polio virus (PV), Sendai virus, Flavivirus, Lentivirus, a pox virus, a retrovirus, an adeno-associated virus, or an adenovirus.

48. The oncolytic virus of claim 46, wherein the nucleic acid encoding the TNFSF-L or functional variant thereof is inserted into the viral genome.

49. The oncolytic virus of claim 46, wherein the nucleic acid encoding the TNFSF-L or functional variant thereof is inserted into a thymidine kinase gene.

50. The oncolytic virus of claim 46, wherein the TNFSF-L comprises a Lymphotoxin alpha, OX40 ligand, CD40 ligand, Fas ligand, CD27 ligand, CD30 ligand, 4-1BBL, TNF-related apoptosis-inducing ligand (TRAIL), Receptor activator of nuclear factor kappa-B ligand (RANKL), TNF-related weak inducer of apoptosis, A proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), LIGHT, Vascular endothelial growth inhibitor (VEGI), TNF superfamily member 18 ligand (GITRL), Ectodysplasin A, or any combination thereof.

51. The oncolytic virus of claim 50, wherein the TNFSF-L is a CD40 ligand.

52. The oncolytic virus of claim 51, wherein the CD40 ligand comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 1.

53. The oncolytic virus of claim 50, wherein the TNFSF-L is an OX40 ligand.

54. The oncolytic virus of claim 53, wherein the OX40 ligand comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 2 or SEQ ID NO: 3.

55. The oncolytic virus of claim 50, wherein the TNFSF-L is a 4-1BBL.

56. The oncolytic virus of claim 55, wherein the 4-1BBL comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 4 or SEQ ID NO: 5.

57. The oncolytic virus of claim 50, wherein the TNFSF-L is a LIGHT.

58. The oncolytic virus of claim 57, wherein the LIGHT comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 6.

59. The oncolytic virus of claim 50, wherein the TNFSF-L is a TNF superfamily member 18 ligand (GITRL).

60. The oncolytic virus of claim 59, wherein the GITRL comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 7 or SEQ ID NO: 8.

61. The oncolytic virus of claim 46, wherein the oligomerization domain comprises a sequence comprising at least 85% sequence identity to SEQ ID NO: 9.

62. The oncolytic virus of any one of claims 46 to 61, wherein the nucleic acid comprises an RNA.

63. The oncolytic virus of any one of claims 46 to 61, wherein the nucleic acid comprises a DNA.

64. Use of a pharmaceutical composition in the manufacture of a medicament for treatment of cancer,

wherein the pharmaceutical composition comprises:

the composition, fusion protein, or oncolytic virus of any one of claims 1 to 63, and a pharmaceutically acceptable carrier, and wherein the pharmaceutical composition is to be administered to a subject in an amount sufficient for treatment of a cancer.

65. The use of claim 64, wherein the cancer comprises a blood cancer or a solid cancer.

66. The use of claim 64, wherein the cancer comprises a melanoma, a hepatocellular carcinoma, a breast cancer, a lung cancer, a peritoneal cancer, a prostate cancer, a bladder cancer, an ovarian cancer, a leukemia, a lymphoma, a renal carcinoma, a pancreatic cancer, an epithelial carcinoma, a gastric cancer, a colon carcinoma, a duodenal cancer, a pancreatic adenocarcinoma, a mesothelioma, a glioblastoma multiforme, an astrocytoma, a multiple myeloma, a prostate carcinoma, a hepatocellular carcinoma, a cholangiosarcoma, a pancreatic adenocarcinoma, a head and neck squamous cell carcinoma, a colorectal cancer, an intestinal-type gastric adenocarcinoma, a cervical squamous-cell carcinoma, an osteosarcoma, an epithelial ovarian carcinoma, an acute lymphoblastic lymphoma, a myeloproliferative neoplasm, or a sarcoma.

67. The use of claim 64, wherein the cancer comprises a cancer of the bladder, blood, bone, bone marrow, brain, breast, colon, esophagus, gastrointestinal tract, gum, head, kidney, liver, lung, nasopharynx, neck, ovary, prostate, skin, stomach, testis, tongue, or uterus.

68. The use of claim 64, wherein the pharmaceutical composition is to be administered via systemic administration or local administration.

69. The use of claim 64, wherein the pharmaceutical composition is to be administered via intratumoral administration, an intravenous administration, a regional administration, an intraperitoneal administration, a parenteral administration, an intramuscular administration, a subcutaneous administration, an intra-arterial administration, or any combination thereof.

70. The use of claim 64, wherein the pharmaceutical composition is to be administered via intratumoral administration.

71. The use of claim 64, wherein the pharmaceutically acceptable carrier comprises a buffer, an emulsion, a bioadsorbable polymer, a gel, or any combination thereof.

72. The use of claim 64, wherein the composition, cell, or fusion protein is to be administered at a dose from about 0.01 μg/dose to about 1 g/dose.

73. The use of claim 64, wherein the oncolytic virus or the vaccinia virus is to be administered at dose from about 10^3 to about 10^{12} PFU/dose.

74. The pharmaceutical composition comprising the composition, fusion protein, or oncolytic virus of any one of claims 1 to 63 and a pharmaceutically acceptable carrier for use in therapy.