CLAIMS

1. An isolated antibody or antibody fragment comprising variable light chain and variable heavy chain polypeptides, which said antibody or antibody fragment specifically binds to V-domain Ig Suppressor of T cell Activation (VISTA), wherein

   (i) the heavy chain of said antibody or antibody fragment comprises a variable heavy chain (V_H) polypeptide comprising a V_H CDR1 consisting of the amino acid sequence of SEQ ID NO:25, a V_H CDR2 consisting of the amino acid sequence of SEQ ID NO:26 and a V_H CDR3 consisting of the amino acid sequence of SEQ ID NO:27, and

   (ii) the light chain of said antibody or antibody fragment comprises a variable light chain (V_L) polypeptide consisting of a V_L CDR1 consisting of the amino acid sequence of SEQ ID NO:28, a V_L CDR2 consisting of the amino acid sequence of SEQ ID NO:29 and a V_L CDR3 having the amino acid sequence of SEQ ID NO:30.

2. The antibody or antibody fragment of claim 1, wherein said antibody fragment is a Fab, $F(ab')_2$, or scFv comprising said CDRs.

3. The antibody or antibody fragment of claim 1, which comprises a human constant region.

4. The antibody or antibody fragment of any one of claims 1-3, wherein said antibody or antibody fragment comprises a variable heavy chain polypeptide of SEQ ID NO: 37 and a variable light chain polypeptide of SEQ ID NO: 44.

5. The antibody or antibody fragment of any one of claims 1 or 3-4, wherein said antibody or antibody fragment comprises a human heavy chain constant region.

6. The antibody or antibody fragment of claim 5, wherein said human heavy chain constant region comprises a human IgG1 heavy chain constant region.

7. The antibody or antibody fragment of claim 6, wherein said human heavy chain constant region comprises the human IgG1 heavy chain constant region contained in SEQ ID NO: 61 or SEQ ID NO: 60.

8. The antibody or antibody fragment of any one of claims 1 or 3-7, wherein said antibody or antibody fragment comprises a human light chain constant region.

9. The antibody or antibody fragment of claim 8, wherein said human light chain constant region comprises a human IgG1 light chain constant region.

10. The antibody or antibody fragment of claim 9, wherein said human IgG1 light chain constant region comprises the amino acid sequence of the light chain constant region in SEQ ID NO: 56.

11. The antibody or antibody fragment of any one of claims 1-5, wherein said heavy chain polypeptide consisting of SEQ ID NO: 55, 59, 60 or 61.

12. The antibody or antibody fragment of any one of claims 1 or 3-4, wherein:

    (i) said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 55 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56;

    (ii) said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 59 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56;

    (iii) said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 60 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56; or

    (iv) said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 61 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56.

13. The antibody according to claim 12, wherein said heavy chain polypeptide comprises the amino acid sequence of SEQ ID NO: 61 and said light chain polypeptide comprises the amino acid sequence of SEQ ID NO: 56.

14. The antibody or antibody fragment of any one of claims 1-13, wherein said antibody or antibody fragment is expressed in a recombinant cell.

15. The antibody or antibody fragment of claim 14 wherein said cell is deficient in fucosylation enzymes.

16. A composition comprising the antibody or antibody fragment of any one of claims 1-14 and a pharmaceutically acceptable carrier, excipient or diluent.

17. A composition comprising the antibody or antibody fragment of claim 13 and a pharmaceutically acceptable carrier, excipient or diluent.

18. A nucleic acid which encodes for the expression of the antibody or antibody fragment according to any one of claims 1-14.

19. A nucleic acid which encodes for the expression of the antibody or antibody fragment according to claim 13.

20. An expression vector comprising the nucleic acid according to claim 18.

21. An expression vector comprising the nucleic acid according to claim 19.

22. A recombinant cell which expresses an antibody or antibody fragment encoded by the nucleic acid according to claim 18.

23. A recombinant cell which expresses an antibody or antibody fragment encoded by the nucleic acid according to claim 19.

24. The recombinant cell of claim 22 which is a CHO cell.

25. The recombinant cell of claim 23 which is a CHO cell.

26. The recombinant cell of claim 22 which is a CHO cell that is deficient in fucosylation enzymes.

27. The recombinant cell of claim 23 which is a CHO cell that is deficient in fucosylation enzymes.

28. A method of expressing the antibody or antibody fragment according to any one of claims 1-12, comprising culturing a cell which comprises nucleic acids encoding said antibody or antibody fragment under conditions that promote expression of said antibody or antibody fragment.

29. A method of expressing the antibody or antibody fragment according to claim 13, comprising culturing a cell which comprises nucleic acids encoding said antibody or antibody fragment under conditions that promote expression of said antibody or antibody fragment.

30. The method of claim 28 or 29, further comprising isolating said antibody or antibody fragment.

31. A medicament composition or compositions comprising: (i) the antibody or antibody fragment according to any one of claims 1-15; and (ii) a vaccine.

32. A medicament composition or compositions comprising: (i) the antibody or antibody fragment according to claim 13; and (ii) a vaccine.

33. The composition or compositions of claim 31, wherein the vaccine is a bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine or a protein vaccine.

34. The composition or compositions of claim 32, wherein the vaccine is a bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine or a protein vaccine.

35. Use of the antibody or antibody fragment according to any one of claims 1-15, in the preparation of a medicament for enhancing monocyte activation; induction of T-cell proliferation, induction of cytokine secretion; antibody-dependent cell-mediated cytotoxicity of cells expressing VISTA; or antibody-dependent cellular phagocytosis of cells expressing VISTA.

36. Use of the antibody or antibody fragment according to claim 13, in the preparation of a medicament for enhancing monocyte activation; induction of T-cell proliferation, induction of cytokine secretion; antibody-dependent cell-mediated cytotoxicity of cells expressing VISTA; or antibody-dependent cellular phagocytosis of cells expressing VISTA.

37. Use of the antibody or antibody fragment according to any one of claims 1-15, in the preparation of a medicament for treatment of cancer involving VISTA-mediated immunosuppression or VISTA expressing cancer cells.

38. Use of the antibody or antibody fragment according to claim 13, in the preparation of a medicament for treatment of cancer involving VISTA-mediated immunosuppression or VISTA expressing cancer cells.

39. The use of claim 37, which promotes monocyte activation; induction of T-cell proliferation, induction of cytokine secretion; antibody-dependent cell-mediated cytotoxicity of cells expressing VISTA; or antibody-dependent cellular phagocytosis of cells expressing VISTA.

40. The use of claim 38, which promotes monocyte activation; induction of T-cell proliferation, induction of cytokine secretion; antibody-dependent cell-mediated cytotoxicity of cells expressing VISTA; or antibody-dependent cellular phagocytosis of cells expressing VISTA.

41. The use of claim 39, wherein said cancer comprises a leukemia, lymphoma, myelodysplastic syndrome or myeloma.

42. The use of claim 40, wherein said cancer comprises a leukemia, lymphoma, myelodysplastic syndrome or myeloma.

43. The use of claim 41, wherein said cancer comprises a solid tumor.

44. The use of claim 42, wherein said cancer comprises a solid tumor.

45. The use of claim 41, wherein said cancer comprises lymphocytic leukemia, myelogenous leukemia, acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid (myelogenous) leukemia (AML), chronic myelogenous leukemia (CML); hairy cell leukemia, T-cell prolymphocytic leukemia, large granular lymphocytic leukemia, or adult T-cell leukemia.

46. The use of claim 42, wherein said cancer comprises lymphocytic leukemia, myelogenous leukemia, acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid (myelogenous) leukemia (AML), chronic myelogenous leukemia (CML); hairy cell leukemia, T-cell prolymphocytic leukemia, large granular lymphocytic leukemia, or adult T-cell leukemia.

47. The use of claim 39, wherein said cancer comprises lung, breast or bladder cancer.

48. The use of claim 40, wherein said cancer comprises lung, breast or bladder cancer.

49. The use of claim 47, wherein said lung cancer comprises non-small cell lung cancer (NSCLC).

50. The use of claim 48, wherein said lung cancer comprises non-small cell lung cancer (NSCLC).

51. The use of claim 39, further comprising a vaccine.

52. The use of claim 40, further comprising a vaccine.

53. The use of claim 51, wherein the vaccine is a viral vector vaccine, bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine, or protein vaccine.

54. The use of claim 52, wherein the vaccine is a viral vector vaccine, bacterial vaccine, DNA vaccine, RNA vaccine, peptide vaccine, or protein vaccine.

55. The use of claim 39, which further comprises the use of one or more other cancer treatments.

56. The use of claim 40, which further comprises the use of one or more other cancer treatments.

57. The use of claim 55, wherein the one or more other cancer treatments is surgery, chemotherapy, radiation therapy, biologic therapy, targeted therapy, immunomodulatory therapy, or a combination thereof.

58. The use of claim 56, wherein the one or more other cancer treatments is surgery, chemotherapy, radiation therapy, biologic therapy, targeted therapy, immunomodulatory therapy, or a combination thereof.

59. The antibody or antibody fragment of any one of claims 1-15, in the preparation of a medicament for use in eliciting an antitumor immune response.

60. The antibody or antibody fragment of claim 13, in the preparation of a medicament for use in enhancing an antitumor immune response.

61. The use of claim 59, wherein the medicament is for use in a human subject.

62. The use of claim 60, wherein the medicament is for use in a human subject.

63. The use of claim 61, wherein the medicament is suitable for parenteral or non-parenteral administration.

64. The use of claim 62, wherein the medicament is suitable for parenteral or non-parenteral administration.

65. The use of claim 61, wherein the medicament is suitable for intravenous, subcutaneous or oral administration.

66. The use of claim 62, wherein the medicament is suitable for intravenous, subcutaneous or oral administration.

67. The use of claim 39, wherein the dosage of the antibody or antibody fragment is 0.1-15 mg/kg per administration.

68. The use of claim 40, wherein the dosage of the antibody or antibody fragment is 0.1-15 mg/kg per administration.

69. The use of claim 39, wherein the medicament is suitable for administering weekly, once every two weeks, once every three weeks, once every month, once every 2 months, or once every 3 months.

70. The use of claim 40, wherein the medicament is suitable for administering weekly, once every two weeks, once every three weeks, once every month, once every 2 months, or once every 3 months.