

epitope including amino acid Tyrosine 37, Arginine 54, Valine 117 and Arginine 127 of VISTA-ECD (extracellular domain).

[0027] In one example, the present disclosure describes an antibody, or an antigen-binding fragment thereof, that binds to V-domain Ig-containing Suppressor of T cell Activation (VISTA), wherein the antibody, or antigen-binding fragment thereof, blocks binding of all five ligands to VISTA at pH 6.0 and pH 7.4, wherein the five known ligands to VISTA are VSIG-3 (V-set and immunoglobulin domain containing 3), VSIG-8 (V-set and immunoglobulin domain containing 8), PSGL-1 (P-selectin glycoprotein ligand-1), LRIG1 (leucine rich repeats and immunoglobulin like domains 1) and VISTA; and wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable region (VH) and a light chain variable region (VL).

[0028] In another aspect, the present disclosure refers to an antibody, or antigen-binding fragment thereof, that binds to V-domain Ig-containing Suppressor of T cell Activation (VISTA), wherein the antibody or antigen-binding fragment thereof, comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises: a VH CDR1 of SEQ ID NO: 249 as defined by Kabat numbering system; a VH CDR2 of SEQ ID NO: 256 as defined by Kabat numbering system; a VH CDR3 of SEQ ID NO: 268 as defined by Kabat numbering system, and wherein the VL comprises: a VL CDR1 of SEQ ID NO: 113 as defined by Kabat numbering system; a VL CDR2 of SEQ ID NO: 125 as defined by Kabat numbering system; and a VL CDR3 of SEQ ID NO: 134 as defined by Kabat numbering system. In another example, there is described an antibody, or an antigen-binding fragment thereof, that binds to V-domain Ig-containing Suppressor of T cell Activation (VISTA), wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to, comprises, or consists of any one of SEQ ID NOs: 584-597, 227-246, and 383-386, and wherein the VL comprises a sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to, comprises, or consists of any one of SEQ ID NOs: 84-110. In one example, the antibody, or antigen-binding fragment thereof, blocks binding of all five ligands to VISTA at pH 6.0 and pH 7.4, wherein the five known ligands to VISTA are VSIG-3 (V-set and immunoglobulin domain containing 3), VSIG-8 (V-set and immunoglobulin domain containing 8), PSGL-1 (P-selectin glycoprotein ligand-1), LRIG1 (leucine rich repeats and immunoglobulin like domains 1) and VISTA. In another example, the antibody, or antigen-binding fragment thereof comprises a VH CDR1 of any one of SEQ ID NOs: 247-253 as defined by Kabat numbering system; any one of SEQ ID NOs: 284-291 as defined by IMGT numbering system; or any one of SEQ ID NOs: 318-325 as defined by Paratome numbering system; a VH CDR2 of any one of SEQ ID NOs: 254-265 as defined by Kabat numbering system; any one of SEQ ID NOs: 292-298 as defined by IMGT numbering system; or any one of SEQ ID NOs: 326-339 as defined by Paratome numbering system; a VH CDR3 of any one of SEQ ID NOs: 266-283 as defined by Kabat numbering system; any

one of SEQ ID NOs: 299-317 as defined by IMGT numbering system; or any one of SEQ ID NOs: 340-359 as defined by Paratome numbering system; a VL CDR1 of any one of SEQ ID NOs: 111-122 as defined by Kabat numbering system; any one of SEQ ID NOs: 152-162 as defined by IMGT numbering system; or any one of SEQ ID NOs: 188-196 or 576-578 as defined by Paratome numbering system; a VL CDR2 of any one of SEQ ID NOs: 123-131 and 575 as defined by Kabat numbering system; any one of SEQ ID NOs: 163-167 as defined by IMGT numbering system; or any one of SEQ ID NOs: 197-206 as defined by Paratome numbering system, a VL CDR3 of any one of SEQ ID NOs: 132-151 as defined by Kabat numbering system; any one of SEQ ID NOs: 168-

What is claimed is:

1. An antibody, or antigen-binding fragment thereof, that binds to V-domain Ig-containing Suppressor of T cell Activation (VISTA), wherein the antibody or antigen-binding fragment thereof, comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises:
a VH CDR1 of SEQ ID NO: 249 as defined by Kabat numbering system;
a VH CDR2 of SEQ ID NO: 256 as defined by Kabat numbering system;
a VH CDR3 of SEQ ID NO: 268 as defined by Kabat numbering system, and
wherein the VL comprises:
a VL CDR1 of SEQ ID NO: 113 as defined by Kabat numbering system;
a VL CDR2 of SEQ ID NO: 125 as defined by Kabat numbering system; and
a VL CDR3 of SEQ ID NO: 134 as defined by Kabat numbering system.
2. The antibody, or antigen-binding fragment thereof, of claim 1,
wherein the VH comprises a sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity SEQ ID NO: 592 and
the VL comprises a sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to SEQ ID NO: 86.
3. The antibody, or antigen-binding fragment thereof, of any one of the previous claims,
wherein the VH comprises a sequence comprising or consisting of SEQ ID NO: 592, and
the VL comprises a sequence comprising or consisting of SEQ ID NO: 86.
4. The antibody, or antigen-binding fragment thereof, of any one of claims 1 to 3,
comprising a heavy chain (HC) sequence comprising or consisting of SEQ ID NO: 573 and
comprising a light chain (LC) sequence comprising or consisting of SEQ ID NO: 391.
5. The antibody, or antigen-binding fragment thereof, of any one of the previous claims, which binds to human VISTA (amino acids 33-311 of SEQ ID NO:377).
6. The antibody, or antigen-binding fragment thereof, of claim 5, which binds to an epitope of human VISTA comprising Tyrosine 37, Arginine 54, Valine 117 and Arginine 127 (amino acids 69, 86, 149 and 159 respectively of SEQ ID NO: 377).

7. The antibody, or antigen-binding fragment thereof, of any one of the previous claims, comprising an Fc region,

optionally wherein the Fc region is a human Fc region or a variant of the human Fc region that has in the range of one to seven amino acid mutations in the Fc region relative to the native human Fc region, and/or

optionally wherein the human Fc region is of a human IgG1, human IgG2, or a human IgG4, further optionally wherein the antibody comprises a constant region of a human IgG1 or a human IgG4 or a variant of the constant region that has in the range of one to seven amino acid mutations in the constant region relative to the native constant region, optionally wherein:

(a) the Fc region is of a human IgG1, and wherein the mutations are selected from the group consisting of C220D, D221C, E233P, L234A, L234E, L234Y, L235A, L235E, L235F, G236A, G236W, G236R, G237A, P238S, S239D, F241A, M252Y, S254T, T256E, T256N, V264A, D265A, S267E, H268F, H268A, D270A, H268Q, E294deletion, N297A, N297G, N297E, S298A, T307P, E318A, K322A, S324T, K326A, K326M, L328R, P329A, P329G, A330L, A330S, P331A, P331S, I332E, E333A, E333S, K334A, A378V, S383N, M428L, N434S, and N434Y, wherein the residues are numbered using the EU numbering system;

(b) the Fc region is of a human IgG2, and wherein the mutations are selected from the group consisting of C220D, G237A, P238S, S239D, F241A, M252Y, S254T, T256E, T256N, V264A, D265A, S267E, H268F, H268A, D270A, H268Q, E294deletion, N297A, N297G, N297E, S298A, T307P, V309L, E318A, K322A, S324T, K326A, K326M, L328R, P329A, P329G, A330L, A330S, P331A, P331S, I332E, E333A, E333S, K334A, S383N, M428L, N434S, and N434Y, wherein the residues are numbered using the EU numbering system; or

(c) the Fc region is of a human IgG4, and wherein the mutations are selected from the group consisting of S228P, E233P, F234A, L235A, L235E, L235F, G236A, G236W, G236R, G237A, P238S, S239D, F241A, M252Y, S254T, T256E, T256N, V264A, D265A, S267E, H268F, H268A, D270A, H268Q, E294deletion, N297A, N297G, N297E, S298A, T307P, V309L, E318A, K322A, S324T, K326A, K326M, L328R, P329A, P329G, I332E, E333A, E333S, K334A, A378V, S383N, M428L, N434S, and N434Y, wherein the residues are numbered using the EU numbering system.

8. The antibody, or antigen-binding fragment thereof, of any one of the previous claims, wherein the Fc region is of a human IgG1, and wherein the mutations are M252Y, S254T, and T256E, wherein the residues are numbered using the EU numbering system.

9. The antibody, or antigen-binding fragment thereof, of any one of the previous claims, which is a bispecific antibody or a multispecific antibody, or wherein the antigen-binding fragment is an Fv fragment, a Fab fragment, a F(ab')₂ fragment, or a single-chain Fv (scFv).
10. An antibody-drug conjugate comprising the antibody, or antigen-binding fragment thereof, of any one of the previous claims and a therapeutic agent.
11. A chimeric antigen receptor (CAR) comprising the scFv of claim 9.
12. A polynucleotide comprising a nucleotide sequence encoding the VH, the VL, or the VH and the VL of the antibody, or antigen-binding fragment thereof, of any one of claims 1-9.
13. A cell comprising one or more polynucleotides encoding the antibody, or antigen-binding fragment thereof, of any one of claims 1-9.
14. A pharmaceutical composition comprising the antibody, or antigen-binding fragment thereof, of any one of claims 1-9, the antibody-drug conjugate of claim 10, or the CAR of claim 11, and a pharmaceutically acceptable carrier.
15. A method of producing an antibody, or antigen-binding fragment thereof, the method comprising culturing the cell of claim 14 under conditions such that said one or more polynucleotides are expressed by the cell to produce the antibody, or antigen-binding fragment thereof, encoded by the polynucleotides.
16. Use of the pharmaceutical composition of claim 14 in the manufacture of a medicament for treating cancer, an autoimmune disease, and/or an infection in a subject in need thereof, optionally wherein the cancer is a non-small cell lung cancer, small cell lung cancer, a head and neck squamous cell carcinoma, an hepatocellular carcinoma, an ovarian cancer, a neuroblastoma, an oral cancer, a thyroid cancer, a breast cancer, a sarcoma, a pancreatic cancer, a colon cancer, a gastric cancer, a choriocarcinoma, a testicular cancer, a mesothelioma, a skin cancer, a renal cell carcinoma, a bladder cancer, a hematological cancer, a cervical cancer, a blood cancer, an acute myeloid leukemia, myelodysplastic syndrome, and/or a metastatic cancer.
17. The use of claim 16, wherein the use further comprises an additional therapy to be administered to the subject, optionally wherein the additional therapy is radiotherapy, a chemotherapeutic agent, a

targeted therapy, a tyrosine kinase inhibitor, hormone therapy, and/or an immune checkpoint inhibitor; optionally wherein the immune checkpoint inhibitor is an inhibitor of Programmed Death-1 (PD-1), or Programmed death-ligand 1 (PDL1), or cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), or lymphocyte-activation gene 3 (LAG-3).