

- a mean residence time (MRT) of at least 100, 200, 300, 350, 400, 450, 500, 600 or 700 hours (e.g., at least 350 hours) in cynomolgus monkeys, measured, e.g., as described in the Examples;
 - stimulating T cell activation by, e.g., enhancing T cell proliferation; enhancing IFN- γ production from T cells; and/or stimulating T cell receptor mediated NF-kB signaling;
 - inhibiting VISTA mediated cell:cell adhesion;
 - specifically binding to hVISTA in samples of human tumor cells or samples of inflamed human tissue that express VISTA;
 - contacting hVISTA through one or more (e.g., at least 1-3, 1-5, 1-10, 5-10, 5-15 or all) energetically important contact residues Y37, T39, R54, F62, H66, V117, I119 or S124, as determined, e.g., using the yeast surface display and NGS assay described in Example 15; and wherein numbering is that of mature hVISTA;
 - binding to Region 1: ₅₇LGPVDKGHDVTF₆₈ (SEQ ID NO: 566); Region 2: ₈₆RRPIRNLTFQDL₉₇ (SEQ ID NO: 567); and Region 3: ₁₄₈VVEIRHHHSEHRVHGAME₁₆₅ (SEQ ID NO: 568) of hVISTA having SEQ ID NO: 1, and optionally wherein the binding is strongest to Region 2, as determined by MS-HDX as described in Example 21;
 - binding to the histidine-rich β -sheet extension of hVISTA, as determined, e.g., by crystallography, as described, e.g., in the Examples;
 - contacting H121, H122 and/or H123 of mature hVISTA (distance of 4.0 Ångströms (Å) or less), such as through hydrogen bonds, as determined, e.g., by crystallography, as described, e.g., in the Examples;
 - contacting hVISTA through at least one or more glutamic acid, aspartic acid or histidine residue that is located in VH CDR1, CDR2 or CDR3; and
- and any additional characteristic set forth in the claims and/or in the Examples.

In certain embodiments, an anti-hVISTA Ab comprises a heavy chain (HC) comprising the amino acid sequence of the heavy chain of any of the anti-hVISTA Abs provided herein. In certain embodiments, an anti-hVISTA Ab comprises a heavy chain comprising the amino acid sequence of the heavy chain of P1-061029 or P1-061015 or progeny thereof, as shown below in the Sequence Table, comprising an IgG1.3 heavy chain

- specifically binding to hVISTA in samples of human tumor cells or samples of inflamed human tissue that express VISTA;
 - contacting hVISTA through one or more (e.g., at least 1-3, 1-5, 1-10, 5-10, 5-15 or all) energetically important contact residues Y37, T39, R54, F62, H66, V117, I119 or S124, as determined, e.g., using the yeast surface display and NGS assay described in Example 15; and wherein numbering is that of mature hVISTA;
 - binding to Region 1: ₅₇LGPVDKGHDVTF₆₈ (SEQ ID NO: 566); Region 2: ₈₆RRPIRNLTQDL₉₇ (SEQ ID NO: 567); and Region 3: ₁₄₈VVEIRHHHSEHRVHGAME₁₆₅ (SEQ ID NO: 568) of hVISTA having SEQ ID NO: 1, and optionally wherein the binding is strongest to Region 2, as determined by MS-HDX as described in Example 21;
 - binding to the histidine-rich β -sheet extension of hVISTA, as determined, e.g., by crystallography, as described, e.g., in the Examples;
 - contacting H121, H122 and/or H123 of mature hVISTA (distance of 4.0 Ångströms (Å) or less), such as through hydrogen bonds, as determined, e.g., by crystallography, as described, e.g., in the Examples;
 - contacting hVISTA through at least one or more glutamic acid, aspartic acid or histidine residue that is located in VH CDR1, CDR2 or CDR3; and
- and any additional characteristic set forth in the claims and/or in the Examples.

Exemplary Antibody Constant Regions

In some embodiments, an antibody described herein comprises one or more human constant regions. In some embodiments, the human heavy chain constant region is of an isotype selected from IgA, IgG, and IgD. In some embodiments, the human light chain constant region is of an isotype selected from κ and λ . In some embodiments, an antibody described herein comprises a human IgG constant region, such as an IgG1, IgG2, IgG3, or IgG4. In some embodiments, an antibody described herein comprises a human IgG4 heavy chain constant region. In some such embodiments, an antibody described herein comprises an S241P mutation in the human IgG4 constant region. In some embodiments, an antibody described herein comprises a human IgG4 constant region and a human κ light chain.

The choice of heavy chain constant region can determine whether or not an antibody will have effector function *in vivo*. Such effector function, in some embodiments, includes

Hydrogen/deuterium exchange mass spectrometry (HDX-MS) was utilized to probe binding epitopes of human VISTA with mAb VISTA.4. HDX-MS probes protein conformation and conformational dynamics in solution by monitoring the rate and extent of deuterium exchange of backbone amide hydrogen atoms (Huang and Chen (2014) *Analytical and Bioanalytical Chemistry* 406, 6541-6558; Wei, et al. *Drug Discovery Today* (2014) 19, 95-102). The level of HDX depends on the solvent accessibility of backbone amide hydrogen atoms and the protein hydrogen bonds. The mass increase of the protein upon HDX can be precisely measured by MS. When this technique is paired with enzymatic digestion, structure features at the peptide level can be resolved, enabling differentiation of surface exposed peptides from those folded inside, or from those sequestered at the interface of a protein-protein complex. Typically, the deuterium labeling and subsequent quenching experiments are performed, followed by enzymatic digestion, peptide separation, and MS analysis.

Prior to epitope mapping experiments, non-deuteriated experiments were carried out to generate a list of common peptides for recombinant human VISTA (15 μ M) and protein complexes of VISTA with mAb VISTA.4 (1:1 molar ratio). In the HDX-MS experiment, 5 μ L of each sample (VISTA or VISTA with mAb VISTA.4) was diluted into 55 μ L of D₂O buffer (10 mM phosphate buffer, D₂O, pH7.0) to start the labeling reactions. The reactions were carried out for different periods of time: 1 min, 10 min and 240 min. By the end of each labeling reaction period, the reaction was quenched by adding quenching buffer (100 mM phosphate buffer with 4M GdnCl and 0.4M TCEP, pH 2.5, 1:1, v/v) and 50 μ L of quenched sample was injected into Waters HDX-MS system for analysis. The deuterium uptake levels of common peptic peptides were monitored in the absence/presence of VISTA.4. The obtained sequence coverage was 82%.

HDX-MS experiments provided 85% sequence coverage for human VISTA. As shown in Figure 19, the HDX-MS data analysis on VISTA.4 in human VISTA indicates that VISTA.4's epitope is comprised of three regions of human VISTA, with region 2 being the primary epitope (residue numbers correspond to native human VISTA sequence, Figure 20):
Region 1: ⁵⁷LGPVDKGHDVTF⁶⁸ (SEQ ID NO: 566)
Region 2: ⁸⁶RRPIRNLTFQDL⁹⁷ (SEQ ID NO: 567)

Region 3: ¹⁴⁸VVEIRHHHSEHRVHGAME¹⁶⁵ (SEQ ID NO: 568)

Antibody VISTA.4 bound equally well at acidic and neutral pH. Further rounds of selection yielded a variant that bound VISTA with 200-fold higher affinity at pH 6.0 than at pH 7.4. Similar efforts with VISTA blocking antibodies produced variants with up to 10,000-
5 fold selectivity for pH 6.0 relative to pH 7.4. We used these antibodies to map VISTA's receptor-ligand binding interface at acidic and neutral pH. pH-independent, neutral pH-selective, and acidic pH-selective VISTA blocking antibodies bound nearly identical epitopes, suggesting that histidine protonation alone, without marked conformational changes, controls VISTA's ability to engage its counter-receptor at acidic pH. (VISTA.4 is
10 further described in another application family by the same applicants.)

Example 22: VISTA.4 inhibits VISTA binding to T cells at acidic pH

This Example shows that VISTA.4 and other antibodies in epitope group A blocked VISTA binding to T cells at acidic pH, whereas VISTA.5 (mAb1) and other antibodies in
15 epitope group B did not (Figure 21A and B).

This example was conducted essentially as described in Example 4.

Example 23: VISTA.4 enhances T cell proliferation and IFN- γ production

This Example shows that VISTA blocking Abs (epitope Group A) enhanced T cell
20 proliferation and IFN- γ production (Fig. 22). VISTA.5 (mAb1), which is not a blocking antibody, did not enhance T cell proliferation or IFN- γ production. VISTA.4 had no effect when T cells were co-cultured with 293T-OKT3 cells that did not express VISTA.

This experiment was conducted by adding VISTA antibodies to CD4+ T cells co-cultured with 293T cells engineered to express human VISTA and a single chain variable
25 fragment of the T cell receptor agonist antibody OKT3 (293T-OKT3-VISTA).

Example 24: VISTA suppressed T cell receptor-mediated NF-kB signaling

This Example was conducted to further assess the effects of pH on VISTA function, and shows that VISTA suppressed T cell receptor-mediated NF-kB signaling more potently

CLAIMS

1. An isolated antibody that binds specifically to human VISTA (hVISTA) in acidic conditions.
2. The isolated antibody of claim 1, which binds specifically to hVISTA in acidic
5 conditions, but not significantly in neutral or physiological conditions.
3. The isolated antibody of claim 1 or 2, wherein the antibody binds to hVISTA in acidic conditions with a K_D that is at least 10 fold lower than its K_D in neutral or physiological conditions.
4. The isolated antibody of any one of claims 1 to 3, wherein the antibody binds to
10 hVISTA in acidic conditions with a K_D that is at least 100 fold lower than its K_D in neutral or physiological conditions.
5. The isolated antibody of any one of claims 1-4, wherein the antibody binds to hVISTA in acidic conditions with a K_D that is at least 1000 fold lower than its K_D in neutral or physiological conditions.
6. The isolated antibody of any one of claims 1-5, wherein the antibody binds to
15 hVISTA in neutral or physiological conditions with a K_D of 10^{-5} M or more.
7. The isolated antibody of any one of claims 1-6, wherein the antibody binds to hVISTA in neutral or physiological conditions with a K_D of 10^{-4} M or more.
8. The isolated antibody of any one of claims 1-7, wherein the antibody binds to
20 hVISTA in neutral or physiological conditions with a K_D of 10^{-3} M or more.
9. The isolated antibody of any one of claims 1-8, wherein the antibody binds to hVISTA in acidic conditions with a K_D of 10^{-7} M or less.
10. The isolated antibody of any one of claims 1-9, wherein the antibody binds to hVISTA in acidic conditions with a K_D of 10^{-8} M or less.
11. The isolated antibody of any one of claims 1-10, wherein the antibody binds to
25 hVISTA in acidic conditions with a K_D of 10^{-9} M or less.
12. The isolated antibody of any one of claims 1-11, wherein the antibody binds to hVISTA in acidic conditions with a K_D of 10^{-7} or less and binds to hVISTA in neutral or physiological conditions with a K_D of 10^{-4} or more.

13. The isolated antibody of any one of claims 1-12, wherein the antibody binds to hVISTA in acidic conditions with a K_D of 10^{-7} or less and binds to hVISTA in neutral or physiological conditions with a K_D of 10^{-5} or more.
- 5 14. The isolated antibody of any one of claims 1-13, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} that is at least 5 fold lower than its k_{off} in neutral or physiological conditions.
15. The isolated antibody of any one of claims 1-14, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} that is at least 10 fold lower than its k_{off} in neutral or physiological conditions.
- 10 16. The isolated antibody of any one of claims 1-15, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} that is at least 50 fold lower than its k_{off} in neutral or physiological conditions.
- 15 17. The isolated antibody of any one of claims 1-16, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} that is at least 100 fold lower than its k_{off} in neutral or physiological conditions.
18. The isolated antibody of any one of claims 1-17, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $7 \times 10^{-3} \text{ s}^{-1}$ or less.
19. The isolated antibody of any one of claims 1-18, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $5 \times 10^{-3} \text{ s}^{-1}$ or less.
- 20 20. The isolated antibody of any one of claims 1-19 wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $3 \times 10^{-3} \text{ s}^{-1}$ or less.
21. The isolated antibody of any one of claims 1-20, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of 10^{-3} s^{-1} or less.
- 25 22. The isolated antibody of any one of claims 1-21, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $7 \times 10^{-4} \text{ s}^{-1}$ or less.
23. The isolated antibody of any one of claims 1-22, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $5 \times 10^{-4} \text{ s}^{-1}$ or less.
24. The isolated antibody of any one of claims 1-23, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $3 \times 10^{-4} \text{ s}^{-1}$ or less.

25. The isolated antibody of any one of claims 1-24, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of 10^{-4} s^{-1} or less.
26. The isolated antibody of any one of claims 1-25, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $7 \times 10^{-5} \text{ s}^{-1}$ or less.
- 5 27. The isolated antibody of any one of claims 1-26, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $5 \times 10^{-5} \text{ s}^{-1}$ or less.
28. The isolated antibody of any one of claims 1-21, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $3 \times 10^{-5} \text{ s}^{-1}$ or less.
- 10 29. The isolated antibody of any one of claims 1-28, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of 10^{-5} s^{-1} or less.
30. The isolated antibody of any one of claims 1-29, wherein the antibody binds to hVISTA in neutral or physiological conditions with a k_{off} of 10^{-3} s^{-1} or more.
31. The isolated antibody of any one of claims 1-30, wherein the antibody binds to hVISTA in neutral or physiological conditions with a k_{off} of $3 \times 10^{-3} \text{ s}^{-1}$ or more.
- 15 32. The isolated antibody of any one of claims 1-31, wherein the antibody binds to hVISTA in neutral or physiological conditions with a k_{off} of $5 \times 10^{-3} \text{ s}^{-1}$ or more.
33. The isolated antibody of any one of claims 1-32, wherein the antibody binds to hVISTA in neutral or physiological conditions with a k_{off} of $7 \times 10^{-3} \text{ s}^{-1}$ or more.
34. The isolated antibody of any one of claims 1-33, wherein the antibody binds to hVISTA in neutral or physiological conditions with a k_{off} of 10^{-2} s^{-1} or more.
- 20 35. The isolated antibody of any one of claims 1-34, wherein the antibody binds to hVISTA in neutral or physiological conditions with a k_{off} of $3 \times 10^{-2} \text{ s}^{-1}$ or more.
36. The isolated antibody of any one of claims 1-35, wherein the antibody binds to hVISTA in neutral or physiological conditions with a k_{off} of $5 \times 10^{-2} \text{ s}^{-1}$ or more.
- 25 37. The isolated antibody of any one of claims 1-36, wherein the antibody binds to hVISTA in neutral or physiological conditions with a k_{off} of $7 \times 10^{-2} \text{ s}^{-1}$ or more.
38. The isolated antibody of any one of claims 1-37, wherein binding of the antibody to hVISTA in neutral or physiological conditions is not detectable, e.g., via surface plasmon resonance (SPR).

39. The isolated antibody of any one of claims 1-38, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of $5 \times 10^{-3} \text{ s}^{-1}$ or less and in neutral or physiological conditions with a k_{off} of $7 \times 10^{-3} \text{ s}^{-1}$ or more.
- 5 40. The isolated antibody of any one of claims 1-39, wherein the antibody binds to hVISTA in acidic conditions with a k_{off} of 10^{-4} s^{-1} or less and in neutral or physiological conditions with a k_{off} of 10^{-2} s^{-1} or more.
- 10 41. The isolated antibody of any one of claims 1-40, wherein the antibody binds to hVISTA in acidic conditions with a K_D of 10^{-8} M or less and a k_{off} of $5 \times 10^{-3} \text{ s}^{-1}$ or less and in neutral of physiological conditions with a K_D of 10^{-6} M or more and a k_{off} of $7 \times 10^{-3} \text{ s}^{-1}$ or more.
42. The isolated antibody of any one of claims 1-41, wherein the antibody binds to hVISTA in acidic conditions with a K_D of 10^{-8} M or less and a k_{off} of $3 \times 10^{-3} \text{ s}^{-1}$ or less and in neutral of physiological conditions with a K_D of 10^{-6} M or more and a k_{off} of 10^{-2} s^{-1} or more.
- 15 43. The isolated antibody of any one of claims 1-42, wherein the antibody binds to hVISTA in acidic conditions with a K_D of 10^{-12} to 10^{-8} M and a k_{off} of 10^{-4} to $5 \times 10^{-3} \text{ s}^{-1}$ and in neutral of physiological conditions with a K_D of 10^{-7} to 10^{-4} M and a k_{off} of 3×10^{-3} to 10^{-2} s^{-1} or more.
- 20 44. The isolated antibody of any one of claims 1-43, wherein the antibody binds to hVISTA in acidic conditions with a K_D of 10^{-12} to 10^{-8} M and a k_{off} of 10^{-4} to $5 \times 10^{-3} \text{ s}^{-1}$ and in neutral of physiological conditions with a K_D of 10^{-7} to 10^{-4} M and a k_{off} of 3×10^{-3} to 10^{-2} s^{-1} or more; and wherein the antibody binds to cyno VISTA with a K_D of 10^{-7} or less.
- 25 45. The isolated antibody of any one of claims 1-44, wherein the antibody binds to hVISTA with a K_D that is at least 10 fold lower at pH 6.9 than at pH 7.4 and/or a K_D that is at least 100 fold lower at pH 6.5 than at pH 7.4 and at least 1000 fold lower at pH 6.0 than at pH 7.4.
46. The isolated antibody of any one of claims 1-45, wherein the antibody binds to cynomolgus (cyno) VISTA.

47. The isolated antibody of claim 46, wherein the antibody binds to cyno VISTA with higher affinity in acidic conditions relative to physiologic conditions.
48. The isolated antibody of any one of claims 45-47, wherein the antibody binds to cyno VISTA in acidic conditions with a K_D of 10^{-8} or less and/or a k_{off} of 10^{-2} or less and in
5 physiologic conditions with a K_D of 10^{-6} or more and/or a k_{off} of 10^{-2} or more.
49. The isolated antibody of any one of claims 1-48, wherein acidic conditions are conditions having a pH of 6.5 or less.
50. The isolated antibody of any one of claims 1-49, wherein acidic conditions are conditions having a pH of 6.0 to 6.5.
- 10 51. The isolated antibody of any one of claim 1-50, wherein neutral conditions are conditions having a pH of 7.0.
52. The isolated antibody of any one of claims 1-51, wherein physiological conditions are conditions having a pH of 7.35 to 7.45.
53. The isolated antibody of any one of claims 1-52, wherein physiological conditions are
15 conditions having a pH of 7.4.
54. The isolated antibody of any one of claims 1-53, wherein the antibody inhibits the binding of hVISTA to human T cells, such as human CD4+ T cells (an antagonist antibody).
55. The isolated antibody of claim 54, wherein the antibody inhibits the binding of
20 hVISTA to human T cells in conditions having a pH of less than pH 7.0.
56. The isolated antibody of any one of claims 1-55, wherein the antibody inhibits the binding of hVISTA to human PSGL-1 (huPSGL-1) and/or competes with huPSGL1 for binding to hVISTA.
57. The isolated antibody of claim 56, wherein the antibody inhibits the binding of
25 hVISTA to huPSGL-1 in conditions having a pH of less than pH 7.0.
58. The isolated antibody of anyone of claims 1-57, wherein the antibody inhibits the binding of hVISTA to heparan sulfate proteoglycans.

59. The isolated antibody of claim 58, wherein the antibody inhibits the binding of hVISTA to heparan sulfate proteoglycans in conditions having a pH of less than pH 7.0.
- 5 60. The isolated antibody of any one of claims 55, 57 or 59, wherein a condition having a pH of less than pH 7.0 is a tumor or any diseased area having a pH of less than pH 7.0 in a subject and in which an immune stimulation is desired.
61. The isolated antibody of any one of claims 1-60, wherein the antibody stimulates T cell activation, as evidenced by, e.g., enhancing T cell proliferation; enhancing IFN- γ production from T cells; and/or stimulating T cell receptor mediated NF-kB signaling.
- 10 62. The isolated antibody of claim 61, wherein the antibody stimulates T cell activation in conditions having a pH of less than pH 7.0.
63. The isolated antibody of any one of claims 1-62, wherein the antibody reduces VISTA mediated cell-cell adhesion.
64. The isolated antibody of any one of claims 1-53, wherein the antibody stimulates the activity of VISTA (an agonist antibody).
- 15 65. The isolated antibody of any one of claims 1-53 and 64, wherein the antibody stimulates the binding of hVISTA to human T cells, such as human CD4+ T cells.
66. The isolated antibody of claim 65, wherein the antibody stimulates the binding of hVISTA to human T cells in conditions having a pH of less than pH 7.0.
- 20 67. The isolated antibody of any one of claims 1-53 and 64-66, wherein the antibody stimulates the binding of hVISTA to huPSGL-1.
68. The isolated antibody of claim 67, wherein the antibody stimulates the binding of hVISTA to huPSGL-1 in conditions having a pH of less than pH 7.0.
69. The isolated antibody of any one of claims 1-53 and 64-68, wherein the antibody stimulates the binding of hVISTA to heparan sulfate proteoglycans.
- 25 70. The isolated antibody of claim 69, wherein the antibody stimulates the binding of hVISTA to heparan sulfate proteoglycans in conditions having a pH of less than pH 7.0.

71. The isolated antibody of any one of claims 66, 68 and 70, wherein a condition having a pH of less than pH 7.0 is an autoimmune (e.g., rheumatoid arthritis and lupus) milieu, an inflammation site, or any diseased area having a pH of less than pH 7.0 in a subject and in which an immune inhibition is desired.
- 5 72. The isolated antibody of any one of claims 1-71, wherein the antibody has a mean residence time (MRT) of at least 100, 200, 300, 400 or 500 days in *Cynomolgus* macaques.
73. The isolated antibody of any one of claims 1-72, wherein the antibody does not significantly bind to VISTA positive cells, e.g., neutrophils, in the peripheral blood of
- 10 a subject to whom it is administered.
74. The isolated antibody of any one of claims 1-73, wherein the antibody does not significantly deplete VISTA positive cells, e.g., neutrophils, in peripheral blood of a subject to whom it is administered.
75. The isolated antibody of any one of claims 1-74, wherein the antibody has been
- 15 engineered to bind to hVISTA at acidic pH, but not at neutral or physiological pH.
76. The isolated antibody of claim 75, wherein the antibody has been engineered by replacing from 1-8 amino acids in VH CDR1, CDR2 and/or CDR3 of a hVISTA binding antibody with a glutamic acid, aspartic acid or histidine residue.
77. The isolated antibody of any one of claims 1-63 and 72-76, wherein the antibody
- 20 comprises VH CDR1, CDR2 and/or CDR3 of P1-061029 or a variant thereof comprising 1 to 6 or 1 to 8 amino acid differences in VH CDR1, CDR2 and/or CDR3 relative to antibody P1-061029, wherein at most 1, 2 or 3 amino acid variations are present in any one CDR.
78. The isolated antibody of claim 77, wherein the antibody comprises VH CDR1, CDR2
- 25 and CDR3 of P1-061029 or a variant thereof comprising 1 to 6 or 1 to 8 amino acid differences in VH CDR1, CDR2 and/or CDR3 relative to P1-061029.
79. The isolated antibody of claim 77 or 78, wherein an amino acid variation is a substitution to a glutamic acid residue (E), aspartic acid residue (D) or a histidine residue (H).

80. The isolated antibody of any one of claims 77-79, wherein the antibody comprises
- a CDR1 comprising GFTX₁X₂DX₃AMH, wherein X₁ is D or L, X₂ is E or D and X₃ is E or Y (SEQ ID NO: 563);

- a CDR2 comprising GIX₄WX₅SX₆X₇IGYADSVKG, wherein X₄ is D or N, X₅ is D or N, X₆ is D, E, H or A and X₇ is D, E, H or N (SEQ ID NO: 564); and/or

- a CDR3 comprising VPGYSX₈GWIDAX₉DX₁₀, wherein X₈ is E, H or G, X₉ is E, D or F and X₁₀ is D, E or V (SEQ ID NO: 565).

81. The antibody of claim 80, wherein the antibody comprises

- a CDR1 comprising GFTX₁X₂DX₃AMH, wherein X₁ is D or L, X₂ is E or D and X₃ is E or Y (SEQ ID NO: 563);

- a CDR2 comprising GIX₄WX₅SX₆X₇IGYADSVKG, wherein X₄ is D or N, X₅ is D or N, X₆ is D, E, H or A and X₇ is D, E, H or N (SEQ ID NO: 564); and

- a CDR3 comprising VPGYSX₈GWIDAX₉DX₁₀, wherein X₈ is E, H or G, X₉ is E, D or F and X₁₀ is D, E or V (SEQ ID NO: 565).

82. The isolated antibody of claim 80 or 81, wherein X₃ is E and X₉ is E.

83. The isolated antibody of any one of claims 80-82, wherein X₂ is E, X₇ is E, and/or X₈ is H.

84. The isolated antibody of claim 83, wherein two or more of the following three conditions are met: X₂ is E, X₇ is E, and/or X₈ is H.

85. The isolated antibody of claim 84, wherein X₂ is E, X₇ is E and X₈ is H.

86. The isolated antibody of any one of claims 80-85, wherein X₆ is E.

87. The isolated antibody of any one of claims 80-85, wherein X₆ is A.

88. The isolated antibody of any one of claims 80-86, wherein X₁ is L, X₄ is N, X₅ is N and/or X₁₀ is V.

89. The isolated antibody of claim 88, wherein two or more of the following four conditions are met: X₁ is L, X₄ is N, X₅ is N and/or X₁₀ is V.

90. The isolated antibody of claim 89, wherein three or more of the following four conditions are met: X₁ is L, X₄ is N, X₅ is N and/or X₁₀ is V.

91. The isolated antibody of claim 90, wherein X₁ is L, X₄ is N, X₅ is N and/or X₁₀ is V.

92. The isolated antibody of any one of claims 80-91, wherein X₁₀ is D.
93. The isolated antibody of any one of claims 80-92, wherein X₉ is E.
94. The isolated antibody of any one of claims 80-93, wherein X₂ is E, X₄ is D and/or X₆ is E.
- 5 95. The isolated antibody of claim 94, wherein two or more of the following conditions are met: X₂ is E, X₄ is D and/or X₆ is E.
96. The isolated antibody of claim 95, wherein X₂ is E, X₄ is D and X₆ is E.
97. The isolated antibody of any one of claims 80-96, wherein X₁ is L, X₃ is Y, X₅ is N, X₇ is N and/or X₈ is G.
- 10 98. The isolated antibody of claim 97, wherein two or more of the following conditions are met: X₁ is L, X₃ is Y, X₅ is N, X₇ is N and/or X₈ is G.
99. The isolated antibody of claim 98, wherein three or more of the following conditions are met: X₁ is L, X₃ is Y, X₅ is N, X₇ is N and/or X₈ is G.
100. The isolated antibody of claim 99, wherein four or more of the following
- 15 conditions are met: X₁ is L, X₃ is Y, X₅ is N, X₇ is N and/or X₈ is G.
101. The isolated antibody of claim 100, wherein X₁ is L, X₃ is Y, X₅ is N, X₇ is N and X₈ is G.
102. The isolated antibody of any one of claims 77-101, wherein the antibody comprises VH CDR1, CDR2 and/or CDR3 of P1-061029, P1-068757, P1-068759, P1-068761, P1-068763, P1-068765, P1-068767, P1-068769, P1-068771, P1-068773, P1-068775, P1-069059, P1-069061, P1-069063, P1-069065, P1-069067, P1-069069, P1-069071, P1-069073, P1-069075, P1-069077, P1-068761_E55A, P1-068761_H100G, P1-068761_E56N, P1-068761_E55A_E56N, P1-068761_E30D, P1-068761_E30D_E55A, P1-068761_E56N_H100G, P1-068761_E30D_H100G, or P1-068761_E30D_E56N, P1-068761_E100fF, P1-068761_E55A_E100fF, P1-068761_H100G_E100fF, P1-068761_E30D_E100fF, P1-068761_E56N_E100fF, P1-068761_E32Y, P1-068761_E32Y_E55A, P1-068761_E32Y_E56N, P1-068761_E30D_E32Y, P1-068761_E32Y_H100G, or P1-068761_E32Y_E100fF, P1-068767_D52N_D102V, P1-068767_D52N, P1-068767_D52N_E55A, P1-

068767_E55A_D102V, P1-068767_D102V, P1-068767_E55A, P1-
068767_E30D_D52N, P1-068767_E30D_D102V, P1-068767_E30D, P1-
068767_E30D_E55A, P1-068767_E100fF_D102V, P1-068767_E55A_E100fF, P1-
068767_D52N_E100fF, P1-068767_E100fF, P1-068767_E30D_E100fF, P1-
5 061029_F100fE_V102D, P1-061029_F100fE, P1-061029_V102D, P1-
061029_Y32E, or P1-061029_Y32E_F100fE.

103. The isolated antibody of claim 102, wherein the antibody comprises VH
CDR1, CDR2 and CDR3 of P1-061029, P1-068757, P1-068759, P1-068761, P1-
068763, P1-068765, P1-068767, P1-068769, P1-068771, P1-068773, P1-068775,
10 P1-069059, P1-069061, P1-069063, P1-069065, P1-069067, P1-069069, P1-
069071, P1-069073, P1-069075, P1-069077, P1-069077, P1-068761_E55A, P1-
068761_H100G, P1-068761_E56N, P1-068761_E55A_E56N, P1-068761_E30D, P1-
068761_E30D_E55A, P1-068761_E56N_H100G, P1-068761_E30D_H100G, or P1-
068761_E30D_E56N, P1-068761_E100fF, P1-068761_E55A_E100fF, P1-
15 068761_H100G_E100fF, P1-068761_E30D_E100fF, P1-068761_E56N_E100fF, P1-
068761_E32Y, P1-068761_E32Y_E55A, P1-068761_E32Y_E56N, P1-
068761_E30D_E32Y, P1-068761_E32Y_H100G, P1-068761_E32Y_E100fF, P1-
068767_D52N_D102V, P1-068767_D52N, P1-068767_D52N_E55A, P1-
068767_E55A_D102V, P1-068767_D102V, P1-068767_E55A, P1-
20 068767_E30D_D52N, P1-068767_E30D_D102V, P1-068767_E30D, P1-
068767_E30D_E55A, P1-068767_E100fF_D102V, P1-068767_E55A_E100fF, P1-
068767_D52N_E100fF, P1-068767_E100fF, P1-068767_E30D_E100fF, P1-
061029_F100fE_V102D, P1-061029_F100fE, P1-061029_V102D, P1-
061029_Y32E, or P1-061029_Y32E_F100fE.

25 104. The isolated antibody of any one of claims 77-103, wherein the antibody
comprises VL CDR1, CDR2 and CDR3 of the VL of P1-061029.

105. The isolated antibody of any one of claims 1-63 and 72-104, wherein the
antibody comprises a VH comprising an amino acid sequence that is at least 90%,
95%, 97%, 98% or 99% identical to that of P1-061029, P1-068757, P1-068759, P1-

068761, P1-068763, P1-068765, P1-068767, P1-068769, P1-068771, P1-068773,
 P1-068775, P1-069059, P1-069061, P1-069063, P1-069065, P1-069067, P1-
 069069, P1-069071, P1-069073, P1-069075, P1-069077, P1-069077, P1-
 068761_E55A, P1-068761_H100G, P1-068761_E56N, P1-068761_E55A_E56N, P1-
 5 068761_E30D, P1-068761_E30D_E55A, P1-068761_E56N_H100G, P1-
 068761_E30D_H100G, or P1-068761_E30D_E56N, P1-068761_E100fF, P1-
 068761_E55A_E100fF, P1-068761_H100G_E100fF, P1-068761_E30D_E100fF, P1-
 068761_E56N_E100fF, P1-068761_E32Y, P1-068761_E32Y_E55A, P1-
 068761_E32Y_E56N, P1-068761_E30D_E32Y, P1-068761_E32Y_H100G, P1-
 10 068761_E32Y_E100fF, P1-068767_D52N_D102V, P1-068767_D52N, P1-
 068767_D52N_E55A, P1-068767_E55A_D102V, P1-068767_D102V, P1-
 068767_E55A, P1-068767_E30D_D52N, P1-068767_E30D_D102V, P1-
 068767_E30D, P1-068767_E30D_E55A, P1-068767_E100fF_D102V, P1-
 068767_E55A_E100fF, P1-068767_D52N_E100fF, P1-068767_E100fF, P1-
 15 068767_E30D_E100fF, P1-061029_F100fE_V102D, P1-061029_F100fE, P1-
 061029_V102D, P1-061029_Y32E, or P1-061029_Y32E_F100fE; or
 comprises the VH of P1-061029, P1-068757, P1-068759, P1-068761, P1-068763,
 P1-068765, P1-068767, P1-068769, P1-068771, P1-068773, P1-068775, P1-
 069059, P1-069061, P1-069063, P1-069065, P1-069067, P1-069069, P1-069071,
 20 P1-069073, P1-069075, P1-069077, P1-069077, P1-068761_E55A, P1-
 068761_H100G, P1-068761_E56N, P1-068761_E55A_E56N, P1-068761_E30D, P1-
 068761_E30D_E55A, P1-068761_E56N_H100G, P1-068761_E30D_H100G, or P1-
 068761_E30D_E56N, P1-068761_E100fF, P1-068761_E55A_E100fF, P1-
 068761_H100G_E100fF, P1-068761_E30D_E100fF, P1-068761_E56N_E100fF, P1-
 25 068761_E32Y, P1-068761_E32Y_E55A, P1-068761_E32Y_E56N, P1-
 068761_E30D_E32Y, P1-068761_E32Y_H100G, P1-068761_E32Y_E100fF, P1-
 068767_D52N_D102V, P1-068767_D52N, P1-068767_D52N_E55A, P1-
 068767_E55A_D102V, P1-068767_D102V, P1-068767_E55A, P1-
 068767_E30D_D52N, P1-068767_E30D_D102V, P1-068767_E30D, P1-

068767_E30D_E55A, P1-068767_E100fF_D102V, P1-068767_E55A_E100fF, P1-068767_D52N_E100fF, P1-068767_E100fF, P1-068767_E30D_E100fF, P1-061029_F100fE_V102D, P1-061029_F100fE, P1-061029_V102D, P1-061029_Y32E, or P1-061029_Y32E_F100fE, modified by 1, 2, 3, 4, or 5 amino acid substitutions, modified by 1, 2, 3, 4, or 5 conservative amino acid substitutions, or modified by one or both of K16R and T84A substitutions.

106. The isolated antibody of any one of claims 1-63 and 72-105, wherein the antibody comprises a VH comprising the amino acid sequence of the VH of P1-061029, P1-068757, P1-068759, P1-068761, P1-068763, P1-068765, P1-068767, P1-068769, P1-068771, P1-068773, P1-068775, P1-069059, P1-069061, P1-069063, P1-069065, P1-069067, P1-069069, P1-069071, P1-069073, P1-069075, P1-069077, P1-068761_E55A, P1-068761_H100G, P1-068761_E56N, P1-068761_E55A_E56N, P1-068761_E30D, P1-068761_E30D_E55A, P1-068761_E56N_H100G, P1-068761_E30D_H100G, or P1-068761_E30D_E56N, P1-068761_E100fF, P1-068761_E55A_E100fF, P1-068761_H100G_E100fF, P1-068761_E30D_E100fF, P1-068761_E56N_E100fF, P1-068761_E32Y, P1-068761_E32Y_E55A, P1-068761_E32Y_E56N, P1-068761_E30D_E32Y, P1-068761_E32Y_H100G, or P1-068761_E32Y_E100fF, P1-068767_D52N_D102V, P1-068767_D52N, P1-068767_D52N_E55A, P1-068767_E55A_D102V, P1-068767_D102V, P1-068767_E55A, P1-068767_E30D_D52N, P1-068767_E30D_D102V, P1-068767_E30D, P1-068767_E30D_E55A, P1-068767_E100fF_D102V, P1-068767_E55A_E100fF, P1-068767_D52N_E100fF, P1-068767_E100fF, P1-068767_E30D_E100fF, P1-061029_F100fE_V102D, P1-061029_F100fE, P1-061029_V102D, P1-061029_Y32E, or P1-061029_Y32E_F100fE; or comprises the VH of P1-061029, P1-068757, P1-068759, P1-068761, P1-068763, P1-068765, P1-068767, P1-068769, P1-068771, P1-068773, P1-068775, P1-069059, P1-069061, P1-069063, P1-069065, P1-069067, P1-069069, P1-069071, P1-069073, P1-069075, P1-069077, P1-068761_E55A, P1-

- 068761_H100G, P1-068761_E56N, P1-068761_E55A_E56N, P1-068761_E30D, P1-068761_E30D_E55A, P1-068761_E56N_H100G, P1-068761_E30D_H100G, or P1-068761_E30D_E56N, P1-068761_E100fF, P1-068761_E55A_E100fF, P1-068761_H100G_E100fF, P1-068761_E30D_E100fF, P1-068761_E56N_E100fF, P1-068761_E32Y, P1-068761_E32Y_E55A, P1-068761_E32Y_E56N, P1-068761_E30D_E32Y, P1-068761_E32Y_H100G, P1-068761_E32Y_E100fF, P1-068767_D52N_D102V, P1-068767_D52N, P1-068767_D52N_E55A, P1-068767_E55A_D102V, P1-068767_D102V, P1-068767_E55A, P1-068767_E30D_D52N, P1-068767_E30D_D102V, P1-068767_E30D, P1-068767_E30D_E55A, P1-068767_E100fF_D102V, P1-068767_E55A_E100fF, P1-068767_D52N_E100fF, P1-068767_E100fF, P1-068767_E30D_E100fF, P1-061029_F100fE_V102D, P1-061029_F100fE, P1-061029_V102D, P1-061029_Y32E, or P1-061029_Y32E_F100fE, modified by one or both of K16R and T84A substitutions.
107. The isolated antibody of any one of claims 1-106, wherein the antibody comprises a VL comprising an amino acid sequence that is at least 90%, 95%, 97%, 98% or 99% identical to that of P1-061029.
108. The isolated antibody of claim 107, wherein the antibody comprises the VL of P1-061029.
109. The isolated antibody of any one of claims 1-63 and 72-76, wherein the antibody comprises VH CDR1, CDR2 and/or CDR3 of P1-061015 or a variant thereof comprising 1-6 or 1-8 amino acid differences in VH CDR1, CDR2 and/or CDR3 relative to P1-061015, wherein at most 1, 2 or 3 amino acid variations are present in any one CDR.
110. The isolated antibody of claim 109, wherein the antibody comprises VH CDR1, CDR2 and CDR3 of P1-061015 or a variant thereof comprising 1-6 amino acid differences in VH CDR1, CDR2 and/or CDR3 relative to the P1-061015, wherein at most 1, 2 or 3 amino acid variations are present in any one CDR.

111. The isolated antibody of claims 108 or 109, wherein an amino acid variation is a substitution to a glutamic acid residue (E), aspartic acid residue (D) or a histidine residue (H).

112. The isolated antibody of any one of claims 108-111, wherein the antibody comprises

- a CDR1 comprising GFTFX₁X₂X₃MH, wherein X₁ is E, D, H or S; X₂ is H or Y; and X₃ is D or A (SEQ ID NO: 569);

- a CDR2 comprising X₄X₅WX₆DGSX₇X₈X₉X₁₀ADSVKG, wherein X₄ is E, H or I; X₅ is D or I; X₆ is D or Y; X₇ is D or N; X₈ is D, H or K; X₉ is D, H or Y; and X₁₀ is E or Y (SEQ ID NO: 570); and/or

- a CDR3 comprising DX₁₁X₁₂FYX₁₃X₁₄YYDFX₁₅, wherein X₁₁ is E or S; X₁₂ is E or G; X₁₃ is D, E or S; X₁₄ is D or S; and X₁₅ is D, E or Y (SEQ ID NO: 571).

113. The antibody of any one of claims 108-112, wherein the antibody comprises

- a CDR1 comprising GFTFX₁X₂X₃MH, wherein X₁ is E, D, H or S; X₂ is H or Y; and X₃ is D or A (SEQ ID NO: 569);

- a CDR2 comprising X₄X₅WX₆DGSX₇X₈X₉X₁₀ADSVKG, wherein X₄ is E, H or I; X₅ is D or I; X₆ is D or Y; X₇ is D or N; X₈ is D, H or K; X₉ is D, H or Y; and X₁₀ is E or Y (SEQ ID NO: 570); and

- a CDR3 comprising DX₁₁X₁₂FYX₁₃X₁₄YYDFX₁₅, wherein X₁₁ is E or S; X₁₂ is E or G; X₁₃ is D, E or S; X₁₄ is D or S; and X₁₅ is D, E or Y (SEQ ID NO: 571).

114. The isolated antibody of any one of claims 98-102, wherein the antibody comprises VH CDR1, CDR2 and/or CDR3 of P1-061015, P1-068736, P1-068738, P1-068740, P1-068742, P1-068744, P1-068748, P1-068750, P1-068752 or P1-068754.

115. The isolated antibody of claim 114, wherein the antibody comprises VH CDR1, CDR2 and CDR3 of P1-061015, P1-068736, P1-068738, P1-068740, P1-068742, P1-068744, P1-068748, P1-068750, P1-068752 or P1-068754.

116. The isolated antibody of any one of claims 98-115, wherein the antibody comprises VL CDR1, CDR2 and CDR3 of the VL of P1-061015.

117. The isolated antibody of any one of claims 98-116, wherein the antibody comprises a VH comprising an amino acid sequence that is at least 90%, 95%, 97%, 98% or 99% identical to that of P1-061015, P1-068736, P1-068738, P1-068740, P1-068742, P1-068744, P1-068748, P1-068750, P1-068752 or P1-068754; or
5 comprising an amino acid sequence of the VH of P1-061015, P1-068736, P1-068738, P1-068740, P1-068742, P1-068744, P1-068748, P1-068750, P1-068752 or P1-068754, modified by 1, 2, 3, 4, or 5 amino acid substitutions, or modified by 1, 2, 3, 4, or 5 conservative amino acid substitutions.
118. The isolated antibody of any one of claims 98-117, wherein the antibody
10 comprises a VH comprising the amino acid sequence of the VH of P1-061015, P1-068736, P1-068738, P1-068740, P1-068742, P1-068744, P1-068748, P1-068750, P1-068752 or P1-068754; or
comprising the amino acid sequence of the VH of P1-061015, P1-068736, P1-068738, P1-068740, P1-068742, P1-068744, P1-068748, P1-068750, P1-068752 or
15 P1-068754, modified by 1, 2, 3, 4, or 5 amino acid substitutions, or modified by 1, 2, 3, 4, or 5 conservative amino acid substitutions.
119. The isolated antibody of any one of claims 98-118, wherein the antibody comprises a VL comprising an amino acid sequence that is at least 90%, 95%, 97%, 98% or 99% identical to that of P1-061015.
- 20 120. The isolated antibody of claim 119, wherein the antibody comprises a VL comprising the amino acid sequence of P1-061015.
121. The isolated isolated antibody of any one of claims 1-120, wherein the antibody binds at or near the histidine rich region of hVISTA, such as the histidine-rich β -sheet extension.
- 25 122. The isolated isolated antibody of claim 121, wherein the antibody binds at or near the histidine rich region of hVISTA, such as the histidine-rich β -sheet extension, in conditions having a pH of 6.0-6.5.
123. The isolated isolated antibody of any one of claims 1-122, wherein the antibody competes or cross-competes for binding to hVISTA with one or more

antibodies described herein, e.g., comprising the VH and VL of P1-061029, P1-068757, P1-068759, P1-068761, P1-068763, P1-068765, P1-068767, P1-068769, P1-068771, P1-068773, P1-068775, P1-069059, P1-069061, P1-069063, P1-069065, P1-069067, P1-069069, P1-069071, P1-069073, P1-069075, P1-069077, P1-069077, P1-068761_E55A, P1-068761_H100G, P1-068761_E56N, P1-068761_E55A_E56N, P1-068761_E30D, P1-068761_E30D_E55A, P1-068761_E56N_H100G, P1-068761_E30D_H100G, or P1-068761_E30D_E56N, P1-068761_E100fF, P1-068761_E55A_E100fF, P1-068761_H100G_E100fF, P1-068761_E30D_E100fF, P1-068761_E56N_E100fF, P1-068761_E32Y, P1-068761_E32Y_E55A, P1-068761_E32Y_E56N, P1-068761_E30D_E32Y, P1-068761_E32Y_H100G, P1-068761_E32Y_E100fF, P1-068767_D52N_D102V, P1-068767_D52N, P1-068767_D52N_E55A, P1-068767_E55A_D102V, P1-068767_D102V, P1-068767_E55A, P1-068767_E30D_D52N, P1-068767_E30D_D102V, P1-068767_E30D, P1-068767_E30D_E55A, P1-068767_E100fF_D102V, P1-068767_E55A_E100fF, P1-068767_D52N_E100fF, P1-068767_E100fF, P1-068767_E30D_E100fF, P1-061029_F100fE_V102D, P1-061029_F100fE, P1-061029_V102D, P1-061029_Y32E, or P1-061029_Y32E_F100fE, P1-061015, P1-068736, P1-068738, P1-068740, P1-068742, P1-068744, P1-068748, P1-068750, P1-068752 or P1-068754), as determined, e.g., by the competitive bio-layer interferometry (BLI) epitope binning assay described in Example 15.

124. The isolated antibody of any one of claims 1-123, wherein the antibody bins to epitope Group A, as determined, e.g., by the competitive bio-layer interferometry (BLI) epitope binning assay described in Example 15.

125. The isolated antibody of any one of claims 1-124, wherein the antibody does not bind significantly to a hVISTA modified in that one or more of the following amino acid residues have been mutated: T35, Y37, K38, T39, Y41, R54, T61, F62, Q63, L65, H66, L67, H68, H69, F97, L115, V117, I119, H121, H122, S124, E125, R127, e.g., as determined by the yeast mutational analysis described in the Examples.

126. An isolated antibody that binds to hVISTA consisting of SEQ ID NO: 1 or 2, but does not bind significantly to a hVISTA modified in that one or more of the following amino acid residues have been mutated: T35, Y37, K38, T39, Y41, R54, T61, F62, Q63, L65, H66, L67, H68, H69, F97, L115, V117, I119, H121, H122, S124, E125, R127.
127. The isolated antibody of any one of claims 1-126, wherein the antibody does not bind significantly to a hVISTA modified in that 2, 3, 4, 5 or more of the following amino acid residues have been mutated: T35, Y37, K38, T39, Y41, R54, T61, F62, Q63, L65, H66, L67, H68, H69, F97, L115, V117, I119, H121, H122, S124, E125, R127.
128. The isolated antibody of any one of claims 125-127, wherein the antibody does not bind to a hVISTA modified in that one or more of the following residues have been mutated to one of the corresponding residues shown in Table 15: H68, F97, L115, V117, I119, H121, H122, S124, E125, R127.
129. An isolated antibody (Ab) that binds to hVISTA under acidic conditions, e.g., at a pH of 6.5 (as measured, e.g., by one of the assays described in the Examples), wherein the Ab inhibits the interaction between hVISTA and (a) T cells and/or (b) PSGL-1, and wherein the Ab contacts hVISTA through one or more (e.g., at least 1-3, 1-5, 1-10, 5-10, 5-15 or all) energetically important contact residues of an antibody described herein, such as P1-061015, P1-061029, P1-068761, or P1-068767, such as one or more amino acids selected from one of the following groups of energetically important contact residues: (i) V34, T35, Y37, K38, T39, Y41, S52, R54, T61, F62, Q63, L65, H66, L67, H68, H69, F97, L115, V117, I119, H121, H122, S124, E125, R127; (ii) V34, T35, Y37, T39, Y41, S52, R54, F62, L65, H66, H68, L115, V117, I119, R120, H121, H122, S124, E125; or (iii) Y37, T39, R54, F62, H66, L115 or V117, as determined, e.g., using the yeast surface display and NGS assay described in Example 15, and wherein numbering is that of mature hVISTA.
130. An isolated Ab that binds to hVISTA under acidic conditions, e.g., at a pH of 6.5 (as measured, e.g., by one of the assays described in the Examples), wherein the

Ab inhibits the interaction between hVISTA and (a) T cells and/or (b) PSGL-1, and wherein the Ab contacts hVISTA through one or more (e.g., at least 1-3, 1-5, 1-10, 5-10, 5-15 or all) energetically important contact residues Y37, T39, R54, F62, H66, V117, I119 or S124, as determined, e.g., using the yeast surface display and NGS assay described in Example 15, and wherein numbering is that of mature hVISTA.

131. An isolated Ab that binds to hVISTA under acidic conditions, e.g., at a pH of 6.5 (as measured, e.g., by one of the assays described in the Examples), wherein the Ab inhibits the interaction between hVISTA and (a) T cells and/or (b) PSGL-1, and wherein the Ab contacts hVISTA through one or more (e.g., at least 1-3, 1-5, 1-10, 5-10, 5-15 or all) energetically important contact residues of P1-061015, P1-061029, P1-068761, or P1-068767 or other antibody described herein, as determined, e.g., using the yeast surface display and NGS assay described in Example 15, and wherein numbering is that of mature hVISTA.

132. The isolated Ab of any one of claims 1-131, wherein the Ab binds to the FG loop of hVISTA.

133. The isolated Ab of any one of claims 1-132, wherein the Ab binds to the histidine-rich β -sheet extension of hVISTA, as determined, e.g., by crystallography, as described, e.g., in the Examples.

134. The isolated Ab of any one of claims 1-133, wherein the Ab contacts H121, H122 and H123 (histidine triad) of mature hVISTA (distance of, e.g., 4.0 Ångströms (Å) or less), such as through hydrogen bonds, as determined, e.g., by crystallography, as described, e.g., in the Examples.

135. The isolated Ab of any one of claims 1-134, wherein the Ab contacts hVISTA through VH CDR1 and VH CDR3, and for example, not significantly through VH CDR2 and/or through a VL CDR.

136. The isolated Ab of any one of claims 1-135, wherein amino acid residues 110 and 112 of the antibody form hydrogen bonds with H121 and H122 of hVISTA, respectively, and optionally, wherein an amino acid residue of the antibody forms a hydrogen bond with H123 of hVISTA.

137. The isolated Ab of any one of claims 1-136, wherein the Ab contacts hVISTA through at least one or more glutamic acid, aspartic acid or histidine residue that is located in VH CDR1, CDR2 or CDR3.

138. The isolated Ab of any one of claims 1-137, wherein the Ab does not bind significantly to hVISTA at neutral or physiological pH (as measured, e.g., by one of the assays described in the Examples).

139. The isolated Ab of any one of claims 1-138, wherein the Ab binds to hVISTA under acidic conditions, e.g., at a pH of 6.5, with a K_D (or k_{off}) that is at least 10 fold, 100 fold or 1000 fold lower than its K_D and/or k_{off} of binding to hVISTA under neutral or physiological pH (as measured, e.g., by one of the assays described in the Examples).

140. The isolated Ab of any one of claims 1-139, wherein the Ab does not bind significantly to hVISTA at neutral or physiological pH (as measured, e.g., by one of the assays described in the Examples).

141. An isolated antibody (Ab) that binds to hVISTA under acidic conditions, e.g., at a pH of 6.5 (as measured, e.g., by one of the assays described in the Examples), wherein the Ab:

- inhibits the interaction between hVISTA and (a) T cells and/or (b) PSGL-1 (e.g., inhibits the interaction between H153 and H154 of hVISTA having SEQ ID NO: 1 and PSGL-1 tyrosines Y46 and Y48);
- enhances T cell activation by, e.g., enhancing T cell proliferation; enhancing IFN- γ production from T cells; and/or stimulating T cell receptor mediated NF-kB signaling;
- contacts hVISTA through one or more (e.g., at least 1-3, 1-5, 1-10, 5-10, 5-15 or all) energetically important contact residues Y37, T39, R54, F62, H66, V117, I119 or S124, as determined, e.g., using the yeast surface display and NGS assay described in Example 15; and wherein numbering is that of mature hVISTA;

- binds to the histidine-rich β -sheet extension of hVISTA, as determined, e.g., by crystallography, as described, e.g., in the Examples;
 - contacts H121, H122 and/or H123 of mature hVISTA (distance of 4.0 Ångströms (Å) or less), such as through hydrogen bonds, as determined, e.g., by crystallography, as described, e.g., in the Examples;
 - binds to Region 1: ₅₇LGPVDKGHDVTF₆₈ (SEQ ID NO: 566); Region 2: ₈₆RRPIRNLTFQDL₉₇ (SEQ ID NO: 567); and Region 3: ₁₄₈VVEIRHHHSEHRVHGAME₁₆₅ (SEQ ID NO: 568) of hVISTA having SEQ ID NO: 1, and optionally wherein the binding is strongest to Region 2, as determined by MS-HDX as described in Example 21;
 - competes for binding to hVISTA (two-way competition) with one or more antibodies described herein, e.g., P1-061015, P1-061029, P1-068761, P1-068767 and VISTA.4;
 - contacts hVISTA through at least one or more glutamic acid, aspartic acid or histidine residue that is located in VH CDR1, CDR2 or CDR3; and/or
 - has low target mediated drug disposition, leading to mean residence time (MRT) of at least 100, 200, 300, 400, 500, 600 or 700 hours, as measured, e.g., as described in the Examples.
142. An isolated antibody (Ab) that binds to hVISTA under acidic conditions, e.g., at a pH of 6.5 with a K_D (and/or k_{off}) that is at least 10 fold, 100 fold or 1000 fold lower than its K_D or k_{off} of binding to hVISTA under neutral or physiological pH (as measured, e.g., by one of the assays described in the Examples), wherein the Ab:
- inhibits the interaction between hVISTA and (a) T cells and/or (b) PSGL-1 (e.g., inhibits the interaction between H153 and H154 of hVISTA having SEQ ID NO: 1 and PSGL-1 tyrosines Y46 and Y48);
 - enhances T cell activation by, e.g., enhancing T cell proliferation; enhancing IFN- γ production from T cells; and/or stimulating T cell receptor mediated NF-kB signaling;

- contacts hVISTA through one or more (e.g., at least 1-3, 1-5, 1-10, 5-10, 5-15 or all) energetically important contact residues Y37, T39, R54, F62, H66, V117, I119 or S124, as determined, e.g., using the yeast surface display and NGS assay described in Example 15; and wherein numbering is that of mature hVISTA;
 - binds to the histidine-rich β -sheet extension of hVISTA, as determined, e.g., by crystallography, as described, e.g., in the Examples;
 - contacts H121, H122 and/or H123 of mature hVISTA (distance of 4.0 Ångströms (Å) or less), such as through hydrogen bonds, as determined, e.g., by crystallography, as described, e.g., in the Examples;
 - binds to Region 1: ₅₇LGPVDKGHDVTF₆₈ (SEQ ID NO: 566); Region 2: ₈₆RRPIRNLTQDL₉₇ (SEQ ID NO: 567); and Region 3: ₁₄₈VVEIRHHHSEHRVHGAME₁₆₅ (SEQ ID NO: 568) of hVISTA having SEQ ID NO: 1, and optionally wherein the binding is strongest to Region 2, as determined by MS-HDX as described in Example 21;
 - competes for binding to hVISTA (two-way competition) with one or more antibodies described herein, e.g., P1-061015, P1-061029, P1-068761, P1-068767 and VISTA.4;
 - contacts hVISTA through at least one or more glutamic acid, aspartic acid or histidine residue that is located in VH CDR1, CDR2 or CDR3; and/or
 - has low target mediated drug disposition, leading to mean residence time (MRT) of at least 100, 200, 300, 400 500, 600 or 700 hours, as measured, e.g., as described in the Examples.
143. The isolated antibody of any one of claims 1-142, wherein the antibody has an isoelectric point (pI) between 6.5 and 6.8, as measured, e.g., by icIEF.
144. The isolated antibody of any one of claims 1-143, wherein the antibody exhibits low aggregation, e.g., an aggregation that is similar or lower than that of antibodies '029, '761 or '767 (P1-061015, P1-061029, P1-068761, or P1-068767, respectively), e.g., as determined in the Examples.

145. The isolated antibody of any one of claims 1-144, wherein the antibody exhibits a viscosity that is similar or lower than that of '029, '761 or '767, e.g., as determined in the Examples.
146. The isolated antibody of any one of claims 1-145, wherein the antibody exhibits a hydrodynamic radius that is similar or lower than that of '029, '761 or '767, e.g., as determined in the Examples.
147. The isolated antibody of any one of claims 1-146, wherein the antibody exhibits a melting temperature (T_{m1}) that is similar or higher than that of '029, '761 or '767, e.g., as determined in the Examples.
148. The isolated antibody of any one of claims 1-147, wherein the antibody exhibits an amount of high molecular weight species that is similar to or lower than that of '029, '761 or '767, e.g., as determined in the Examples.
149. The isolated antibody of any one of claims 1-148, which is an IgG antibody.
150. The isolated antibody of claim 149, which is an IgG1, IgG2 or IgG4 antibody (IgG4 optionally with S228P).
151. The isolated antibody of any one of claims 1-150, wherein the antibody is an effectorless antibody, e.g., lacks ADCC and/or CDC, and/or an antibody that does not significantly bind to one or more FcγRs, e.g., FcγRIII.
152. The isolated antibody of claim 151, wherein the constant region comprises 1-5 mutations in a wild type heavy chain constant region that reduce the effector function of the antibody and/or the ability to bind to one or more FcγRs, e.g., FcγRIII, relative to that of the corresponding wildtype heavy chain constant region.
153. The isolated antibody of any one of claims 1-152, wherein the constant region of the antibody is IgG1.3, IgG1.1 or is an IgG1 with a P238K substitution (e.g., IgG1.P238K).
154. The isolated antibody of any one of claims 1-150, wherein the antibody has effector function and/or binds to one or more FcγRs, e.g., FcγRIII.
155. The isolated antibody of claim 154, wherein the antibody is afucosylated (e.g., an afucosylated IgG1 antibody).

156. The isolated antibody of claim 154 or 155, wherein the constant region comprises 1-5 mutations that enhance the effector function of the antibody and/or the ability to bind to one or more FcγRs, e.g., FcγRIII, relative to the corresponding wildtype constant region.
- 5 157. The isolated antibody of any one of claims 1- 156, which is a full length antibody or an antibody comprising a full length heavy chain (with or without a C-terminal lysine) and a full length light chain.
158. The isolated antibody of any one of claims 1-156, which is an antigen binding fragment of the antibody.
- 10 159. The isolated antibody of anyone of claims 1-158, which is a multimeric (e.g., dimeric or trimeric) antibody.
160. The isolated antibody of anyone of claims 1-159, which is linked (e.g., covalently) to another molecule.
161. The isolated antibody of claim 160, wherein the other molecule is a label.
- 15 162. The isolated antibody of claim 160 or 161, wherein the other molecule is a peptide.
163. The isolated antibody of any one of claims 1-162, which is an antibody drug conjugate (ADC) or an activatable antibody.
164. An isolated nucleic acid encoding an antibody of any one of claims 1-163 or
20 206-212.
165. An isolated nucleic acid encoding the heavy chain and/or the light chain of an antibody of any one of claims 1-163 or 206-212.
166. A composition comprising an isolated nucleic acid encoding the heavy chain of an antibody of any one of claims 1-163 or 206-212 and a nucleic acid encoding the
25 light chain of the antibody.
167. A cell comprising the isolated nucleic acid of any one of claims 164-166.
168. A method of preparing an antibody, comprising culturing the cell of claim 167 in conditions under which the antibody is expressed.

169. A composition comprising an isolated antibody, nucleic acid, composition or cell of any one of claims 1-168 and a pharmaceutically acceptable carrier.
170. The composition of claim 169, comprising a second therapeutic agent.
171. The composition of claim 170, wherein the second therapeutic agent is an immunostimulatory agent or a chemotherapeutic agent.
172. The composition of claim 171, wherein the second therapeutic agent is an immunostimulating agent that is an antagonist of an immunosuppressive molecule, e.g., the PD-1/PD-L1, a CTLA-4 and LAG-3, or an agonist of an immunostimulating molecule, e.g., GITR and OX40.
173. A method of treating cancer in a subject, comprising administering to the subject a therapeutically effective amount of a composition or isolated antibody of any one of claims 1-172 or 206-212 that stimulates an immune response and/or is a VISTA antagonist antibody.
174. The method of claim 173, wherein the subject has VISTA positive cells, e.g., in a tumor of the cancer.
175. The method of claim 174, wherein cells are VISTA positive infiltrating lymphocytic (e.g., T cells) or myelomonocytic cells.
176. The method of any one of claims 173-175, wherein the subject is first tested for the presence of VISTA positive cells in a tumor.
177. The method of any one of claims 173-176, wherein the method further comprises administering a second therapy.
178. The method of claim 177, wherein the second therapy is chemotherapy, radiotherapy, surgery or administration of a second agent.
179. The method of claim 178, wherein the second therapy is a second agent and the second agent is an immunostimulatory agent or a chemotherapeutic agent.
180. The method of claim 179, wherein the second therapeutic agent is an immunostimulatory agent that is an antagonist of an immunosuppressive molecule, e.g., the PD-1/PD-L1, an CTLA-4 and LAG-3, or an agonist of an immunostimulating molecule, e.g., GITR and OX40.

181. A method of treating an infectious disease (e.g., viral disease) in a subject, comprising administering to the subject a therapeutically effective amount of a composition or isolated antibody of any one of claims 1-172 or 206-212 that stimulates an immune response and/or is a VISTA antagonist.
- 5 182. A method of treating an inflammation, an inflammatory condition, and autoimmune disease, graft versus host disease or a disease that benefits from reducing an immune response, comprising administering to the subject a therapeutically effective amount of a composition or isolated antibody of any one of claims 1-172 or 206-212 that inhibits an immune response, e.g., T cell activation or is a VISTA
- 10 agonist.
183. A method for identifying an antibody (Ab) that binds to human VISTA extracellular domain (hVISTA-ECD) at pH 6.5 or less with a K_D of 10^{-7} M or less, comprising contacting a test Ab or a plurality of test Abs with a polypeptide comprising hVISTA-ECD or a fragment thereof comprising the IgV domain of
- 15 hVISTA-ECD or comprising amino acids 20-95, 20-70, 35-70-127, or 35-127 of SEQ ID NO:2 at pH 6.5 or less, and selecting the test Ab or Abs that bind to the polypeptide with a K_D of 10^{-7} M or less.
184. A method for identifying an antibody (Ab) that binds to human VISTA extracellular domain (hVISTA-ECD) at pH 6.5 or less with a k_{off} of $5 \times 10^{-3} \text{ sec}^{-1}$ or
- 20 less, comprising contacting a test Ab or a plurality of test Abs with a polypeptide comprising hVISTA-ECD or a fragment thereof comprising the IgV domain of hVISTA-ECD or comprising amino acids 20-95, 20-70, 35-70, or 35-127 of SEQ ID NO:2 at pH 6.5 or less, and selecting the test Ab or Abs that bind to the polypeptide with a k_{off} of $5 \times 10^{-3} \text{ sec}^{-1}$ or less.
- 25 185. A method for identifying an antibody (Ab) that binds to human VISTA extracellular domain (hVISTA-ECD) at pH 6.5 with similar affinity at pH 7.0 comprising:
- a. contacting a test Ab or plurality of test Abs at pH 6.5 with a polypeptide comprising hVISTA-ECD or a fragment thereof comprising the IgV domain

of hVISTA-ECD or comprising amino acids 20-95, 20-70, or 35-70, or 35-127 of SEQ ID NO:2;

- b. contacting the test Ab or plurality of test Abs at pH 7.0 with the polypeptide of (a); and
- 5 c. selecting a test Ab if it binds to the polypeptide with a K_D of 10^{-7} M or less at pH 6.5 and at pH 7.0.

186. A method for identifying an antibody (Ab) that binds with higher affinity to human VISTA extracellular domain (hVISTA-ECD) at pH 6.5 than at pH 7.0 comprising:

- 10 a. contacting a test Ab or plurality of test Abs at pH 6.5 with a polypeptide comprising hVISTA-ECD or a fragment thereof comprising the IgV domain of hVISTA-ECD or comprising amino acids 20-95, 20-70, 35-70, or 35-127 of SEQ ID NO:2;
- b. contacting the test Ab or plurality of test Abs at pH 7.0 with the polypeptide
- 15 of (a); and
- c. selecting a test Ab if it binds to the polypeptide with a K_D or k_{off} at least 2-fold lower at pH 6.5 than at pH 7.0.

187. A method for identifying an antibody (Ab) that specifically binds to human VISTA extracellular domain (hVISTA-ECD) for use in treating cancer, comprising

- 20 a. identifying Abs that specifically bind to hVISTA-ECD at pH 6.5 or less, such as according to the methods of claims 183-186; and
- b. selecting the Abs of (a) that trigger or enhance an immune response in a tumor model or that inhibit tumor growth at pH 6.5 or less.

188. The method of claim 187, wherein step (b) comprises measuring T cell

25 activity.

189. The method of claim 187 or 188, further comprising measuring the anti-tumor effect of the Ab.

190. A method for improving the anti-tumor efficacy of an antibody (Ab) that binds to human VISTA extracellular domain (hVISTA-ECD), comprising

- a. Providing an Ab that binds to hVISTA-ECD at pH 6.5 or less with an affinity that is less than a desired value;
 - b. substituting 1 to 5 amino acid residues in the heavy or light chain of the Ab with a different amino acid residue (e.g, with a glutamic acid, aspartic acid or histidine residue), wherein the 1 to 5 amino acid residues are contact residues with hVISTA-ECD, e.g., one or more of amino acid residues 26, 30, 31, 32, 110 and 112 (shown in Table 24; numbering in SEQ ID NOs: 67, 51 or 55;
 - c. Determining if the Ab obtained in (b) has higher affinity for hVISTA-ECD at pH 6.5 or less relative to the Ab of (a); and
 - d. Repeating steps (a) - (c), for a number of rounds sufficient to obtain an Ab that binds to hVISTA-ECD at pH 6.5 or less with a K_D of 10^{-7} M or less.
191. A method for improving the anti-tumor efficacy of an antibody (Ab) that binds to human VISTA extracellular domain (hVISTA-ECD), comprising:
 - a. Providing an Ab that binds to hVISTA-ECD at pH 6.5 or less with an affinity that is less than a desired value;
 - b. Preparing a library of variants of the Ab of (a), wherein each variant comprises a substitution of 1 to 5 amino acid residues in the heavy or light chain of the Ab with a different amino acid residue (e.g, with a glutamic acid, aspartic acid or histidine residue), wherein the 1 to 5 amino acid residues are contact residues with hVISTA-ECD, e.g., one or more of amino acid residues 26, 30, 31, 32, 110 and 112 (shown in Table 24; numbering in SEQ ID NOs: 67, 51 or 55;
 - c. Selecting Abs of the library of variants of (b) that bind to hVISTA-ECD at pH 6.5 or less with a K_D of 10^{-7} M or less; and
 - d. Optionally testing the anti-tumor efficacy of the Abs of (c) in a tumor model.
192. A method for improving the pharmacokinetics of an antibody that binds to human VISTA extracellular domain (ECD), comprising enhancing the ability of the

antibody to bind to human VISTA in acidic conditions, e.g., equal to or lower than pH 6.5.

193. A method for selecting an antibody that binds to human VISTA and having an extended half-life (good pharmacokinetic properties), wherein the method comprises selecting an antibody that binds to human VISTA in acidic conditions, e.g., equal to or lower than pH 6.5.

194. A method for improving the efficacy of antibodies that bind to human VISTA (hVISTA), comprising increasing the number of aspartic acid, glutamic acid and/or histidine residues in one or more VH CDRs of the antibody, to enhance binding of the antibody to hVISTA at acidic pH.

195. A method for isolating antibodies that bind to human VISTA (hVISTA) and have a long half-life in human blood and/or stimulate T cells in a tumor environment, comprising screening a library of antibodies binding to hVISTA for those that bind at acidic pH, but not at neutral pH.

196. The method of any one of claims 183-195, comprising counter selecting for those antibodies that bind at physiological pH.

197. The method of any one of claims 183-196, further comprising selecting antibodies that are either a VISTA antagonist or a VISTA agonist.

198. The method of any one of claims 183-197, comprising selecting for those antibodies that inhibit the interaction between VISTA and a VISTA co-receptor (e.g., PSGL-1) and/or the interaction between VISTA and T cells or myelomonocytic cells.

199. The method of any one of claims 183-198, further comprising selecting antibodies that have one or more of the properties of P1-068761 or P1-068767.

200. A method for improving the anti-tumor efficacy of an antibody (Ab) that binds to human VISTA extracellular domain (hVISTA-ECD), comprising

- a. providing an Ab that binds to hVISTA-ECD at pH 7.0, but not significantly at pH 6.5;
- b. substituting 1 to 5 amino acid residues in the heavy or light chain, e.g., CDRs, of the Ab with a different amino acid residue, wherein, e.g., the 1 to 5 amino

acid residues are contact residues with hVISTA-ECD, e.g., one or more of amino acid residues 26, 30, 31, 32, 110 and 112 (shown in Table 24; numbering in SEQ ID NOs: 67, 51 or 55;

- c. determining if the Ab obtained in (b) has higher affinity for hVISTA-ECD at pH 6.5 than at pH 7.0 and/or determining whether the Ab obtained in (b) has similar or higher affinity at pH 6.5 relative to the parent antibody (antibody of (a) and lower affinity at pH 7.0 relative to the antibody of (a); and
- d. repeating steps (a) - (c), for a number of rounds sufficient to obtain an Ab that binds to hVISTA-ECD at pH 6.5 or less with a K_D of 10^{-7} M or less and binds to hVISTA-ECD at pH 7.0 or more with a K_D of 10^{-6} M or more.

201. A method of detecting VISTA in a sample, comprising contacting the sample with a VISTA antibody of any one of claims 1-163 or 206-212.

202. A method of treating cancer in a subject, comprising administering to the subject an isolated antibody that binds to human VISTA (hVISTA) and inhibits the activity of hVISTA (e.g., T cell activation) and a PD1/PD-L1 pathway antagonist, which results in the increase of the number of CD4+ and CD8+ T cells, e.g., in a tumor of the subject.

203. A method of treating cancer in a subject, comprising administering to the subject an isolated antibody that binds to human VISTA (hVISTA) and inhibits the activity of hVISTA (e.g., T cell activation) and a PD1/PD-L1 pathway antagonist, which results in the reduction of the number of exhausted T cells and/or T cells expressing PD-1, LAG3 and/or TIM-3, e.g., in a tumor of the subject.

204. A method of treating cancer in a subject, comprising administering to the subject an isolated antibody that binds to human VISTA (hVISTA) and inhibits the activity of hVISTA (e.g., T cell activation) and a PD1/PD-L1 pathway antagonist, which results in the increase of the number of CD4+ and CD8+ T cells, e.g., in a tumor of the subject and a reduction of the number of exhausted T cells and/or T cells expressing PD-1, LAG3 and/or TIM-3, e.g., in a tumor of the subject and/or other features described herein.

205. The method of any one of claims 202-204, wherein the antibody that binds to hVISTA is an antibody described herein, such as an antibody of any one of claims 1-163 or 206-212.

206. The antibody, composition or a method of any one of claims 1-205, wherein the antibody comprises one or more (e.g., 1-5, 5-10, 10-15, 10-20 or 15-20) interactions with hVISTA listed in Table 24.

207. An antibody, composition or method of any one of claims 1-206, wherein the antibody comprises a glutamic acid, aspartic acid or histidine at one or more of positions 26, 30, 31, 110, 111 and 112 (e.g., the contact residues identified by crystallography in Table 24), wherein the numbering is according to that in SEQ ID NOs: 67, 51 and 55.

208. An isolated antibody that binds to human VISTA extracellular domain at a pH of 6.5 and optionally not significantly at pH 7.0, wherein the antibody comprises a glutamic acid, aspartic acid or histidine at one or more of positions 26, 30, 31, 110, 111 and 112 (e.g., the contact residues identified by crystallography in Table 24), wherein the numbering is according to that in SEQ ID NOs: 67, 51 and 55.

209. The antibody, composition or method of any one of claims 1-208, wherein the antibody does not comprise the heavy chain variable region of any of P1-069059, P1-069061, P1-069063, P1-069065, P1-069067, P1-069071, P1-069073, P1-069075, P1-069077, P1-068761, P1-068767, P1-068773, P1-068765, P1-061029, P1-068757, P1-068771, P1-068775, P1-068769, P1-068759, P1-068763, P1-061015, P1-068748, P1-068744, P1-068736, P1-068752, P1-068740, P1-068742, P1-068746, P1-068750, P1-068738, P1-068754, P1-069293, P1-069298, P1-069302, P1-069312, P1-069309, P1-069307, P1-070864, P1-070866, P1-070868, P1-070870, P1-070872, P1-070874, P1-070876, P1-070878, P1-070880, P1-070882, P1-070884, P1-070886, P1-070888, P1-070890, P1-070892, P1-070894, P1-070896, P1-070898, P1-070900, P1-070902, P1-070904, P1-070906, P1-070908, P1-070910, P1-070912, P1-070914, P1-070916, P1-070918, P1-070920, P1-070922, P1-070924, P1-070926, P1-070928, P1-070930, P1-070932 (i.e., SEQ ID Nos: 11, 15, 19, 23, 27, 31, 35, 39, 43, 47, 51, 55, 59, 63, 67,

71, 75, 79, 83, 87, 91, 95, 99, 103, 107, 111, 115, 119, 123, 127, 131, 135, 139, 143, 147, 151, 155, 159, 185, 189, 193, 197, 201, 205, 209, 213, 217, 221, 225, 229, 233, 237, 241, 245, 249, 253, 257, 261, 265, 269, 273, 277, 281, 285, 289, 293, 297, 301, 305, 309, 313, 317, 321), or does not comprise the heavy chain variable region of any antibody disclosed in international publication WO2018/169993.

210. The antibody, composition or method of any one of claims 1-209, wherein the antibody inhibits the interaction between hVISTA extracellular domain (ECD) and PSGL-1.

211. The antibody, composition or method of any one of claims 1-210, wherein the antibody competes for binding to hVISTA ECD with an antibody described herein (e.g., using BLI described herein), such as '761 and '767, and/or which binds to hVISTA ECD via the same amino acid residues as an antibody described herein, such as '761 and '767.

212. The antibody, composition or method of any one of claims 1-211, wherein the antibody interacts with the histidine triad (H121, 122 and 123 of mature hVISTA), as determined by X-ray crystallography, e.g., as determined herein.