

CLAIMS

WHAT IS CLAIMED IS:

1. A composition comprising an antibody molecule that binds to NKp30, wherein the antibody molecule comprises:
 - (a) (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) comprising the sequence of SEQ ID NO: 19, a heavy chain complementarity determining region 2 (VHCDR2) comprising the sequence of SEQ ID NO: 21, and a heavy chain complementarity determining region 3 (VHCDR3) comprising the sequence of SEQ ID NO: 23; and
 - (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) comprising the sequence of SEQ ID NO: 26, a light chain complementarity determining region 2 (VLCDR2) comprising the sequence of SEQ ID NO: 28, and a light chain complementarity determining region 3 (VLCDR3) comprising the sequences of SEQ ID NO: 30, SEQ ID NO: 7395, or SEQ ID NO: 113; or
 - (b)(i) a VH comprising a VHCDR1 comprising the sequence of SEQ ID NO: 19, a VHCDR2 comprising the sequence of SEQ ID NO: 7399, and a VHCDR3 comprising the sequence of the sequence of SEQ ID NO: 23; and
 - (ii) a VL comprising a VLCDR1 comprising the sequence of SEQ ID NO: 26, a VLCDR2 comprising the sequence of SEQ ID NO: 28, and a VLCDR3 comprising the sequences of SEQ ID NO: 30, SEQ ID NO: 7395, SEQ ID NO: 86, or SEQ ID NO: 113.
2. The composition of claim 1, wherein the antibody molecule comprises:
 - (i) a VH comprising an amino acid sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1 or SEQ ID NO: 2; and/or
 - (ii) a VL comprising an amino acid sequence having at least 80% sequence identity to any one sequence selected from the group consisting of SEQ ID NOs: 9-16.
 3. The composition of claim 1 or 2, wherein the antibody molecule comprises:
 - (i) a VH comprising the amino acid sequence of SEQ ID NO: 1; and/or
 - (ii) a VL comprising any one of the amino acid sequences selected from the group consisting of SEQ ID NOs: 9-12, 15, and 16.

4. The composition of claim 1 or 2, wherein the antibody molecule comprises:
 - (i) a VH comprising the amino acid sequence of SEQ ID NO: 2; and/or
 - (ii) a VL comprising any one of the amino acid sequences selected from the group consisting of SEQ ID NOs: 9-16.
5. The composition of any one of claims 1-4, wherein the antibody molecule comprises an amino acid sequence having at least 80% sequence identity to any one sequence selected from the group consisting of SEQ ID NOs: 17 and 7386-7392.
6. The composition of any one of claims 1-5, wherein the antibody molecule comprises any one amino acid sequences selected from the group consisting of SEQ ID NOs: 17 and 7386-7392.
7. The composition of any one of claims 1-6, wherein the antibody molecule is a multifunctional antibody molecule.
8. The composition of any one of claims 1-7, wherein the antibody molecule is a multispecific antibody molecule.
9. The composition of any one of claims 1-8, wherein the antibody molecule is a full antibody or an antigen-binding fragment thereof, a bivalent antibody, or a bispecific antibody.
10. The composition of any one of claims 1-9, wherein the antibody molecule is a Fab, F(ab')₂, Fv, a single chain Fv, a single domain antibody, a diabody, or a camelid antibody.
11. The composition of any one of claims 1-10, wherein the antibody molecule comprises an immunoglobulin heavy chain constant region selected from the group consisting of IgG1 heavy chain constant region or fragment thereof, IgG2 heavy chain constant region or fragment thereof, IgG3 heavy chain constant region or fragment thereof, and IgG4 heavy chain constant region or fragment thereof.
12. The composition of claim 11, wherein the immunoglobulin heavy chain constant region is altered to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function.
13. The composition of claim 11 or 12, wherein the antibody molecule comprises a first immunoglobulin heavy chain constant region and a second immunoglobulin heavy chain constant region,

wherein the first immunoglobulin heavy chain constant region comprises a first Fc region, and the second immunoglobulin heavy chain constant region comprises a second Fc region, and

wherein the dimerization of the first immunoglobulin heavy chain constant region and the second immunoglobulin heavy chain constant region is enhanced by providing an Fc interface of the first Fc region and the second Fc region with one or more of: a paired cavity-protuberance, an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer:homomultimer forms relative to a non-engineered interface.

14. The composition of claim 13, wherein the immunoglobulin heavy chain constant region comprises an amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409 of the Fc region of human IgG1.

15. The composition of claim 13 or 14, wherein the immunoglobulin chain heavy constant region comprises an amino acid substitution selected from the group consisting of: (i) T366S, L368A, or Y407V, (ii) T366W, and (iii) a combination thereof.

16. The composition of any one of claims 13-15, wherein the first Fc region comprises an amino acid substitution selected from the group consisting of T366S, L368A, Y407V, and any combination thereof, and the second Fc region comprises an amino acid substitution of T366W, or the first Fc region comprises an amino acid substitution of T366W, and the second Fc region comprises an amino acid substitution selected from the group consisting of T366S, L368A, Y407V, and any combination thereof.

17. The composition of any one of claims 1-16, wherein the antibody molecule further comprises a light chain constant region selected from the group consisting of the kappa light chain constant region or fragment thereof, and the lambda light chain constant region or fragment thereof.

18. The composition of any one of claims 7-17, wherein the antibody molecule further comprises a targeting moiety selected from the group consisting of a tumor targeting moiety, a targeting moiety that targets an autoreactive T cell, and a targeting moiety that targets an infected cell.

19. The composition of claim 18, wherein the targeting moiety that targets an autoreactive T cell binds to an antigen present on the surface of the autoreactive T cell, wherein the antigen present on the surface of the autoreactive T cell is associated with an inflammatory or autoimmune disorder.

20. The composition of claim 19, wherein the antigen present on the surface of the autoreactive T cell is selected from the group consisting of CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, and CD226.
21. The composition of claim 18, wherein the targeting moiety that targets an infected cell binds to an antigen associated with a viral infection or a bacterial infection.
22. The composition of any one of claims 7-21, wherein the antibody molecule further comprises a cytokine molecule.
23. The composition of any one of claims 7-22, wherein the antibody molecule comprises one, two, three, four or more of:
- (a) a tumor targeting moiety;
 - (b) a cytokine molecule;
 - (c) a T cell engager; or
 - (d) a stromal modifying moiety.
24. The composition of claim 22 or 23, wherein the cytokine molecule is interleukin-2 (IL-2) or a functional variant thereof, interleukin-12 (IL-12) or a functional variant thereof, interleukin-15 (IL-15) or a functional variant thereof, interleukin-18 (IL-18) or a functional variant thereof, interleukin-21 (IL-21) or a functional variant thereof, interleukin-7 (IL-7) or a functional variant thereof, or interferon gamma or a functional variant thereof.
25. A recombinant polynucleotide comprising a sequence encoding the antibody molecule of the composition of any one of claims 1-24.
26. A pharmaceutical composition comprising the composition of any one of claims 1-24, and a pharmaceutically acceptable carrier, excipient, diluent, or stabilizer for use in therapy.
27. Use of a pharmaceutical composition comprising the composition of any one of claims 1-24 or the pharmaceutical composition of claim 26 in the manufacture of a medicament for treating cancer, an autoimmune or an inflammatory disorder, or an infectious disorder in a subject in need thereof, wherein the composition or the pharmaceutical composition comprises an effective amount of the antibody molecule to treat the cancer, the autoimmune or the inflammatory disorder, or the infectious disorder in the subject.

28. The use of claim 27, wherein the cancer is a solid tumor cancer, a hematological cancer, or a metastatic cancer.
29. The use of claim 28, wherein the solid tumor cancer is one or more of pancreatic cancer, breast cancer, colorectal cancer, lung cancer, skin cancer, ovarian cancer, or liver cancer.
30. The use of claim 27, wherein the infectious disorder is associated with a viral infection or a bacterial infection.