

and soft-tissue tumors), as well as autoimmune and infectious diseases. Thus, compositions and methods for detecting NKp30, as well as methods for treating various disorders including cancer, autoimmune and/or infectious diseases, using the anti- NKp30 antibody molecules are disclosed herein.

Accordingly, in one example, the disclosure features an antibody molecule (*e.g.*, an isolated or recombinant antibody molecule), comprising one or more sequences according to the following enumerated examples. Additional features of any of the disclosed antibody molecules, multifunctional molecules, nucleic acids, vectors, host cells, or methods include one or more of the following enumerated examples.

In one aspect, the present disclosure refers to an antibody ~~molecule or an antigen-binding fragment thereof~~ that binds to NKp30 comprising: a heavy chain complementarity determining region 1 (VHCDR1), a heavy chain complementarity determining region 2 (VHCDR2), and a heavy chain complementarity determining region 3 (VHCDR3) comprising the sequences of:

- (1) SEQ ID NO: 7313, SEQ ID NO: 6008, and SEQ ID NO: 6009, respectively;
- (2) SEQ ID NO: 6000, SEQ ID NO: 6001, and SEQ ID NO: 6002, respectively;
- (3) SEQ ID NO: 6007, SEQ ID NO: 6008, and SEQ ID NO: 6009, respectively;
- (4) SEQ ID NO: 7313, SEQ ID NO: 7385, and SEQ ID NO: 7315, respectively; or
- (5) SEQ ID NO: 7313, SEQ ID NO: 6001, and SEQ ID NO: 7315, respectively; and

(b) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1), a light chain complementarity determining region 2 (VLCDR2), and a light chain complementarity determining region 3 (VLCDR3) comprising the sequences of:

- (1) SEQ ID NO: 6070, SEQ ID NO: 6071, and SEQ ID NO: 6072, respectively;
- (2) SEQ ID NO: 6063, SEQ ID NO: 6064, and SEQ ID NO: 7239, respectively;
- (3) SEQ ID NO: 6070, SEQ ID NO: 6064, and SEQ ID NO: 7321, respectively; or
- (4) SEQ ID NO: 7326, SEQ ID NO: 7327, and SEQ ID NO: 7329, respectively,

wherein the antibody molecule activates NK cells upon binding.

~~(a) a heavy chain variable region (VH) comprising~~

- ~~(i) a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313,~~

- (ii) a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and
- (iii) a VHCDR3 amino acid sequence of SEQ ID NO: 7315; and/or
- (b) a light chain variable region (VL) comprising
 - (i) a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326,
 - (ii) a VLCDR2 amino acid sequence of SEQ ID NO: 7327, and
 - (iii) a VLCDR3 amino acid sequence of SEQ ID NO: 7329.

In another aspect, the present disclosure refers to an antibody or an antigen-binding fragment thereof that binds to NKp30 comprising:

- (a) a heavy chain variable region (VH) comprising
 - (i) a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000,
 - (ii) a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and
 - (iii) a VHCDR3 amino acid sequence of SEQ ID NO: 6002; and/or
- (b) a light chain variable region (VL) comprising
 - (i) a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063, (ii) a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and
 - (iii) a VLCDR3 amino acid sequence of SEQ ID NO: 7239.

In another aspect, the present disclosure refers to an antibody or an antigen-binding fragment thereof that binds to NKp30 comprising:

- (a) a heavy chain variable region (VH) comprising
 - (i) a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007,
 - (ii) a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and
 - (iii) a VHCDR3 amino acid sequence of SEQ ID NO: 6009; and/or
- (b) a light chain variable region (VL) comprising
 - (i) a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070,
 - (ii) a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and
 - (iii) a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

In another aspect, the present disclosure refers to a multispecific molecule comprising the antibody or an antigen-binding fragment thereof as described herein.

In another aspect, the present disclosure refers to a polynucleotide comprising a sequence encoding the antibody or an antigen-binding fragment thereof as described herein or the multispecific molecule as described herein.

In another aspect, the present disclosure refers to an expression vector comprising a sequence encoding the antibody or an antigen-binding fragment thereof as described herein or the multispecific molecule as described herein.

In yet another aspect, the present disclosure refers to a recombinant polynucleotide comprising a sequence encoding the antibody molecule host cell comprising the polynucleotide as described herein ~~or the expression vector as described herein.~~

In yet another aspect, the present disclosure refers to a method of making the antibody molecule or an antigen-binding fragment thereof as described herein ~~or the multispecific molecule as described herein~~ comprising culturing ~~the~~ host cell comprising the recombinant polynucleotide as described herein under conditions suitable for gene expression and/or homo- or heterodimerization ~~as described herein under suitable conditions for gene expression and/or homo- or heterodimerization.~~

In yet another aspect, the present disclosure refers to a medicament comprising the antibody molecule or an antigen-binding fragment thereof as described herein ~~or the multispecific molecule as described herein~~, and a pharmaceutically acceptable carrier, excipient, or stabilizer.

In yet another aspect, the present disclosure refers to a use of the pharmaceutical composition comprising the antibody molecule or an antigen-binding fragment thereof as described herein ~~or the multispecific molecule as described herein~~ in the manufacture of a medicament for treating a disease or condition in a subject in need thereof,

~~optionally~~, wherein the disease or condition is cancer, an autoimmune or inflammatory disorder, or an infectious disorder.

In yet another aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody ~~molecule or an antigen-binding fragment thereof~~ as described herein ~~or the multispecific molecule as described herein~~ for use in therapy.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific examples of the disclosure described herein. Such equivalents are intended to be encompassed by the following enumerated examples.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a graph showing binding of NKp30 antibodies to NK92 cells. Data was calculated as the percent-AF747 positive population.

FIG. 2 is a graph showing activation of NK92 cells by NKp30 antibodies. Data were generated using hamster anti-NKp30 mAbs.

Enumerated Embodiments

1. An isolated antibody molecule that binds to NKp30, comprising:
 - (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 7315 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions; and/or
 - (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326 (or a sequence with

What is claimed is:

1. An antibody molecule or an antigen-binding fragment thereof that binds to NKp30 comprising:

(a) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1), a heavy chain complementarity determining region 2 (VHCDR2), and a heavy chain complementarity determining region 3 (VHCDR3) comprising the sequences of:

- (1) SEQ ID NO: 7313, SEQ ID NO: 6008, and SEQ ID NO: 6009, respectively;
- (2) SEQ ID NO: 6000, SEQ ID NO: 6001, and SEQ ID NO: 6002, respectively;
- (3) SEQ ID NO: 6007, SEQ ID NO: 6008, and SEQ ID NO: 6009, respectively;
- (4) SEQ ID NO: 7313, SEQ ID NO: 7385, and SEQ ID NO: 7315, respectively; or
- (5) SEQ ID NO: 7313, SEQ ID NO: 6001, and SEQ ID NO: 7315, respectively; and
- (i) a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313,
- (ii) a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and
- (iii) a VHCDR3 amino acid sequence of SEQ ID NO: 7315; and/or

(b) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1), a light chain complementarity determining region 2 (VLCDR2), and a light chain complementarity determining region 3 (VLCDR3) comprising the sequences of:

- (1) SEQ ID NO: 6070, SEQ ID NO: 6071, and SEQ ID NO: 6072, respectively;
- (2) SEQ ID NO: 6063, SEQ ID NO: 6064, and SEQ ID NO: 7239, respectively;
- (3) SEQ ID NO: 6070, SEQ ID NO: 6064, and SEQ ID NO: 7321, respectively; or
- (4) SEQ ID NO: 7326, SEQ ID NO: 7327, and SEQ ID NO: 7329, respectively,

wherein the antibody molecule activates NK cells upon binding (i) a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326, (ii) a VLCDR2 amino acid sequence of SEQ ID NO: 7327, and (iii) a VLCDR3 amino acid sequence of SEQ ID NO: 7329.

2. The antibody molecule or an antigen-binding fragment thereof of claim 1, wherein the antibody molecule comprises:

(a) a VH comprising a VHCDR1, a VHCDR2, and a VHCDR3 comprising the sequences of SEQ ID NO: 7313, SEQ ID NO: 6008, and SEQ ID NO: 6009, respectively; and a VL comprising a VLCDR1, a VLCDR2, and a VLCDR3 comprising the sequences of SEQ ID NO: 6070, SEQ ID NO: 6071, and SEQ ID NO: 6072, respectively;

(b) a VH comprising a VHCDR1, a VHCDR2, and a VHCDR3 comprising the sequences of SEQ ID NO: 6000, SEQ ID NO: 6001, and SEQ ID NO: 6002, respectively; and a VL comprising a VLCDR1, a VLCDR2, and a VLCDR3 comprising the sequences of SEQ ID NO: 6063, SEQ ID NO: 6064, and SEQ ID NO: 7239, respectively;

(c) a VH comprising a VHCDR1, a VHCDR2, and a VHCDR3 comprising the sequences of SEQ ID NO: 6007, SEQ ID NO: 6008, and SEQ ID NO: 6009, respectively; and a VL comprising a VLCDR1, a VLCDR2, and a VLCDR3 comprising the sequences of SEQ ID NO: 6070, SEQ ID NO: 6071, and SEQ ID NO: 6072, respectively;

(d) a VH comprising a VHCDR1, a VHCDR2, and a VHCDR3 comprising the sequences of SEQ ID NO: 7313, SEQ ID NO: 7385, and SEQ ID NO: 7315, respectively; and a VL comprising a VLCDR1, a VLCDR2, and a VLCDR3 comprising the sequences of SEQ ID NO: 6070, SEQ ID NO: 6064, and SEQ ID NO: 7321, respectively; or

(e) a VH comprising a VHCDR1, a VHCDR2, and a VHCDR3 comprising the sequences of SEQ ID NO: 7313, SEQ ID NO: 6001, and SEQ ID NO: 7315, respectively; and a VL comprising a VLCDR1, a VLCDR2, and a VLCDR3 comprising the sequences of SEQ ID NO: 7326, SEQ ID NO: 7327, and SEQ ID NO: 7329, respectively-~~(a) the VH comprises an amino acid sequence with at least 75% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 7298 and 7300-7304; and (b) the VL comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 7299 or 7305-7309.~~

3. The antibody molecule ~~or an antigen-binding fragment thereof~~ of claim 1 or 2, wherein the antibody molecule comprises:

(i) a VH comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 6121, 6122, 6129-6134, 7295, 7298, and 7300-7304; and/or

- (ii) a VL comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 6136, 6142-6147, 7294, 7296, 7299, and 7305-7309~~(a) the VH comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7302; and (b) the VL comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7305.~~
4. The antibody molecule ~~or an antigen-binding fragment thereof~~ of any one of claims 1-3, wherein the antibody molecule comprises:
- (i) a VH comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6121, 6122, 6129-6134, 7295, 7298, and 7300-7304; and/or
(ii) a VL comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6136, 6142-6147, 7294, 7296, 7299, and 7305-7309
~~(a) the VH comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7302; and (b) the VL comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NOs: 7305 or SEQ ID NO: 7309.~~
5. The antibody molecule ~~or an antigen-binding fragment thereof~~ of any one of claims 1-4, wherein the antibody molecule ~~or an antigen-binding fragment thereof~~ comprises:
- (a) a VH comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 6122 and 6129-6134; and a VL comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 6136 and 6142-6147;
(b) a VH comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 6121 and 6123-6128; and a VL comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 7294 and 6137-6141,
(c) a VH comprising an amino acid sequence with at least 85% sequence identity to the sequence of SEQ ID NO: 7295; and a VL comprising an amino acid sequence with at least 85% sequence identity to the sequence of SEQ ID NO: 7296; or
(d) a VH comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 7298 and 7300-7304; and a VL comprising an amino acid sequence with at least 85% sequence identity to a sequence

selected from the group consisting of SEQ ID NOs: 7299 and 7305-7309~~an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 7310 or SEQ ID NO: 7311.~~

6. The~~An~~ antibody molecule of any one of claims 1-5, wherein the antibody molecule comprises:~~or an antigen-binding fragment thereof that binds to NKp30 comprising:~~

(a) a VH comprising a sequence selected from the group consisting of SEQ ID NOs: 6122 and 6129-6134, and a VL comprising a sequence selected from the group consisting of SEQ ID NOs: 6136 and 6142-6147;

(b) a VH comprising a sequence selected from the group consisting of SEQ ID NOs: 6121 and 6123-6128; and a VL comprising a sequence selected from the group consisting of SEQ ID NOs: 7294 and 6137-6141

(c) a VH comprising the sequence of SEQ ID NO: 7295, and a VL comprising the sequence of SEQ ID NO: 7296; or

(d) a VH comprising a sequence selected from the group consisting of SEQ ID NOs: 7298 and 7300-7304, and a VL comprising a sequence selected from the group consisting of SEQ ID NOs: 7299 and 7305-7309(a) a heavy chain variable region (VH) comprising

(i) a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000,

(ii) a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and

(iii) a VHCDR3 amino acid sequence of SEQ ID NO: 6002; and/or

(b) a light chain variable region (VL) comprising

(i) a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063,

(ii) a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and

(iii) a VLCDR3 amino acid sequence of SEQ ID NO: 7239.

7. The antibody ~~or an antigen-binding fragment thereof of~~ any one of claims 1-6,
wherein the antibody molecule comprises:

(i) a heavy chain comprising an amino acid sequence with at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NOs: 6148, 6149, 6151, and 6152; and/or

(ii) a light chain comprising an amino acid sequence with at least 85% sequence identity to the sequence of SEQ ID NO: 6150 or SEQ ID NO: 6153 ~~(a) the VH comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 6121; and/or~~
~~(b) the VL comprises an amino acid sequence with at least 85% sequence identity to SEQ ID NO: 7294.~~

8. The antibody molecule ~~or an antigen-binding fragment thereof~~ of any one of claims 1-6 or 7, wherein the antibody molecule comprises:

(i) a heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6148, 6149, 6151, and 6152; and/or

(ii) a light chain comprising the amino acid sequence of SEQ ID NO: 6150 or SEQ ID NO: 6153 ~~(a) the VH comprises:~~

~~(i) a heavy chain framework region 1 (VHFWR1) amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6003,~~

~~(ii) a VHFWR2 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6004,~~

~~(iii) a VHFWR3 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6005,~~

~~(iv) a VHFWR4 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6006; and~~

~~(b) the VL comprises~~

~~(i) a light chain framework region 1 (VLFWR1) amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6066,~~

~~(ii) a VLFWR2 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6067,~~

~~(iii) a VLFWR2 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 7292, and~~

~~(iv) a VLFWR2 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6069.~~

9. ~~The~~ An antibody molecule of any one of claims 1-8, wherein the antibody molecule comprises ~~or an antigen-binding fragment thereof that binds to NKp30 comprising:~~

(i) a heavy chain comprising an amino acid sequence with at least 85% sequence identity to the sequence of SEQ ID NO: 6151 or the sequence of SEQ ID NO: 6152; and
(ii) a light chain comprising an amino acid sequence with at least 85% sequence identity to the sequence of SEQ ID NO: 6153(a) a heavy chain variable region (VH) comprising
(i) a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6007,
(ii) a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and
(iii) a VHCDR3 amino acid sequence of SEQ ID NO: 6009; and/or
(b) a light chain variable region (VL) comprising
(i) a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070,
(ii) a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and
(iii) a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

10. The antibody molecule or an antigen-binding fragment thereof of any one of claims 1-9, wherein the antibody molecule comprises a heavy chain comprising the sequence of SEQ ID NO: 6151 or the sequence of SEQ ID NO: 6152, and a light chain comprising to the sequence of SEQ ID NO: 6153(a) the VH comprises an amino acid sequence with at least 75% sequence identity to SEQ ID NO: 6122; and
(b) the VL comprises an amino acid sequence with at least 85% sequence identity to SEQ ID NOs: 7305 or SEQ ID NO: 6136.

11. The antibody molecule or an antigen-binding fragment thereof of any one of claims 1-9 or 10, wherein the antibody molecule is a full antibody, a Fab, a F(ab')₂, a Fv, a single chain Fv, a diabody, a bivalent antibody, or a bispecific antibody molecule(a) the VH comprises:
(i) a heavy chain framework region 1 (VHFWR1) amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6010,
(ii) a VHFWR2 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6011,
(iii) a VHFWR3 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6012,
(iv) a VHFWR4 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6013; and
(b) the VL comprises

- (i) a light chain framework region 1 (VLFWR1) amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6073,
- (ii) a VLFWR2 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6074,
- (iii) a VLFWR2 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6075, and
- (iv) a VLFWR2 amino acid sequence with at least 90% sequence identity to SEQ ID NO: 6076.
12. ~~The~~ A multispecific molecule comprising the antibody molecule or an antigen-binding fragment thereof of any one of claims 1-11, wherein the antibody molecule comprises a single chain Fv comprising an amino acid sequence with at least 85% sequence identity to the sequence of SEQ ID NO: 7310 or the sequence of SEQ ID NO: 7311.
13. The antibody multispecific molecule of any one of claims 1-12, wherein the antibody molecule comprises a single chain Fv comprising the sequence of SEQ ID NO: 7310 or the sequence of SEQ ID NO: 7311~~the multispecific molecule further comprises one, two, three, four or more of:~~(a) a tumor targeting moiety;
- (b) a cytokine molecule;
- (c) a T cell engager; and
- (d) a stromal modifying moiety.
14. The antibody multispecific molecule of any one of claims 1-12 or 13, wherein the antibody multispecific molecule further comprises:
- (i) a 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; and/or
- (ii) a kappa light chain constant region or fragment thereof or a lambda light chain constant region or fragment thereof (a) a T cell engager that binds to an antigen present on the surface of an autoreactive T cell that is associated with an inflammatory or autoimmune disorder, or
- (b) a binding moiety that binds to an antigen present on the surface of a cell infected by a virus or a bacteria.
15. The antibody multispecific molecule of any one of claims 112-14, wherein the antibody molecule further comprises one or more of: a tumor targeting moiety, a T cell engager, a binding

specificity that binds to a viral or bacterial infected cell, or a binding specificity that binds to an autoreactive T cell,

optionally, wherein the binding specificity that binds to an autoreactive T cell binds to an antigen present on the surface of an autoreactive T cell that is associated with an inflammatory or an autoimmune disorder~~multispecific molecule comprises an immunoglobulin chain constant region.~~

16. The antibody ~~multispecific molecule~~ of any one of claims 1-15, wherein the antibody molecule comprises a first immunoglobulin chain constant region and a second immunoglobulin chain constant region;

wherein the antibody molecule is connected to the first immunoglobulin chain constant region;

wherein the first immunoglobulin chain is a first Fc region, and the second immunoglobulin chain is a second Fc region;

wherein the first Fc region and the second Fc region dimerize; and

wherein dimerization of the first Fc region and the second Fc 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~~the immunoglobulin chain constant region is an IgG1 chain constant region that comprises an amino acid substitution at a position selected from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, and 409.~~

17. The antibody ~~multispecific molecule~~ of claim ~~15 or~~ 16, wherein the first Fc region comprises an amino acid substitution selected from the group consisting of Y407T, T366S, L368A, and/or Y407V and the second Fc region comprises an amino acid substitution of T366Y or T366W, or the first Fc region comprises an amino acid substitution of T366Y or T366W and the second Fc region comprises an amino acid substitution selected from the group consisting of Y407T, T366S, L368A, and/or Y407V ~~the multispecific molecule comprises an IgG1 chain constant region that comprises an amino acid substitution at a position selected from the group consisting of T366S, L368A, Y407V, T366W, and any combination thereof.~~

18. The antibody multispecific molecule of any one of claims 16 or 13-17, wherein the first Fc region and/or the second Fc 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~~the multispecific molecule comprises a linker between one or more of:~~
(a) ~~the targeting moiety and the cytokine molecule or the stromal modifying moiety;~~
(b) ~~the targeting moiety and the immune cell engager, the cytokine molecule, or the stromal modifying moiety;~~
(c) ~~the immune cell engager, the cytokine molecule, or the stromal modifying moiety and the immunoglobulin chain constant region;~~
(d) ~~the targeting moiety and the immunoglobulin chain constant region, and~~
(e) ~~the immune cell engager and the immunoglobulin chain constant region.~~
19. The antibody molecule of any one of claims 1-18, wherein the antibody molecule further comprises a cytokine molecule selected from the group consisting of interleukin-2 (IL-2) or functional variant thereof, interleukin-7 (IL-7) or functional variant thereof, interleukin-12 (IL-12) or functional variant thereof, interleukin-15 (IL-15) or functional variant thereof, interleukin-18 (IL-18) or functional variant thereof, interleukin-21 (IL-21) or functional variant thereof, and interferon gamma or functional variant thereof~~A polynucleotide comprising a sequence encoding the antibody or an antigen-binding fragment thereof of any one of claims 1-11 or the multispecific molecule of any one of claims 12-18.~~
20. The antibody molecule of any one of claims 1-19, wherein the antibody molecule further comprises one or more of: a linker between the antibody molecule and the cytokine molecule, a linker between the tumor targeting moiety and the cytokine molecule, a linker between the cytokine molecule and the T cell engager, a linker between the cytokine molecule and the first immunoglobulin chain constant region, a linker between the cytokine molecule and the second immunoglobulin chain constant region, a linker between the tumor targeting moiety and the first immunoglobulin chain constant region, a linker between the tumor targeting moiety and the second immunoglobulin chain constant region, a linker between the T cell engager and the first immunoglobulin chain constant region, or a linker between the T cell engager and the second immunoglobulin chain constant region.

optionally, wherein the linker is selected from the group consisting of a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, and a non-helical linker~~An expression vector comprising a sequence encoding the antibody or an antigen-binding fragment thereof of any one of claims 1-11 or the multispecific molecule of any one of claims 12-18.~~

21. A recombinant polynucleotide comprising a sequence encoding the antibody molecule according to any one of claims 1-20~~A host cell comprising the polynucleotide of claim 19 or the expression vector of claim 20.~~
22. A method of making the antibody molecule according to any one of claims 1-20 comprising culturing a host cell comprising the recombinant polynucleotide of claim 21 under conditions suitable for gene expression and/or homo- or heterodimerization~~A method of making the antibody or an antigen-binding fragment thereof of any one of claims 1-11 or the multispecific molecule of any one of claims 12-18 comprising culturing the host cell of claim 21 under suitable conditions for gene expression and/or homo- or heterodimerization.~~
23. A medicament comprising the antibody molecule ~~or an antigen-binding fragment thereof~~ of any one of claims 1-~~20~~11 ~~or the multispecific molecule of any one of claims 12-18~~, and a pharmaceutically acceptable carrier, excipient, or stabilizer.
24. Use of the pharmaceutical composition comprising the antibody molecule ~~or an antigen-binding fragment thereof~~ of any one of claims 1-~~20~~11 ~~or the multispecific molecule of any one of claims 12-18~~ in the manufacture of a medicament for treating a disease or condition in a subject in need thereof, optionally, wherein the disease or condition is cancer, an autoimmune or inflammatory disorder, or an infectious disorder.
25. The use of claim 24, wherein the disease or condition is cancer, and the cancer is a solid tumor cancer, a metastatic cancer~~lesion~~, or a hematological cancer,
optionally, wherein the solid tumor cancer is one or more of pancreatic cancer, breast cancer, colorectal cancer, lung cancer, skin cancer, ovarian cancer, ~~and or~~ liver cancer.
26. A pharmaceutical composition comprising the antibody molecule ~~or an antigen-binding fragment thereof~~ of any one of claims 1-~~20~~11 ~~or the multispecific molecule of any one of claims 12-18~~ for use in therapy.