

CLAIMS

1. An antibody or antigen binding fragment thereof which specifically binds human NKp30.
2. The antibody of claim 1, wherein the antibody binds human NKp30 at least at amino acids isoleucine 50 and Leucine 86 of SEQ ID NO:1.
3. The antibody of claim 2, wherein the antibody reduces the interaction of NKp30 with the B6H7 ligand.
4. The antibody of claim 3, wherein the antibody has NKp30 agonist activity.
5. The antibody or antigen binding fragment thereof of claim 1, which comprises:
 - (i) a heavy chain variable region that comprises (a) a HCDR1 (Heavy Chain Complementarity Determining Region 1) of SEQ ID NO: 19, (b) a HCDR2 of SEQ ID NO:4, (c) a HCDR3 of SEQ ID NO:29 and a light chain variable region that comprises: (d) a LCDR1 (Light Chain Complementarity Determining Region 1) of SEQ ID NO:6, (e) a LCDR2 of SEQ ID NO:7, and (f) a LCDR3 of SEQ ID NO:8;
 - (ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO:19, (b) a HCDR2 of SEQ ID NO:4, (c) a HCDR3 of SEQ ID NO:20; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:6, (e) a LCDR2 of SEQ ID NO:7, and (f) a LCDR3 of SEQ ID NO: 8; or
 - (iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO:3, (b) a HCDR2 of SEQ ID NO:4, (c) a HCDR3 of SEQ ID NO:5; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:6, (e) a LCDR2 of SEQ ID NO:7, and (f) a LCDR3 of SEQ ID NO:8.
6. The antibody or antigen-binding fragment of claim 1, that comprises:
 - (i) a heavy chain variable region (VH) comprising an amino acid sequence at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identical to SEQ ID NO:30, and a light chain variable region (VL) comprising an amino acid sequence at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identical to SEQ ID NO: 32;
 - (ii) a heavy chain variable region (VH) comprising an amino acid sequence at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identical to SEQ ID NO: 21, and a light chain variable region (VL) comprising an amino acid sequence at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identical to SEQ ID NO: 23; or

(iii) a heavy chain variable region (VH) comprising an amino acid sequence at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identical to SEQ ID NO: 11, and a light chain variable region (VL) comprising an amino acid sequence at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identical to SEQ ID NO: 13.

7. The antibody or antigen-binding fragment of claim 2, wherein one, two, three, four, five, six, seven, eight, nine, or ten amino acids within SEQ ID NO:30, 32, 21, 23, 11, or 13 have been inserted, deleted or substituted.

8. The antibody or antigen-binding fragment of claim 1, that comprises:

(i) a heavy chain variable region (VH) comprising SEQ ID NO:30, and a light chain variable region (VL) that comprises SEQ ID NO:32;

(ii) a heavy chain variable region (VH) comprising SEQ ID NO: 21, and a light chain variable region (VL) that comprises SEQ ID NO: 23; or

(iii) a heavy chain variable region (VH) comprising SEQ ID NO: 11, and a light chain variable region (VL) that comprises SEQ ID NO: 13.

9. The antibody or antigen-binding fragment of any one of claims 1 to 4, which is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human engineered antibody, a single chain antibody (scFv), a Fab fragment, a Fab' fragment, or a F(ab')₂ fragment.

10. The antibody of claim 1, wherein the antibody is a multispecific antibody.

11. A multispecific antibody comprising at least a first antigen binding domain that specifically binds human NKp30 and at least a second antigen binding domain that specifically binds a human tumor-associated antigen (TAA).

12. The multispecific antibody of claim 11, wherein the first antigen binding domain comprises:

(i) a heavy chain variable region that comprises (a) a HCDR1 (Heavy Chain Complementarity Determining Region 1) of SEQ ID NO: 19, (b) a HCDR2 of SEQ ID NO:4, (c) a HCDR3 of SEQ ID NO:29 and a light chain variable region that comprises: (d) a LCDR1 (Light Chain Complementarity Determining Region 1) of SEQ ID NO:6, (e) a LCDR2 of SEQ ID NO:7, and (f) a LCDR3 of SEQ ID NO:8;

(ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO:19, (b) a HCDR2 of SEQ ID NO:4, (c) a HCDR3 of SEQ ID NO:20; and a light chain variable region

that comprises: (d) a LCDR1 of SEQ ID NO:6, (e) a LCDR2 of SEQ ID NO:7, and (f) a LCDR3 of SEQ ID NO: 8; or

(iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO:3, (b) a HCDR2 of SEQ ID NO:4, (c) a HCDR3 of SEQ ID NO:5; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:6, (e) a LCDR2 of SEQ ID NO:7, and (f) a LCDR3 of SEQ ID NO:8,

and at least a second antigen binding domain that specifically binds a human tumor associated antigen (TAA).

13. The multispecific antibody of claim 12, wherein the multispecific antibody is a bispecific antibody.

14. The bispecific antibody of claim 13, wherein the bispecific antibody is a bispecific tetravalent antibody.

15. The bispecific tetravalent antibody of claim 14, comprising VD1-CL-(X1)_n-VD2-CH1-Fc or VD1-CH-(X1)_n-VD2-CL-Fc, wherein VD1 is a first variable domain of an antigen binding domain, VD2 is a second variable domain of an antigen binding domain, Fc is one polypeptide chain of an Fc region, CH or CL is a constant heavy or constant light domain, and (X1)_n is a linker of at least 2 amino acids.

16. The bispecific tetravalent antibody of claim 15, wherein the linker is any sequence of SEQ ID NO:43 to SEQ ID NO 85.

17. The bispecific tetravalent antibody of claim 16, wherein the linker is SEQ ID NO: 44.

18. The bispecific tetravalent antibody of claim 16, wherein the linker is SEQ ID NO: 50.

19. The bispecific tetravalent antibody of claim 16, wherein the linker is SEQ ID NO: 55.

20. The antibody or antigen-binding fragment of any one of claims 1 to 19, wherein the antibody or antigen-binding fragment thereof has antibody dependent cellular cytotoxicity (ADCC) or complement dependent cytotoxicity (CDC).

21. The antibody or antigen-binding fragment of any one of claims 1 to 19, wherein the antibody or antigen-binding fragment thereof has reduced glycosylation or no glycosylation or is hypofucosylated.

22. The antibody or antigen-binding fragment of any one of claims 1 to 19, wherein the antibody or antigen-binding fragment thereof comprises increased bisecting GlcNAc structures.

23. The antibody or antigen-binding fragment of any one of claims 1 to 19, wherein the Fc domain is of an IgG1.
24. The antibody or antigen-binding fragment of any one of claims 1 to 19, wherein the Fc domain is of an IgG4.
25. The antibody or antigen-binding fragment of claim 24, wherein the IgG4 has an S228P substitution (according to EU numbering system).
26. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof, of any one of claims 1 to 19 further comprising a pharmaceutically acceptable carrier.
27. A method of treating cancer comprising administering to a patient in need an effective amount of the antibody or antigen-binding fragment of claim 1 or claim 11.
28. The method of claim 27, wherein the cancer is gastric cancer, colon cancer, pancreatic cancer, breast cancer, head and neck cancer, kidney cancer, liver cancer, small cell lung cancer, non-small cell lung cancer, ovarian cancer, skin cancer, mesothelioma, lymphoma, leukemia, myeloma and sarcoma.
29. The method of claim 27, wherein the antibody or antigen-binding fragment is administered in combination with another therapeutic agent.
30. The method of claim 28, wherein the therapeutic agent is paclitaxel or a paclitaxel agent, docetaxel, carboplatin, topotecan, cisplatin, irinotecan, doxorubicin, lenalidomide or 5-azacytidine.
31. The method of claim 30, wherein the therapeutic agent is a paclitaxel agent, lenalidomide or 5-azacytidine.
32. An isolated nucleic acid that encodes the antibody or antigen-binding fragment of any one of claims 1 to 19.
33. A vector comprising the nucleic acid of claim 32.
34. A host cell comprising the nucleic acid of claim 32 or the vector of claim 33.
35. A process for producing an antibody or antigen-binding fragment thereof comprising cultivating the host cell of claim 35 and recovering the antibody or antigen-binding fragment from the culture.
36. A diagnostic reagent comprising the antibody or antigen-binding fragment thereof of claim 1.

37. The diagnostic reagent of claim 36, wherein the label is selected from the group consisting of a radiolabel, a fluorophore, a chromophore, an imaging agent, and a metal ion.