

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.~~

15. The An antibody or antigen binding fragment thereof of claim 1, which specifically binds human NKp30 that 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.

26. 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.

37. 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.

48. The antibody or antigen-binding fragment of claim ~~12~~, 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.

59. 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.~~

611. A multispecific antibody-comprising at least a first antigen binding domain that specifically binds human NKp30 ~~of any one of claims 1 to 5~~ 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).

713. The multispecific antibody of claim 612, wherein the multispecific antibody is a bispecific antibody.

814. The multispecificbispecific antibody of claim 713, wherein the bispecific antibody is a bispecific tetravalent antibody.

915. The multispecificbispecific tetravalent antibody of claim 148, 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.

1016. The multispecificbispecific tetravalent antibody of claim 159, wherein the linker is any sequence of SEQ ID NO:43 to SEQ ID NO 85.

1117. The multispecificbispecific tetravalent antibody of claim 1016, wherein the linker is SEQ ID NO: 44.

1218. The multispecificbispecific tetravalent antibody of claim 1016, wherein the linker is SEQ ID NO: 50.

~~1319. The multispecific ~~bispecific~~ tetravalent antibody of claim 1016, wherein the linker is SEQ ID NO: 55.~~

~~1420. The multispecific antibody or antigen-binding fragment of any one of claims 616 to 1319, wherein the antibody or antigen-binding fragment thereof has antibody dependent cellular cytotoxicity (ADCC) or complement dependent cytotoxicity (CDC).~~

~~1521. The multispecific antibody or antigen-binding fragment of any one of claims 61 to 1319, wherein the antibody or antigen-binding fragment thereof has reduced glycosylation or no glycosylation or is hypofucosylated.~~

~~1622. The multispecific antibody or antigen-binding fragment of any one of claims 61 to 1319, 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).~~

~~1726. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof, of any one of claims 1 to 519 or the multispecific antibody of any one of claims 6 to 16 further comprising a pharmaceutically acceptable carrier.~~

~~2718. Use of the antibody or antigen-binding fragment thereof, of any one of claims 1 to 5 or the multispecific antibody of any one of claims 6 to 16 in the manufacture of a medicament for 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.~~

~~1929. The use method of claim 2718, wherein the antibody or antigen-binding fragment or the multispecific antibody is to be administered in combination with another therapeutic agent.~~

~~2030. The use method of claim 1928, 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.~~