

CLAIMS

1. An antibody or antigen binding fragment thereof, which specifically binds to an epitope of ASCT2, wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region (VH) and three light chain complementarity determining regions (LCDRs) of a light chain variable region (VL), wherein the antibody or antigen-binding fragment thereof comprises:

- (a) an HCDR1 of the amino acid sequence of SEQ ID NO: 10; an HCDR2 of the amino acid sequence of SEQ ID NO: 11; an HCDR3 of the amino acid sequence of SEQ ID NO: 12; an LCDR1 of the amino acid sequence of SEQ ID NO: 13; an LCDR2 of the amino acid sequence of SEQ ID NO: 14; and an LCDR3 of the amino acid sequence of SEQ ID NO: 15; or
- (b) an HCDR1 of the amino acid sequence of SEQ ID NO: 16; an HCDR2 of the amino acid sequence of SEQ ID NO: 17; an HCDR3 of the amino acid sequence of SEQ ID NO: 18; an LCDR1 of the amino acid sequence of SEQ ID NO: 19; an LCDR2 of the amino acid sequence of SEQ ID NO: 20; and an LCDR3 of the amino acid sequence of SEQ ID NO: 21.

2. The antibody or antigen binding fragment of claim 1, wherein:

- (a) the VH comprises an amino acid sequence of SEQ ID NO: 1 and wherein the VL comprises an amino acid sequence of SEQ ID NO: 2;
- (b) the VH comprises an amino acid sequence of SEQ ID NO: 3, and wherein the VL comprises an amino acid sequence of SEQ ID NO: 4;
- (c) the VH comprises an amino acid sequence of SEQ ID NO: 5, and wherein the VL comprises an amino acid sequence of SEQ ID NO: 6; or
- (d) the VH comprises an amino acid sequence of SEQ ID NO: 7, and wherein the VL comprises an amino acid sequence of SEQ ID NO: 8.

3. The antibody or antigen binding fragment according to any one of claims 1 or 2, wherein the VH comprises the amino acid sequence of SEQ ID NO: 5 and the VL comprises the amino acid sequence of SEQ ID NO: 6.

4. The antibody or antigen binding fragment according to any one of claims 1 or 2, wherein the VH comprises the amino acid sequence SEQ ID NO: 7 and the VL comprises the amino acid sequence SEQ ID NO: 8.

5. The antibody or antigen binding fragment according to any one of claims 1 to 4, wherein the antibody or antigen-binding fragment comprises an IgG constant region comprising a cysteine (C) insertion between the serine (S) at position 239 and the valine (V) at position 240, wherein the numbering corresponds to the EU index in Kabat.

6. The antibody or antigen binding fragment according to claim 5, wherein the antibody comprises a heavy chain of an amino acid sequence of SEQ ID NO: 9.

7. The antibody or antigen binding fragment according to any one of claims 1 to 6, wherein upon the antibody binding to ASCT2 on the cell surface, the antibody internalizes into the cell.

8. The antibody or antigen binding fragment according to any one of claims 1 to 7, which comprises a light chain constant region selected from the group consisting of a human kappa constant region and a human lambda constant region.

9. The antibody or antigen binding fragment according to claim 8, wherein the antibody comprises a human kappa constant region of SEQ ID NO: 26.

10. The antibody or antigen binding fragment according to any one of claims 1 to 9, further conjugated to a cytotoxin selected from the group consisting of an antimicrobial agent, a therapeutic agent, a prodrug, a peptide, a protein, an enzyme, a lipid, a biological response modifier, a pharmaceutical agent, a lymphokine, a heterologous antibody, a fragment of a heterologous antibody, a detectable label, a polyethylene glycol (PEG), a radioisotope, and a combination of two or more of any said cytotoxins.

11. The antibody or antigen binding fragment according to claim 10, which is conjugated to a cytotoxin.

12. The antibody or antigen binding fragment according to claim 11, wherein the cytotoxin is selected from a tubulysin derivative and a pyrrolobenzodiazepine.

13. The antibody or antigen binding fragment according to claim 12, wherein the tubulysin derivative is tubulysin AZ1508.

14. The antibody or antigen binding fragment according to claim 12, wherein the pyrrolobenzodiazepine is selected from SG3315 and SG3249.

15. The antibody or antigen binding fragment according to any one of claims 1 to 14, wherein the antibody binds to human ASCT2 and cynomolgus monkey ASCT2.

16. The antibody or antigen binding fragment according to any one of claims 1 to 15, wherein the antibody does not specifically bind to human ASCT1.

17. A pharmaceutical composition comprising an antibody or antigen binding fragment of any one of claims 1 to 16 and a pharmaceutically acceptable carrier.

18. A polynucleotide or combination of polynucleotides encoding the antibody or antigen binding fragment thereof according to any one of claims 1 to 16.

19. A method of making an antibody or antigen binding fragment thereof of any one of claims 1 to 16 comprising culturing a host comprising a polynucleotide of claim 18.

20. The antibody or antigen binding fragment of any one of claims 1 to 16 or a pharmaceutical composition of claim 17 for use in the treatment of a cancer characterized by overexpression of ASCT2, wherein an effective amount of said antibody or antigen binding fragment or said pharmaceutical composition is to be administered to a subject in need thereof.