Claims

1. An antibody or a functional fragment of the antibody characterized by having the following properties of:

(a) specifically binding to B7-H3;

(b) having an antibody-dependent cell-mediated phagocytosis (ADCP) activity; and

(c) having an in vivo antitumor activity,

~~or a functional fragment of the antibody.~~

~~2. The antibody or a functional fragment of the antibody according to claim 1,~~ wherein B7-H3 is a molecule comprising an amino acid sequence represented by SEQ ID NO: 6 or 10~~.~~, and wherein

~~3. T~~the antibody or ~~a~~ the functional fragment of the antibody ~~according to claim 1 or 2, which~~ binds to IgC1 and/or IgC2 each of which is a domain of B7-H3.

~~4~~2. The antibody or a functional fragment of the antibody according to claim ~~3~~1, wherein IgC1 is a domain comprising an amino acid sequence represented by amino acid numbers 140 to 244 in SEQ ID NO: 6, and IgC2 is a domain comprising an amino acid sequence represented by amino acid numbers 358 to 456 in SEQ ID NO: 6.

~~5~~3. The antibody or a functional fragment of the antibody according to any one of claims 1 to ~~4~~2, which has a competitive inhibitory activity against M30 antibody for the binding to B7-H3.

~~6~~4. The antibody or a functional fragment of the antibody according to any one of claims 1 to ~~5~~3, which has an antibody-dependent cellular cytotoxicity (ADCC) activity and/or a complement-dependent cytotoxicity (CDC) activity.

~~7~~5. The antibody or a functional fragment of the antibody according to any one of claims 1 to ~~6~~4, wherein the tumor is cancer.

~~8~~6. The antibody or a functional fragment of the antibody according to claim ~~7~~5, wherein the cancer is lung cancer, breast cancer, prostate cancer, pancreatic cancer, colorectal cancer, a melanoma, liver cancer, ovarian cancer, bladder cancer, stomach cancer, esophageal cancer, or kidney cancer.

~~9~~7. The antibody or a functional fragment of the antibody according to any one of claims 1 to ~~8~~6, which comprises CDRH1 consisting of an amino acid sequence represented by SEQ ID NO: 92, CDRH2 consisting of an amino acid sequence represented by

SEQ ID NO: 93, and CDRH3 consisting of an amino acid sequence represented by SEQ ID NO: 94 as complementarity determining regions of the heavy chain and comprises CDRL1 consisting of an amino acid sequence represented by SEQ ID NO: 95, CDRL2 consisting of an amino acid sequence represented by SEQ ID NO: 96, and CDRL3 consisting of an amino acid sequence represented by SEQ ID NO: 97 as complementarity determining regions of the light chain.

~~10~~8. The antibody or a functional fragment of the antibody according to any one of claims 1 to ~~9~~7, which comprises a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 51 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 23 to 130 in SEQ ID NO: 53.

~~11~~9. The antibody or a functional fragment of the antibody according to any one of claims 1 to ~~10~~8, wherein a constant region is a human-derived constant region.

~~12~~10. The antibody or a functional fragment of the antibody according to claim ~~11~~9, which comprises a heavy chain consisting of an amino acid sequence represented by SEQ ID NO:

63 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 59.

~~13~~11. The antibody or a functional fragment of the antibody according to any one of claims 1 to ~~12~~10, which is humanized.

~~14~~12. The antibody or a functional fragment of the antibody according to claim ~~13~~11, which comprises: a heavy chain variable region consisting of an amino acid sequence selected from the group consisting of (a) an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 85, (b) an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 87, (c) an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 89, (d) an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 91, (e) an amino acid sequence having a homology of at least 95% or more with any of the sequences (a) to (d), and (f) an amino acid sequence wherein one or several amino acids are deleted, substituted or added in any of the sequences (a) to (d); and a light chain variable region consisting of an amino acid sequence selected from the group consisting of (g) an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 71, (h) an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 73, (i) an amino

acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 75, (j) an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 77, (k) an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 79, (l) an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 81, (m) an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 83, (n) an amino acid sequence having a homology of at least 95% or more with any of the sequences (g) to (m), and (o) an amino acid sequence wherein one or several amino acids are deleted, substituted or added in any of the sequences (g) to (m).

~~15~~13. The antibody or a functional fragment of the antibody according to claim ~~14~~12, which comprises a heavy chain variable region and a light chain variable region selected from the group consisting of: a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 85 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 71; a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 85 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 73; a heavy chain

variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 85 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 75; a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 85 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 77; a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 85 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 79; a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 85 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 81; a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 85 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 83; a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 91 and a light chain variable region consisting of

an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 71; a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 91 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 73; a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 91 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 75; and a heavy chain variable region consisting of an amino acid sequence represented by amino acid numbers 20 to 141 in SEQ ID NO: 91 and a light chain variable region consisting of an amino acid sequence represented by amino acid numbers 21 to 128 in SEQ ID NO: 77.

~~16~~14. The antibody or a functional fragment of the antibody according to claim ~~14~~ 12 or ~~15~~13, which comprises a heavy chain and a light chain selected from the group consisting of: a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 71; a heavy chain consisting of an amino acid sequence represented by amino acid numbers

20 to 471 in SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 73; a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 75; a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 77; a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 79; a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 81; a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 83; a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 91 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to

233 in SEQ ID NO: 71; a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 91 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 73; a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 91 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 75; and a heavy chain consisting of an amino acid sequence represented by amino acid numbers 20 to 471 in SEQ ID NO: 91 and a light chain consisting of an amino acid sequence represented by amino acid numbers 21 to 233 in SEQ ID NO: 77.

~~17~~15. The antibody or a functional fragment of the antibody according to any one of claims ~~14~~ 12 to ~~16~~14, which comprises a heavy chain and a light chain selected from the group consisting of: a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 71; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 73; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 85 and a light chain consisting of an amino acid sequence

represented by SEQ ID NO: 75; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 77; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 79; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 81; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 85 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 83; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 91 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 71; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 91 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 73; a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 91 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 75; and a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 91 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 77.

~~18. The functional fragment of the antibody according to any~~

~~one of claims 1 to 17, wherein the functional fragment is selected from the group consisting of Fab, F(ab)2, Fab' and Fv.~~

~~19~~16. A polynucleotide encoding the antibody or a functional fragment of the antibody according to any one of claims 1 to ~~18~~15.

~~20~~17. The polynucleotide according to claim ~~19~~16, which comprises a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 50 and a nucleotide sequence represented by nucleotide numbers 67 to 390 in SEQ ID NO: 52.

~~21~~18. The polynucleotide according to claim ~~19~~ 16 or ~~20~~17, which comprises a nucleotide sequence represented by SEQ ID NO: 62 and a nucleotide sequence represented by SEQ ID NO: 58.

~~22~~19. The polynucleotide according to claim ~~19~~ 16 or ~~20~~17, which comprises: a nucleotide sequence selected from the group consisting of (a) a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 84, (b) a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 86, (c) a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 88, (d) a nucleotide sequence

represented by nucleotide numbers 58 to 423 in SEQ ID NO: 90, and (e) a nucleotide sequence comprising a polynucleotide which hybridizes to a polynucleotide consisting of a nucleotide sequence complementary to any of the nucleotide sequences (a) to (d) under stringent conditions; and a nucleotide sequence selected from the group consisting of (f) a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 70, (g) a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 72, (h) a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 74, (i) a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 76, (j) a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 78, (k) a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 80, (l) a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 82, and (m) a nucleotide sequence comprising a polynucleotide which hybridizes to a polynucleotide consisting of a nucleotide sequence complementary to any of the nucleotide sequences (f) to (l) under stringent conditions.

~~23~~20. The polynucleotide according to claim ~~22~~19, which comprises nucleotide sequences selected from the group consisting of: a nucleotide sequence represented by nucleotide

numbers 58 to 423 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 70; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 72; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 74; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 76; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 78; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 80; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 82; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 90 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 70; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 90 and a nucleotide sequence represented by nucleotide numbers

61 to 384 in SEQ ID NO: 72; a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 90 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 74; and a nucleotide sequence represented by nucleotide numbers 58 to 423 in SEQ ID NO: 90 and a nucleotide sequence represented by nucleotide numbers 61 to 384 in SEQ ID NO: 76.

~~24~~21. The polynucleotide according to claim ~~22~~ 19 or ~~23~~20, which comprises nucleotide sequences selected from the group consisting of: a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 70; a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 72; a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 74; a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 76; a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 78; a nucleotide sequence represented by nucleotide

numbers 58 to 1413 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 80; a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 84 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 82; a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 90 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 70; a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 90 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 72; a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 90 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 74; and a nucleotide sequence represented by nucleotide numbers 58 to 1413 in SEQ ID NO: 90 and a nucleotide sequence represented by nucleotide numbers 61 to 699 in SEQ ID NO: 76.

~~25~~22. The polynucleotide according to any one of claims ~~22~~ 19 to ~~24~~21, which comprises nucleotide sequences selected from the group consisting of: a nucleotide sequence represented by SEQ ID NO: 84 and a nucleotide sequence represented by SEQ ID NO: 70; a nucleotide sequence represented by SEQ ID NO: 84 and a nucleotide sequence represented by SEQ ID NO: 72; a nucleotide sequence represented by SEQ ID NO: 84 and a nucleotide sequence

represented by SEQ ID NO: 74; a nucleotide sequence represented by SEQ ID NO: 84 and a nucleotide sequence represented by SEQ ID NO: 76; a nucleotide sequence represented by SEQ ID NO: 84 and a nucleotide sequence represented by SEQ ID NO: 78; a nucleotide sequence represented by SEQ ID NO: 84 and a nucleotide sequence represented by SEQ ID NO: 80; a nucleotide sequence represented by SEQ ID NO: 84 and a nucleotide sequence represented by SEQ ID NO: 82; a nucleotide sequence represented by SEQ ID NO: 90 and a nucleotide sequence represented by SEQ ID NO: 70; a nucleotide sequence represented by SEQ ID NO: 90 and a nucleotide sequence represented by SEQ ID NO: 72; a nucleotide sequence represented by SEQ ID NO: 90 and a nucleotide sequence represented by SEQ ID NO: 74; and a nucleotide sequence represented by SEQ ID NO: 90 and a nucleotide sequence represented by SEQ ID NO: 76.

~~26~~23. An expression vector comprising a polynucleotide according to any one of claims ~~19~~ 16 to ~~25~~22.

~~27~~24. A host cell, which is transformed with the expression vector according to claim ~~26~~23.

~~28~~25. The host cell according to claim ~~27~~24, wherein the host cell is a eukaryotic cell.

~~29~~26. A method of producing an antibody or a functional fragment of the antibody, characterized by comprising a step of culturing the host cell according to claim ~~27~~ 24 or ~~28~~ 25 and a step of collecting a desired antibody or a functional fragment of the antibody from a cultured product obtained in the culturing step.

~~30~~27. An antibody or a functional fragment of the antibody, characterized by being obtained by the production method according to claim ~~29~~26.

~~31. The functional fragment of the antibody according to claim 30, wherein the functional fragment is selected from the group consisting of Fab, F(ab)2, Fab' and Fv.~~

~~32~~28. The antibody or a functional fragment of the antibody according to any one of claims 1 to ~~18~~15~~,~~ and ~~30~~27~~, and 31~~, wherein the modification of a glycan is regulated to enhance an antibody-dependent cellular cytotoxic activity.

~~33~~29. A pharmaceutical composition characterized by comprising at least one of the antibodies or functional fragments of the antibodies according to claims 1 to ~~18~~15, ~~and 30~~ 27 and 28~~to 32~~.

~~34~~30. The pharmaceutical composition according to claim ~~33~~29, which is for treating a tumor.

~~35~~31. A pharmaceutical composition for treating a tumor characterized by comprising at least one of the antibodies or functional fragments of the antibodies according to claims 1 to ~~18~~ 15, ~~and 30~~27 ~~to 32~~and 28 and at least one therapeutic agent for cancer.

~~36~~32. The pharmaceutical composition according to claim ~~34~~ 30 or ~~35~~31, wherein the tumor is cancer.

~~37~~33. The pharmaceutical composition according to claim ~~36~~32, wherein the cancer is lung cancer, breast cancer, prostate cancer, pancreatic cancer, colorectal cancer, a melanoma, liver cancer, ovarian cancer, bladder cancer, stomach cancer, esophageal cancer, or kidney cancer.

~~38~~34. Use of an antibody or functional fragment of the antibody according to claims 1 to ~~18~~ 15, ~~and 30~~27 ~~to 32~~and 28 for the manufacture of a medicament for treating a tumor.

~~39~~35. Use of an antibody or functional fragment of the antibody according to claims 1 to ~~18~~ 15, ~~and 30~~27 ~~to 32~~and 28 for the

manufacture of a medicament for use in a method of treating a tumor wherein the method comprises administering the medicament and at least one therapeutic agent for cancer simultaneously, separately, or sequentially to an individual.

~~40~~36. The use according to claim ~~38~~ 34 or ~~39~~35, wherein the tumor is cancer.

~~41~~37. The use according to claim ~~40~~36, wherein the cancer is lung cancer, breast cancer, prostate cancer, pancreatic cancer, colorectal cancer, a melanoma, liver cancer, ovarian cancer, bladder cancer, stomach cancer, esophageal cancer, or kidney cancer.