

Claims

[Claim 1] An anti-B7-H4/anti-4-1BB bispecific antibody, comprising an anti-B7-H4 antibody or an antigen-binding fragment thereof and an anti-4-1BB antibody or an antigen-binding fragment thereof,

wherein the anti-B7-H4 antibody or an antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region comprising:

(1) a heavy chain complementarity-determining region 1 (CDR-H1) of SEQ ID NO: 2, a CDR-H2 of SEQ ID NO: 3, a CDR-H3 of SEQ ID NO: 4, a CDR-L1 of SEQ ID NO: 7, a CDR-L2 of SEQ ID NO: 9, and a CDR-L3 of SEQ ID NO: 10;

(2) a CDR-H1 of SEQ ID NO: 2, a CDR-H2 of SEQ ID NO: 3, a CDR-H3 of SEQ ID NO: 4, a CDR-L1 of SEQ ID NO: 8, a CDR-L2 of SEQ ID NO: 9, and a CDR-L3 of SEQ ID NO: 10;

wherein the anti-4-1BB antibody or an antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region comprising:

(1) a CDR-H1 of SEQ ID NO: 44, a CDR-H2 of SEQ ID NO: 46, a CDR-H3 of SEQ ID NO: 48, a CDR-L1 of SEQ ID NO: 54, a CDR-L2 of SEQ ID NO: 55, and a CDR-L3 of SEQ ID NO: 56;

(2) a CDR-H1 of SEQ ID NO: 44, a CDR-H2 of SEQ ID NO: 46, a CDR-H3 of SEQ ID NO: 49, a CDR-L1 of SEQ ID NO: 54, a CDR-L2 of SEQ ID NO: 55, and a CDR-L3 of SEQ ID NO: 56;

(3) a CDR-H1 of SEQ ID NO: 44, a CDR-H2 of SEQ ID NO: 46, a CDR-H3 of SEQ ID NO: 50, a CDR-L1 of SEQ ID NO: 54, a CDR-L2 of SEQ ID NO: 55, and a CDR-L3 of SEQ ID NO: 56; or

(4) a CDR-H1 of SEQ ID NO: 45, a CDR-H2 of SEQ ID NO: 47, a CDR-H3 of SEQ ID NO: 51, a CDR-L1 of SEQ ID NO: 54, a CDR-L2 of SEQ ID NO: 55, and a CDR-L3 of SEQ ID NO: 56.

[Claim 2] The anti-B7-H4/anti-4-1BB bispecific antibody of claim 1, wherein the anti-B7-H4 antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region of SEQ ID NO: 1 and a light chain variable region of SEQ ID NOs: 5 or 6.

[Claim 3] The anti-B7-H4/anti-4-1BB bispecific antibody of claim 1 or 2, wherein the anti-B7-H4 antibody or antigen-binding fragment thereof comprises:

a heavy chain framework 1 (H-FR1) comprising an amino acid sequence of SEQ ID NO: 12;

a heavy chain framework 2 (H-FR2) comprising an amino acid sequence of SEQ ID NO: 13;

a heavy chain framework 3 (H-FR3) comprising an amino acid sequence of SEQ ID NO: 14;

a heavy chain framework 4 (H-FR4) comprising an amino acid sequence of SEQ ID NO: 15;

a light chain framework 1 (L-FR1) comprising an amino acid sequence of SEQ ID NO: 17;

a light chain framework 2 (L-FR2) comprising an amino acid sequence of SEQ ID NO: 18;

a light chain framework 3 (L-FR3) comprising an amino acid sequence of SEQ ID NO: 19; and

a light chain framework 4 (L-FR4) comprising an amino acid sequence of SEQ ID NO: 20.

[Claim 4] The anti-B7-H4/anti-4-1BB bispecific antibody of any of claim 1 to 3, wherein each of the anti-B7-H4 antibody or the antigen-binding fragment thereof and the anti-4-1BB antibody or the antigen-binding fragment thereof is independently a chimeric antibody, a humanized antibody, or a human antibody.

[Claim 5] An isolated polynucleotide encoding the antibody or the antigen-binding fragment according to any one of claims 1 to 4.

[Claim 6] A pharmaceutical composition for treatment of cancer, comprising the anti-B7-H4/anti-4-1BB bispecific antibody or the antigen-binding fragment of any one of claims 1 to 4.

[Claim 7] The pharmaceutical composition of claim 6, wherein the cancer is selected from the group consisting of bladder cancer, liver cancer, colon cancer, rectal cancer, endometrial cancer, leukemia, lymphoma, pancreatic cancer, small cell lung cancer, non-small cell lung cancer, breast cancer, urethral cancer, head and neck cancer, gastrointestinal cancer, stomach cancer, oesophageal cancer, ovarian cancer, renal cancer, melanoma, prostate cancer and thyroid cancer.

[Claim 8] Use of the anti-B7-H4/anti-4-1BB bispecific antibody or the antigen-binding fragment of any one of claims 1 to 4 or the pharmaceutical composition of claim 6 or 7 for the manufacture of a medicament for treating cancer.

[Claim 9] An anti-B7-H4/anti-4-1BB bispecific antibody or an antigen-binding fragment thereof of any one of claims 1 to 4 for use in the treatment of cancer.

[Claim 10] An anti-B7-H4 antibody or antigen-binding fragment thereof, having specificity to a B7-H4 protein, wherein the anti-B7-H4 antibody or an antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region comprising:

(1) a CDR-H1 of SEQ ID NO: 2, a CDR-H2 of SEQ ID NO: 3, a CDR-H3 of SEQ ID NO: 4, a CDR-L1 of SEQ ID NO: 7, a CDR-L2 of SEQ ID NO: 9, and a CDR-L3 of SEQ ID NO: 10;

(2) a CDR-H1 of SEQ ID NO: 2, a CDR-H2 of SEQ ID NO: 3, a CDR-H3 of SEQ ID NO: 4, a CDR-L1 of SEQ ID NO: 8, a CDR-L2 of SEQ ID NO: 9, and a CDR-L3 of SEQ ID NO: 10.

[Claim 11] The anti-B7-H4 antibody or antigen-binding fragment of claim 10, comprising:

a heavy chain variable region of SEQ ID NO: 1 and a light chain variable region of SEQ ID NOs: 5 or 6.

[Claim 12] The anti-B7-H4 antibody of claim 10 or 11, which is a chimeric antibody, a humanized antibody, or a human antibody.

[Claim 13] An isolated polynucleotide encoding the antibody or the antigen-binding fragment according to claim 10 or 11, or the antibody of claim 12.

[Claim 14] A pharmaceutical composition for treatment of cancer, comprising the anti-B7-H4 antibody or the antigen-binding fragment of claim 10 or 11, or the anti-B7-H4 antibody of claim 12.

[Claim 15] The pharmaceutical composition of claim 14, wherein the cancer is selected from the group consisting of bladder cancer, liver cancer, colon cancer, rectal cancer, endometrial cancer, leukemia, lymphoma, pancreatic cancer, small cell lung cancer, non-small cell lung cancer, breast cancer, urethral cancer, head and neck cancer, gastrointestinal cancer, stomach cancer, oesophageal cancer, ovarian cancer, renal cancer, melanoma, prostate cancer and thyroid cancer.

[Claim 16] Use of the anti-B7-H4 antibody or the antigen-binding fragment of claim 10 or 11, or the anti-B7-H4 antibody of claim 12 for the manufacture of a medicament for treating cancer.

[Claim 17] An anti-B7-H4 antibody or an antigen-binding fragment thereof of claim 10 or 11, or the anti-B7-H4 antibody of claim 12 for use in the treatment of cancer.