

Claims

It is claimed:

1. An isolated antibody, which specifically binds to Cluster of Differentiation 70 (CD70), wherein the antibody comprises

a) a heavy chain variable (VH) region comprising (i) a VH complementarity determining region one (CDR1) comprising the sequence shown in SEQ ID NO: 97, 98, or 99; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 100 or 101; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 102; and

a light chain variable (VL) region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 217; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 218; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 219;

or

b) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 428, 429, or 430; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 431 or 432; and (iii) a VH CDR3 comprising the sequences shown in SEQ ID NO: 433; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 512; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 513; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 514;

or

c) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 332, 333, or 334; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 335 or 336; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 337; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 464; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 465; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 466;

or

d) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 344, 345, or 346; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 347 or 348; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 349; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 470; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 471; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 472;

or

e) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 350, 351, or 352; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 353 or 354; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 355; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 473; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 474; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 475;

or

f) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 362, 363, or 364; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 365 or 366; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 367; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 479; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 480; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 481;

or

g) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 368, 369, or 370; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 371 or 372; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 373; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 482; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 483; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 484;

or

h) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 380, 381, or 382; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 383 or 384; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 385; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 488; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 489; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 490;

or

i) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 386, 387, or 388; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 389 or 390; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 391; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 491; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 492; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 493;

or

j) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 392, 393, or 394; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 395 or 396; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 397; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 494; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 495; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 496;

or

k) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 398, 399, or 400; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 401 or 402; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 403; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 497; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 498; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 499;

or

I) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 410, 411, or 412; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 413 or 414; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 415; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 503; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 504; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 505.

2. An isolated antibody which specifically binds to Cluster of Differentiation 70 (CD70), wherein the antibody comprises:

a) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 18; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 17; or

b) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 321; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 320; or

c) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 289; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 288; or

d) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 293; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 292; or

e) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 295; and
a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 294; or

f) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 299; and
a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 298; or

g) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 301; and
a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 300; or

h) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 305; and
a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 304; or

i) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 307; and
a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 306; or

j) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 309; and
a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 308; or

k) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 311; and
a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 310; or

l) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 315; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 314

3. A bispecific antibody wherein the bispecific antibody is a full-length antibody, comprising a first antibody variable domain of the bispecific antibody specifically binding to a target antigen, and comprising a second antibody variable domain of the bispecific antibody capable of recruiting the activity of a human immune effector cell by specifically binding to an effector antigen located on the human immune effector cell, wherein the first antibody variable domain comprises a) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 18; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 17; or

b) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 321; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 320; or

c) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 289; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 288; or

d) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 293; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 292; or

e) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 295; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 294; or

f) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 299; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 298; or

g) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 301; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 300; or

h) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 305; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 304; or

i) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 307; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 306; or

j) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 309; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 308; or

k) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 311; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 310; or

l) a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 315; and

a VL region comprising a VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 314.

4. A bispecific antibody wherein the bispecific antibody is a full-length antibody, comprising a first antibody variable domain of the bispecific antibody specifically binding to a target antigen, and comprising a second antibody variable domain of the bispecific antibody capable of recruiting the activity of a human immune effector cell by

specifically binding to an effector antigen located on the human immune effector cell, wherein the first antibody variable domain comprises

a) a heavy chain variable (VH) region comprising (i) a VH complementarity determining region one (CDR1) comprising the sequence shown in SEQ ID NO: 97, 98, or 99; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 100 or 101; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 102; and

a light chain variable (VL) region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 217; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 218; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 219;

or

b) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 428, 429, or 430; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 431 or 432; and (iii) a VH CDR3 comprising the sequences shown in SEQ ID NO: 433; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 512; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 513; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 514;

or

c) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 332, 333, or 334; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 335 or 336; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 337; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 464; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 465; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 466;

or

d) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 344, 345, or 346; (ii) a VH CDR2 comprising the sequence shown in

SEQ ID NO: 347 or 348; and iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 349; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 470; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 471; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 472;

or

e) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 350, 351, or 352; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 353 or 354; and iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 355; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 473; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 474; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 475;

or

f) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 362, 363, or 364; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 365 or 366; and iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 367; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 479; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 480; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 481;

or

g) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 368, 369, or 370; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 371 or 372; and iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 373; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 482; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 483; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 484;

or

h) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 380, 381, or 382; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 383 or 384; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 385; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 488; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 489; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 490;

or

i) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 386, 387, or 388; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 389 or 390; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 391; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 491; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 492; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 493;

or

j) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 392, 393, or 394; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 395 or 396; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 397; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 494; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 495; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 496;

or

k) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 398, 399, or 400; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 401 or 402; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 403; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 497; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 498; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 499;

or

l) a VH region comprising (i) a VH CDR1 comprising the sequence shown in SEQ ID NO: 410, 411, or 412; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 413 or 414; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 415; and

a VL region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 503; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 504; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 505.

5. The bispecific antibody of claim 4, wherein the second antibody variable domain specifically binds to the effector antigen CD3.

6. The bispecific antibody of claim 5, wherein the second antibody variable domain comprises

- a. a heavy chain variable (VH) region comprising (i) a VH complementary determining region one (CDR1) comprising the sequence shown in SEQ ID NO: 267, 268, or 269; (ii) a VH CDR2 comprising the sequence shown in SEQ ID NO: 270 or 271; and (iii) a VH CDR3 comprising the sequence shown in SEQ ID NO: 272; and/or
- b. a light chain variable (VL) region comprising (i) a VL CDR1 comprising the sequence shown in SEQ ID NO: 273; (ii) a VL CDR2 comprising the sequence shown in SEQ ID NO: 274; and (iii) a VL CDR3 comprising the sequence shown in SEQ ID NO: 275.

7. The bispecific antibody of claim 3, wherein both the first and the second antibody variable domains of the heterodimeric protein comprise amino acid modifications at positions 223, 225, and 228 in the hinge region and at position 409 or 368 (EU numbering scheme) in the CH3 region of a human IgG2 (SEQ ID NO: 279).

8. The bispecific antibody of claim 7, further comprising an amino acid modification at one or more of positions 265, 330 and 331 of the human IgG2.

9. A nucleic acid encoding the antibody of any one of claims 1 to 8.

10. A vector comprising the nucleic acid of claim 9.

11. A host cell comprising the nucleic acid of claim 9.

12. The antibody of claim 1 or claim 2 for use as a medicament.
13. A pharmaceutical composition comprising the antibody of any one of claims 1 to 8.
14. Use of the antibody of claim 1 or claim 2 or a pharmaceutical composition comprising the antibody of claim 1 or claim 2 in the manufacture of a medicament for the treatment of a condition associated with malignant cells expressing CD70, wherein an effective amount of the medicament is to be administered to a subject in need thereof.
15. The use of claim 14, wherein the condition is a cancer.
16. The use of claim 15, wherein the cancer is an CD70 related cancer selected from the group consisting of Renal Cell Carcinoma, Glioblastoma, glioma such as low grade glioma, Non-Hodgkin's Lymphoma (NHL), Hodgkin's Disease (HD), Waldenstrom's macroglobulinemia, Acute Myeloid Leukemia, Multiple Myeloma, diffuse large-cell lymphoma, follicular lymphoma or Non-Small Cell Lung Cancer.
17. Use of the pharmaceutical composition of claim 13 in the manufacture of a medicament for inhibiting tumor growth or progression of malignant cells expressing CD70, wherein an effective amount of the medicament is to be administered to the subject.
18. Use of the pharmaceutical composition of claim 13 in the manufacture of a medicament for inhibiting metastasis of malignant cells expressing CD70, wherein an effective amount of the medicament is to be administered to the subject .
19. Use of the pharmaceutical composition of claim 13 in the manufacture of a medicament for inducing tumor regression of malignant cells expressing CD70, wherein an effective amount of the medicament is to be administered to the subject.
20. The pharmaceutical composition of claim 13 for use in therapy.
21. A method of producing an antibody, comprising culturing the host cell of claim 11 under conditions that result in production of the antibody, and isolating the antibody from the host cell or culture.