

WHAT IS CLAIMED IS:

1. An anti-TROP2/EGFR antibody or antigen-binding fragment thereof, comprising: a first antigen-binding domain that specifically binds to EGFR; and a second antigen-binding domain that specifically binds to TROP2,

wherein the first antigen-binding domain comprises a first heavy chain variable region (VH1) and a first light chain variable region (VL1); and the second antigen-binding domain comprises a second heavy chain variable region (VH2) and a second light chain variable region (VL2).

2. The anti-TROP2/EGFR antibody or antigen-binding fragment thereof of claim 1, wherein the first heavy chain variable region (VH1) comprises VH1 CDR1, VH1 CDR2 and VH1 CDR3,

wherein the VH1 CDRs 1, 2 and 3 comprise a combination selected from the group consisting of:

(1) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 7-9, respectively;

(2) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 10-12, respectively;

(3) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 16-18, respectively; and

(4) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 19-21, respectively;

and

the first light chain variable region (VL1) comprises VL1 CDR1, VL1 CDR2 and VL1 CDR3, wherein the VL1 CDRs 1, 2 and 3 comprise amino acid sequences set forth in SEQ ID NOs: 1-3, respectively.

3. The anti-TROP2/EGFR antibody or antigen-binding fragment thereof of claim 1 or 2, wherein

the second heavy chain variable region (VH2) comprises VH2 CDR1, VH2 CDR2 and VH2 CDR3,

wherein the VH2 CDRs 1, 2 and 3 comprise a combination selected from the group consisting of:

(1) the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4-6, respectively, and

(2) the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 13-15, respectively;

and

the second light chain variable region (VL2) comprises VL2 CDR1, VL2 CDR2 and VL2 CDR3, wherein the VL2 CDRs 1, 2, and 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively.

4. The anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein

(1) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 7-9, respectively, and the VL1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively, and the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4-6, respectively, and the VL2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively;

(2) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 7-9, respectively, and the VL1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively, and the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 13-15, respectively, and the VL2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively;

(3) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 16-18, respectively, and the VL1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively, and the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4-6, respectively, and the VL2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively;

(4) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 16-18, respectively, and the VL1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively, and the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 13-15, respectively, and the VL2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively;

(5) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 10-12, respectively, and the VL1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively, and the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4-6, respectively, and the VL2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively;

(6) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 10-12, respectively, and the VL1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively, and the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 13-15, respectively, and the VL2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively;

(7) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 19-21, respectively, and the VL1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively, and the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4-6, respectively, and the VL2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively; or

(8) the VH1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 19-21, respectively, and the VL1 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively, and the VH2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 13-15, respectively, and the VL2 CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3, respectively.

5. The anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein

the first heavy chain variable region comprises a sequence that is at least 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 23, the first light chain

variable region comprises a sequence that is at least 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 22, or

the first heavy chain variable region comprises a sequence that is at least 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 24, the first light chain variable region comprises a sequence that is at least 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 22; and

the second heavy chain variable region comprises a sequence that is at least 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 25, and the second light chain variable region comprises a sequence that is at least 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 22.

6. The anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the VH1 comprises an amino acid sequence that is at least 90% identical to a selected VH sequence, and the VL1 comprises an amino acid sequence that is at least 90% identical to a selected VL sequence, wherein the selected VH sequence and the selected VL sequence are one of the following:

(1) the selected VH sequence is SEQ ID NO: 23, and the selected VL sequence is SEQ ID NO: 22; and

(2) the selected VH sequence is SEQ ID NO: 24, and the selected VL sequence is SEQ ID NO: 22;

and/or

the VH2 comprises an amino acid sequence that is at least 90% identical to SEQ ID NO: 25 and the VL2 comprises an amino acid sequence that is at least 90% identical to SEQ ID NO: 22.

7. The anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the VH1 comprises VH CDR1, VH CDR2, and VH CDR3 that are identical to VH CDR1, VH CDR2, and VH CDR3 of a selected VH sequence; and the VL1 comprising VL CDR1, VL CDR2, and VL CDR3 that are identical to VL CDR1, VL CDR2, and VL CDR3 of a selected VL sequence, wherein the selected VH sequence and the selected VL sequence are one of the following:

(1) the selected VH sequence is SEQ ID NO: 23, and the selected VL sequence is SEQ ID NO: 22; and

(2) the selected VH sequence is SEQ ID NO: 24, and the selected VL sequence is SEQ ID NO: 22;

and/or

the VH2 comprises VH CDR1, VH CDR2, and VH CDR3 that are identical to VH CDR1, VH CDR2, and VH CDR3 of SEQ ID NO: 25; and the VL2 comprises VL CDR1, VL CDR2, and VL CDR3 that are identical to VL CDR1, VL CDR2, and VL CDR3 of SEQ ID NO: 22.

8. The anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the first antigen-binding domain specifically binds to human or monkey EGFR; and/or the second antigen-binding domain specifically binds to human or monkey TROP2;

the first antigen-binding domain is human or humanized; and/or the second antigen-binding domain is human or humanized;

the antibody is a multi-specific antibody;

the first antigen-binding domain is a single-chain variable fragment (scFv); and/or the second antigen-binding domain is a scFv; and/or

the first light chain variable region and the second light chain variable region are identical.

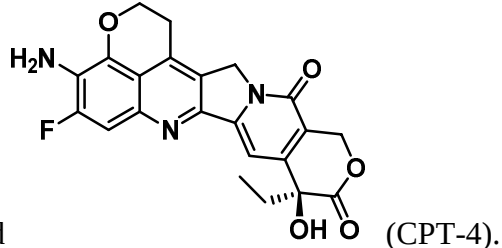
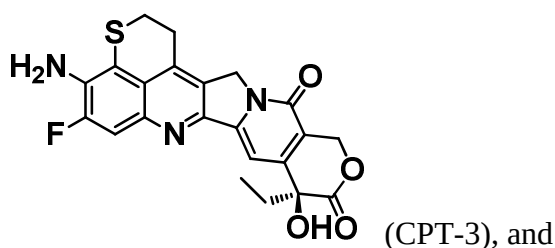
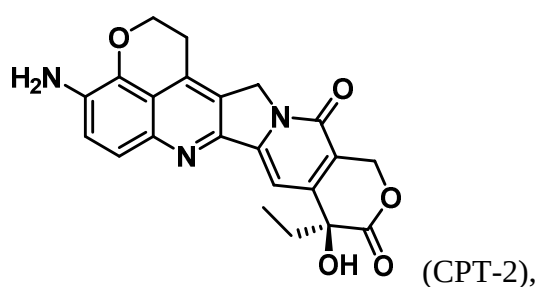
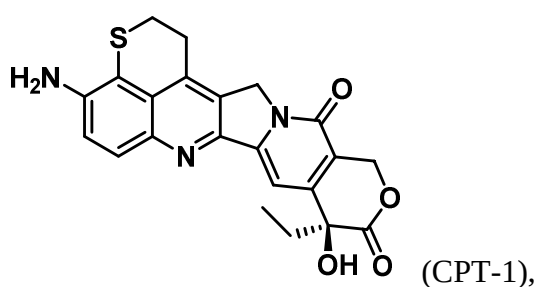
9. An anti-TROP2/EGFR antibody or antigen-binding fragment thereof that cross-competes with the anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-8.

10. A nucleic acid comprising a polynucleotide encoding the anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-9.

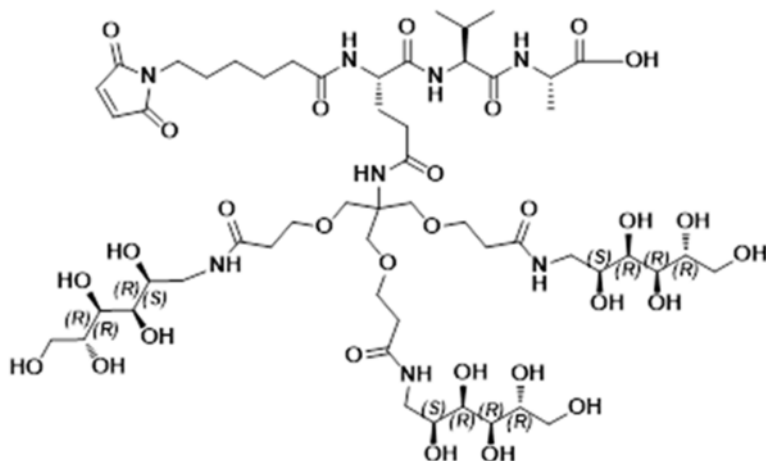
11. An anti-TROP2/EGFR antibody-drug conjugate (ADC) comprising a therapeutic agent covalently bound to the anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-9.

12. The anti-TROP2/EGFR antibody drug conjugate of claim 11, wherein the therapeutic agent is a cytotoxic or cytostatic agent.

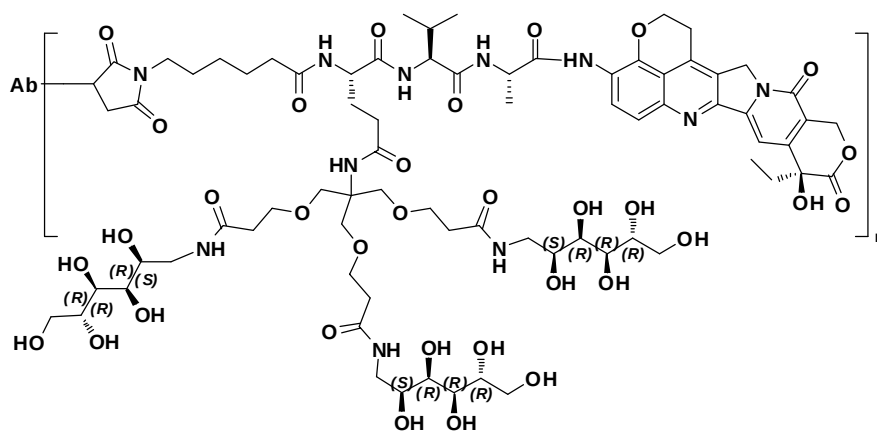
13. The antibody-drug conjugate of claim 11, wherein the therapeutic agent is selected from the group consisting of MMAE, MMAF,



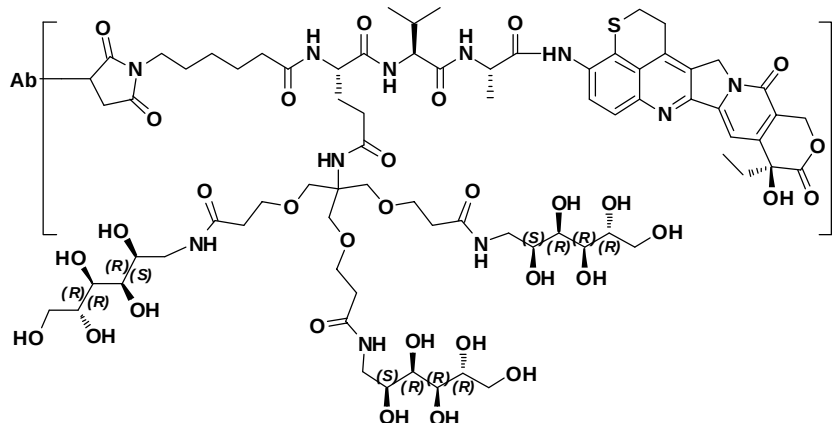
14. The antibody-drug conjugate of claim 11, wherein the therapeutic agent is linked to the antibody or antigen-binding fragment thereof via a linker, wherein the linker has a structure of:



15. The antibody-drug conjugate of any one of claims 11-14, wherein the antibody-drug conjugate has a structure of:



, or



wherein n = 1-8; wherein “Ab” represents the antibody or antigen-binding fragment thereof.

16. Use of the anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-9, or the anti-TROP2/EGFR antibody-drug conjugate of any one of claims 11-15 in the manufacture of a medicament for treating a cancer, wherein the cells of the cancer express EGFR and/or TROP2.

17. The use of claim 16, wherein the cancer is a solid tumor, lung cancer, gastric cancer, skin cancer, colorectal cancer, breast cancer, head and neck cancer, ovarian cancer, prostate cancer, thyroid cancer, pancreatic cancer, CNS cancer, liver cancer, nasopharynx cancer, brain cancer, colon cancer, bladder cancer, oral squamous cell carcinoma, cervical cancer, or oesophageal cancer.

18. A method of decreasing the rate of tumor growth in vitro, the method comprising contacting a tumor cell with an effective amount of a composition comprising the anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-9, or the anti-TROP2/EGFR antibody-drug conjugate of any one of claims 11-15.

19. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and

(a) the anti-TROP2/EGFR antibody or antigen-binding fragment thereof of any one of claims 1-9, and/or

(b) the anti-TROP2/EGFR antibody-drug conjugate of any one of claims 11-15.

20. The anti-TROP2/EGFR ADC of any one of claims 11-15, wherein the drug-to-antibody ratio (DAR) is about 4 or 8.