description referring to "about X" includes description of "X." Numeric ranges are inclusive of the numbers defining the range.

It is understood that wherever embodiments are described herein with the language "comprising," otherwise analogous embodiments described in terms of "consisting of" and/or "consisting essentially of" are also provided.

Where aspects or embodiments of the invention are described in terms of a Markush group or other grouping of alternatives, the present invention encompasses not only the entire group listed as a whole, but each member of the group individually and all possible subgroups of the main group, but also the main group absent one or more of the group members. The present invention also envisages the explicit exclusion of one or more of any of the group members in the claimed invention.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. In case of conflict, the present specification, including definitions, will control. Throughout this specification and claims, the word "comprise," or variations such as "comprises" or "comprising" will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers. Unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular.

Exemplary methods and materials are described herein, although methods and materials similar or equivalent to those described herein can also be used in the practice or testing of the present invention. The materials, methods, and examples are illustrative only and not intended to be limiting.

Trop-2 Antibodies and Methods of Making Thereof

The present invention provides an antibody that binds to Trop-2. In one aspect, the invention provides an isolated antibody, or an antigen binding fragment thereof, which specifically binds to domain 3 (e.g., amino acid residues 153~~2~~-206) and domain 4 (e.g., amino acid residues 209-273~~4~~) of human Trop-2 (e.g., SEQ ID NO:27) with a monovalent antibody binding affinity (K_D) of 6.5 nM or less as measured by surface plasmon resonance. In another aspect, the invention provides an isolated antibody, or an antigen binding fragment thereof, which specifically binds to domain 1 (e.g., amino

Claims

1. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to trophoblast cell-surface antigen-2 (Trop-2), wherein the antibody comprises

(a) a heavy chain variable (VH) region complementary determining regions comprising (i) a VH complementary determining region one (CDR1) comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTX$_1$GX$_2$TDYNSALMX$_3$, wherein X$_1$ is G or S; X$_2$ is S or V; X$_3$ is S or G (SEQ ID NO: 49), or WTX$_1$GX$_2$, wherein X$_1$ is G or S, X$_2$ is S or V (SEQ ID NO: 50); and iii) a VH CDR3 comprising the sequence DYDRYTX$_1$DY, wherein X$_1$ is E or M (SEQ ID NO: 82); and/or

(b) a light chain variable region (VL) region complementary determining regions comprising (i) a VL CDR1 comprising the sequence RASKSVSTSX$_1$YSYMH, wherein X$_1$ is G, L, or N (SEQ ID NO: 63); (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56).

2. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises:

a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 5 or 85; and/or

a VL region comprising VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO:3 or 6.

3. The antibody or the antigen binding fragment of claim 2, wherein the VH region comprises (i) a VH CDR1 comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTSGVTDYNSALMG (SEQ ID NO: 38) or WTSGV (SEQ

ID NO: 39); and (iii) a VH CDR3 comprising the sequence DGDYDRYTMDY (SEQ ID NO: 35), DYDRYTMDY (SEQ ID NO: 99), or DYDRYTEDY (SEQ ID NO: 100).

4. The antibody or antigen binding fragment of claim 3, wherein the VL region comprises (i) a VL CDR1 comprising the sequence RASKSVSTSGYSYMH (SEQ ID NO: 54) or RASKSVSTSLYSYMH (SEQ ID NO: 57) ; (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56).

5. The antibody or the antigen binding fragment of claim 4, wherein the VH region comprises the sequence shown in SEQ ID NO: 5, 85 or a variant with one or several conservative amino acid substitutions in residues that are not within a CDR and/or the VL region comprises the amino acid sequence shown in SEQ ID NO: 3, 6 or a variant thereof with one or several amino acid substitutions in amino acids that are not within a CDR.

6. The antibody or the antigen binding fragment of claim 5, wherein the antibody comprises a light chain comprising the sequence shown in SEQ ID NO: 66 and a heavy chain comprising the sequence shown in SEQ ID NO: 65 or 102 .

7. The antibody or the antigen binding fragment of claim 3, wherein the antibody comprises a VH region produced by the expression vector with ATCC Accession No. PTA-12872.

8. The antibody or the antigen binding fragment of claim 4, wherein the antibody comprises a VL region produced by the expression vector with ATCC Accession No. PTA-12871.

9. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to domain 3 and domain 4 of human Trop-2 (SEQ ID NO:27) with a monovalent antibody binding affinity (K_D) of about 6.5 nM or less as measured by surface plasmon resonance.

10. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises

(a) a heavy chain variable (VH) region complementary determining regions comprising (i) a VH complementary determining region one (CDR1) comprising the sequence SYWIN (SEQ ID NO: 40), GYTFTSY (SEQ ID NO: 41), or GYTFTSYWIN (SEQ ID NO: 42); (ii) a VH CDR2 comprising the sequence $NIX_1PSDSYSNYNX_2KFKD$ wherein X_1 is Y or F; X_2 is Q or K, or X_1PSDSY wherein X_1 is Y or F (SEQ ID NO: 52); and iii) a VH CDR3 comprising the sequence GSX_1FDY wherein X_1 is S or G (SEQ ID NO: 53); and/or

(b) a light chain variable region (VL) region complementary determining regions comprising (i) a VL CDR1 comprising the sequence RASQTIGTSIH (SEQ ID NO: 59); (ii) a VL CDR2 comprising the sequence YASESIS (SEQ ID NO: 60); and (iii) a VL CDR3 comprising the sequence X_1QSX_2SWPFT wherein X_1 is Q or S; X_2 is N or F (SEQ ID NO:64).

11. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises:

a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 13; and/or

a VL region comprising VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 12.

12. The antibody or the antigen binding fragment of claim 11, wherein the VH region comprises (i) a VH CDR1 comprising the sequence SYWIN (SEQ ID NO: 40), GYTFTSY (SEQ ID NO: 41), or GYTFTSYWIN (SEQ ID NO: 42); (ii) a VH CDR2 comprising the sequence NIFPSDSYSNYNKKFKD (SEQ ID NO: 46) or FPSDSY (SEQ ID NO: 47); and (iii) a VH CDR3 comprising the sequence GSGFDY (SEQ ID NO: 48).

13. The antibody or antigen binding fragment of claim 12, wherein the VL region comprises (i) a VL CDR1 comprising the sequence RASQTIGTSIH (SEQ ID NO:

59); (ii) a VL CDR2 comprising the sequence YASESIS (SEQ ID NO: 60); and (iii) a VL CDR3 comprising the sequence SQSFSWPFT (SEQ ID NO: 62).

14. The antibody or the antigen binding fragment of claim 13, wherein the VH region comprises the sequence shown in SEQ ID NO: 13 or a variant with one or several conservative amino acid substitutions in residues that are not within a CDR and/or the VL region comprises the amino acid sequence shown in SEQ ID NO: 12 or a variant thereof with one or several amino acid substitutions in amino acids that are not within a CDR.

15. The antibody or the antigen binding fragment of claim 14, wherein the antibody comprises a light chain comprising the sequence shown in SEQ ID NO: 68 and a heavy chain comprising the sequence shown in SEQ ID NO: 67.

16. An isolated antibody which specifically binds to Trop-2 and competes with the antibody of claim 2 or 4.

17. The antibody of claim 16, wherein the antibody has a monovalent antibody binding affinity (K_D) of about 6.5 nM or less as measured by surface plasmon resonance.

18. The antibody of any one of claims 1-15, wherein the antibody comprises an acyl donor glutamine-containing tag engineered at a specific site.

19. The antibody of claim 18, wherein the tag comprises an amino acid sequence GGLLQGG (SEQ ID NO: 78), LLQGA (SEQ ID NO:79), or LLQ.

20. The antibody of claim 19, wherein the antibody further comprises an amino acid modification at position 222, 340, or 370.

21. The antibody of claim 20, wherein the amino acid modification is a substitution from lysine to arginine.

22. A conjugate of the antibody or the antigen binding fragment of any one of claims 1-15 and 18-21, wherein the antibody or the antigen binding fragment is

conjugated to an agent, wherein the agent is selected from the group consisting of a cytotoxic agent, an immunomodulating agent, an imaging agent, a therapeutic protein, a biopolymer, and an oligonucleotide.

23. The conjugate of claim 22, wherein the agent is a cytotoxic agent.

24. The conjugate of claim 23, wherein the cytotoxic agent is MMAD (Monomethyl Auristatin D) or 0101 (2-methylalanyl-*N*-[(3*R*,4*S*,5*S*)-3-methoxy-1-{(2*S*)-2-[(1*R*,2*R*)-1-methoxy-2-methyl-3-oxo-3-{[(1*S*)-2-phenyl-1-(1,3-thiazol-2-yl)ethyl]amino}propyl]pyrrolidin-1-yl}-5-methyl-1-oxoheptan-4-yl]-*N*-methyl-L-valinamide).

25. The conjugate of claim 24, wherein the conjugate comprises the formula: antibody-(acyl donor glutamine-containing tag)-(linker)-(cytotoxic agent).

26. The conjugate of claim 25, wherein the acyl donor glutamine-containing tag comprises an amino acid sequence GGLLQGG (SEQ ID NO: 78), LLQGA (SEQ NO: 79), LLQ, or $LLQX_1X_2X_3X_4X_5$, wherein X_1 is G or P, wherein X_2 is A, G, P, or absent, wherein X_3 is A, G, K, P, or absent, wherein X_4 is G, K, or absent, and wherein X_5 is K or absent (SEQ ID NO: 88), and wherein the linker comprises acetyl-lysine-valine-citrulline-*p*-aminobenzyloxycarbonyl or amino-PEG6-propionyl.

27. The conjugate of claim 26, wherein the conjugate is selected from the group consisting of 1) antibody-LLQGA (SEQ ID NO: 79)- (acetyl-lysine-valine-citrulline-*p*-aminobenzyloxycarbonyl (AcLys-VC-PABC))-0101; 2) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-MMAD; 3) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; 4) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD; 5) antibody –GGLLQGG (SEQ ID NO: 78)- (AcLys-VC-PABC)-0101; and 6) antibody–GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-MMAD.

28. The conjugate of claim 27, wherein the conjugate 1) antibody –GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-0101; 2) antibody–GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-MMAD; 3) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; 4) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD;

5) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101; or 6) antibody-LLQGA (SEQ ID NO: 79)- AcLys-VC-PABC-MMAD comprises an amino acid substitution from lysine to arginine at position 222.

29. The conjugate of claim 27, wherein the conjugate 1) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101; 2) antibody-LLQGA (SEQ ID NO: 79)-AcLys-VC-PABC-MMAD; 3) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; or 4) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD, wherein the amino acid lysine at the C-terminus of heavy chain of the antibody is deleted.

30. The conjugate of claim 24, wherein the conjugate comprises amino acid substitutions at position N297Q and K222R, a linker comprising amino-PEG6-propionyl, and a cytotoxic agent comprising MMAD.

31. A pharmaceutical composition comprising a therapeutically effective amount of the antibody of any one of claims 1-15 or the conjugate of any one of claims 22-30 and a pharmaceutically acceptable carrier.

32. An isolated polynucleotide comprising a nucleotide sequence encoding the antibody of any one of claims 1-15.

33. A vector comprising the polynucleotide of claim 32.

34. An isolated host cell that recombinantly produces the antibody of any one of claims 1-15.

35. A method of producing an antibody, comprising culturing the host cell of claim 34 under conditions that result in production of the antibody, and isolating the antibody from the host cell or culture.

36. The pharmaceutical composition of claim 31 for use in the treatment of a condition associated with Trop-2 expression in a subject in need thereof.

37. The composition of claim 36, wherein the condition is a cancer.

38. The composition of claim 37, wherein the cancer is selected from the group consisting of bladder, breast, cervical, choriocarcinoma, colon, esophageal, gastric, glioblastoma, head and neck, kidney, lung, oral, ovarian, pancreatic, prostate, and skin cancer.

39. The pharmaceutical composition of claim 31 for use in the treatment of inhibiting tumor growth or progression in a subject who has a Trop-2 expressing tumor.

40. The pharmaceutical composition of claim 31 for use in the treatment of inhibiting metastasis of Trop-2 expressing cancer cells in a subject need thereof.

41. The pharmaceutical composition of claim 31 for use in the treatment of inducing regression in a subject who has a Trop-2 expressing tumor.

42. Use of the pharmaceutical composition of claim 31 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a condition associated with Trop-2 expression in a subject in need thereof.

43. The use of claim 42, wherein the condition is a cancer.

44. The use of claim 43, wherein the cancer is selected from the group consisting of bladder, breast, cervical, choriocarcinoma, colon, esophageal, gastric, glioblastoma, head and neck, kidney, lung, oral, ovarian, pancreatic, prostate, and skin cancer.

45. Use of the pharmaceutical composition of claim 31 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inhibiting tumor growth or progression in a subject who has a Trop-2 expressing tumor.

46. Use of the pharmaceutical composition of claim 31 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inhibiting metastasis of Trop-2 expressing cancer cells in a subject need thereof.

47. Use of the pharmaceutical composition of claim 31 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inducing regression in a subject who has a Trop-2 expressing tumor.

Claims

1. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to trophoblast cell-surface antigen-2 (Trop-2), wherein the antibody comprises

(a) a heavy chain variable (VH) region comprising (i) a VH complementary determining region one (CDR1) comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTX$_1$GX$_2$TDYNSALMX$_3$, wherein X$_1$ is G or S; X$_2$ is S or V; X$_3$ is S or G (SEQ ID NO: 49), or WTX$_1$GX$_2$, wherein X$_1$ is G or S, X$_2$ is S or V (SEQ ID NO: 50); and iii) a VH CDR3 comprising the sequence DYDRYTX$_1$DY, wherein X$_1$ is E or M (SEQ ID NO: 82); and

(b) a light chain variable region (VL) comprising (i) a VL CDR1 comprising the sequence RASKSVSTSX$_1$YSYMH, wherein X$_1$ is G, L, or N (SEQ ID NO: 63); (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56).

2. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises:

a VH region comprising VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 4 or 5; and

a VL region comprising VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 3, 6, or 7.

3. The antibody or the antigen binding fragment of claim 2, wherein the VH region comprises (i) a VH CDR1 comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTSGVTDYNSALMG (SEQ ID NO: 38) or WTSGV (SEQ ID NO: 39); and (iii) a VH CDR3 comprising the sequence DGDYDRYTMDY (SEQ ID

NO: 35), and wherein the VL region comprises (i) a VL CDR1 comprising the sequence RASKSVSTSGYSYMH (SEQ ID NO: 54); (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56).

4. The antibody or the antigen binding fragment of claim 3, wherein the VH region comprises the sequence shown in SEQ ID NO: 5 or a variant with one or several conservative amino acid substitutions in residues that are not within a CDR and the VL region comprises the amino acid sequence shown in SEQ ID NO: 3 or a variant thereof with one or several amino acid substitutions in amino acids that are not within a CDR.

5. The antibody or the antigen binding fragment of claim 4, wherein the antibody comprises a light chain comprising the sequence shown in SEQ ID NO: 66 and a heavy chain comprising the sequence shown in SEQ ID NO: 65.

6. The antibody or the antigen binding fragment of claim 3, wherein the antibody comprises a VH region produced by the expression vector with ATCC Accession No. PTA-12872.

7. The antibody or the antigen binding fragment of claim 3, wherein the antibody comprises a VL region produced by the expression vector with ATCC Accession No. PTA-12871.

8. The antibody, or the antigen binding fragment thereof of claim 1, which specifically binds to domain 3 and domain 4 of human Trop-2 (SEQ ID NO:27) with a monovalent antibody binding affinity (KD) of about 0.25 nM or less as measured by surface plasmon resonance.

9. The antibody of any one of claims 1-8, wherein the antibody comprises an acyl donor glutamine-containing tag engineered at a specific site.

10. The antibody of claim 9, wherein the tag comprises an amino acid sequence GGLLQGG (SEQ ID NO: 78), LLQGA (SEQ ID NO:79), or LLQ.

11. The antibody of claim 10, wherein the antibody further comprises an amino acid modification at position K222, K340, or K370.

12. The antibody of claim 11, wherein the amino acid modification is a substitution from lysine to arginine.

13. A conjugate of the antibody or the antigen binding fragment of any one of claims 1-12, wherein the antibody or the antigen binding fragment is conjugated to an agent, wherein the agent is selected from the group consisting of a cytotoxic agent, an immunomodulating agent, an imaging agent, a therapeutic protein, a biopolymer, and an oligonucleotide.

14. The conjugate of claim 13, wherein the agent is a cytotoxic agent.

15. The conjugate of claim 14, wherein the cytotoxic agent is MMAD (Monomethyl Auristatin D) or 0101 (2-methylalanyl-*N*-[(3*R*,4*S*,5*S*)-3-methoxy-1-{(2*S*)-2-[(1*R*,2*R*)-1-methoxy-2-methyl-3-oxo-3-{[(1*S*)-2-phenyl-1-(1,3-thiazol-2-yl)ethyl]amino}propyl]pyrrolidin-1-yl}-5-methyl-1-oxoheptan-4-yl]-*N*-methyl-L-valinamide).

16. The conjugate of claim 15, wherein the conjugate comprises the formula: antibody-(acyl donor glutamine-containing tag)-(linker)-(cytotoxic agent).

17. The conjugate of claim 16, wherein the acyl donor glutamine-containing tag comprises an amino acid sequence GGLLQGG (SEQ ID NO: 78), LLQGA (SEQ NO: 79), LLQ, or $LLQX_1X_2X_3X_4X_5$, wherein X_1 is G or P, wherein X_2 is A, G, P, or absent, wherein X_3 is A, G, K, P, or absent, wherein X_4 is G, K, or absent, and wherein X_5 is K or absent (SEQ ID NO: 88), and wherein the linker comprises acetyl-lysine-valine-citrulline-*p*-aminobenzyloxycarbonyl or amino-PEG6-propionyl.

18. The conjugate of claim 17, wherein the conjugate is selected from the group consisting of 1) antibody-LLQGA (SEQ ID NO: 79)- (acetyl-lysine-valine-citrulline-*p*-aminobenzyloxycarbonyl (AcLys-VC-PABC))-0101; 2) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-MMAD; 3) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-

VC-PABC)-0101; 4) antibody-LLQX$_1$X$_2$X$_3$X$_4$X$_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD; 5) antibody –GGLLQGG (SEQ ID NO: 78)- (AcLys-VC-PABC)-0101; and 6) antibody–GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-MMAD.

19. The conjugate of claim 18, wherein the conjugate 1) antibody –GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-0101; 2) antibody–GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-MMAD; 3) antibody-LLQX$_1$X$_2$X$_3$X$_4$X$_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; 4) antibody-LLQX$_1$X$_2$X$_3$X$_4$X$_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD; 5) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101; or 6) antibody-LLQGA (SEQ ID NO: 79)- AcLys-VC-PABC-MMAD comprises an amino acid substitution from lysine to arginine at position 222 of the antibody.

20. The conjugate of claim 18, wherein the conjugate is 1) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101; 2) antibody-LLQGA (SEQ ID NO: 79)-AcLys-VC-PABC-MMAD; 3) antibody-LLQX$_1$X$_2$X$_3$X$_4$X$_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; or 4) antibody-LLQX$_1$X$_2$X$_3$X$_4$X$_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD, wherein the amino acid lysine at the C-terminus of heavy chain of the antibody is deleted.

21. The conjugate of claim 15, wherein the conjugate comprises amino acid substitutions at position N297Q and K222R of the antibody, a linker comprising amino-PEG6-propionyl, and a cytotoxic agent comprising MMAD.

22. A pharmaceutical composition comprising a therapeutically effective amount of the antibody of any one of claims 1-12 or the conjugate of any one of claims 22-30 and a pharmaceutically acceptable carrier.

23. An isolated polynucleotide comprising a nucleotide sequence encoding the antibody of any one of claims 1-8.

24. A vector comprising the polynucleotide of claim 23.

25. An isolated host cell that recombinantly produces the antibody of any one of claims 1-8.

26. A method of producing an antibody, comprising culturing the host cell of claim 25 under conditions that result in production of the antibody, and isolating the antibody from the host cell or culture.

27. The pharmaceutical composition of claim 22 for use in the treatment of a condition associated with Trop-2 expression in a subject in need thereof.

28. The composition of claim 27, wherein the condition is a cancer.

29. The composition of claim 28, wherein the cancer is selected from the group consisting of bladder, breast, cervical, choriocarcinoma, colon, esophageal, gastric, glioblastoma, head and neck, kidney, lung, oral, ovarian, pancreatic, prostate, and skin cancer.

30. The pharmaceutical composition of claim 22 for use in the treatment of inhibiting tumor growth or progression in a subject who has a Trop-2 expressing tumor.

31. The pharmaceutical composition of claim 22 for use in the treatment of inhibiting metastasis of Trop-2 expressing cancer cells in a subject need thereof.

32. The pharmaceutical composition of claim 22 for use in the treatment of inducing regression in a subject who has a Trop-2 expressing tumor.

33. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a condition associated with Trop-2 expression in a subject in need thereof, wherein the condition is selected from the group consisting of bladder, breast, cervical, choriocarcinoma, colon, esophageal, gastric, glioblastoma, head and neck, kidney, lung, oral, ovarian, pancreatic, prostate, and skin cancer.

34. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inhibiting tumor growth or progression in a subject who has a Trop-2 expressing tumor.

35. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inhibiting metastasis of Trop-2 expressing cancer cells in a subject need thereof.

36. Use of the pharmaceutical composition of claim 22 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inducing regression in a subject who has a Trop-2 expressing tumor.

37. The conjugate of claim 15, wherein the conjugate is antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101, wherein the conjugate comprises an amino acid substitution from lysine to arginine at position 222 of the antibody, and wherein the amino acid lysine at the C-terminus of heavy chain of the antibody is deleted.

38. An antibody-drug conjugate which specifically binds to trophoblast cell-surface antigen-2 (Trop-2), wherein the conjugate is antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101, wherein the antibody comprises a heavy chain variable (VH) region comprising (i) a VH complementary determining region (CDR)1 comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTSGVTDYNSALMG (SEQ ID NO: 38) or WTSGV (SEQ ID NO: 39); and (iii) a VH CDR3 comprising the sequence DGDYDRYTMDY (SEQ ID NO: 35), and a VL region comprising (i) a light chain variable (VL) CDR1 comprising the sequence RASKSVSTSGYSYMH (SEQ ID NO: 54); (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56), wherein the conjugate comprises an amino acid substitution from lysine to arginine at position 222 of the antibody, and wherein the amino acid lysine at the C-terminus of heavy chain of the antibody is deleted.