Claims

1. An antibody drug conjugate comprising an antibody or antigen binding fragment thereof conjugated to monomethyl auristatin E (MMAE), wherein the antibody or fragment comprises a heavy chain variable region comprising complementarity determining regions (CDRs) having the amino acid sequences of the CDRs in the heavy chain variable region sequence set forth in SEQ ID NO: 7 and a light chain variable region comprising complementaity determining regions (CDRs) having the amino acid sequences of the CDRs in the light chain variable region sequence set forth in SEQ ID NO: 8.

2. The antibody drug conjugate of claim 1, wherein the antibody comprises the heavy chain consisting of the amino acid sequence ranging from 1st Q to the 115th S of SEQ ID NO: 7 and the light chain consisting of the amino acid sequence ranging from 1st D to the 106th R of SEQ ID NO: 8.

3. The antibody drug conjugate of claims 1 or 2, wherein the antibody comprises the heavy chain consisting of the amino acid sequence ranging from 1st Q to the 441th K of SEQ ID NO: 7 and the light chain consisting of the amino acid sequence ranging from 1st D to the 212th C of SEQ ID NO: 8.

4. An antibody drug conjugate comprising an antibody or antigen-binding fragment to conjugated to monomethyl auristatin E (MMAE), wherein the antibody or fragment comprises a heavy chain variable region comprising the amino acid sequence of the heavy chain variable region of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under American Type Culture Collection (ATCC) Accession No. PTA-120464, and a light chain variable region comprising the amino acid sequence of the light chain variable region of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC Accession No. PTA-120464.

5. The antibody drug conjugate of claim 4, wherein the antibody comprises a heavy chain consisting of the amino acid sequence of the heavy chain of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC. Accession No. PTA-120464, and a

light chain consisting of the amino acid sequence of the light chain of an antibody produced by a Chinese Hamster Ovary (CHO) deposited under ATCC. Accession No. PTA-120464.

6. The antibody drug conjugate of claims 1 to 5, wherein the antidoby or fragment is the fragment, which is an Fab, $F(ab')_2$, Fv or scFv fragment.

7. The antibody drug conjugate of claims 1 to 6, wherein the antibody is a fully human antibody.

8. The antibody drug conjugate of claims 1 to 7, wherein the antibody or fragment is recombinantly produced.

9. A pharmaceutical composition that comprises the antibody drug conjugate of claims 1 to 8 in a human unit dose form.

10. The pharmaceutical composition of claim 9, wherein the composition is for cancer treatment.

11. The pharmaceutical composition of claim 10, wherein the cancer is -Non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), or Multiple Myeloma (MM).

12. The pharmaceutical composition of claim 9, wherein the composition is administered in combination with radiation or a chemotherapeutic agent.

13. The pharmaceutical composition of claim 9 comprising the antibody drug conjugate of claim 1 and a chemotherapeutic agent in a human unit dose form.

14. A method of treating cancer in a subject, comprising administering to said subject an antibody drug conjugate of claims 1 to 8.

15. A method for treating cancer in a subject, comprising administering to said subject an effective amount of a combination of an antibody drug conjugate of claims 1 to 8 and radiation.

16. A method for treating cancer in a subject, comprising administering to said subject an effective amount of a combination of an antibody drug conjugate of claim 1 to 8 and a chemotherapeutic agent.

17. An antibody drug conjugate comprising an antibody or antigen binding fragment thereof conjugated to monomethyl auristatin E (MMAE), wherein the antibody or fragment is produced by a method comprising culturing a host cell to allow expression of antibody or antigen binding fragment, wherein the host cell is selected from the group consisting of the following (a) to (d):

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding a heavy chain variable region consisting of the amino acid sequence ranging from the 1st Q to the 115th S of SEQ ID NO: 7 and a polynucleotide comprising a base sequence encoding a light chain variable region consisting of the amino acid sequence ranging from the 1st D to the 106th R SEQ ID NO: 8;

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding a heavy chain variable region consisting of the amino acid sequence ranging from the 1st Q to the 115th S of SEQ ID NO: 7 and an expression vector comprising a polynucleotide comprising a base sequence encoding a light chain variable region consisting of the amino acid sequence ranging from the 1st D to the 106th R SEQ ID NO: 8

(c) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding a heavy chain variable region consisting of the amino acid sequence ranging from the 1st Q to the 115th S of SEQ ID NO: 7; and

(d) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding a light chain variable region consisting of the amino acid sequence ranging from the 1st D to the 106th R SEQ ID NO: 8.

18. An antibody drug conjugate comprising an antibody or antigen binding fragment thereof conjugated to monomethyl auristatin E (MMAE), wherein the antibody or fragment is produced by a method comprising culturing a host cell to allow expression of antibody or fragment, wherein the host cell is selected from the group consisting of the following (a) to (d):

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding a heavy chain consisting of the amino acid sequence ranging

from the 1st Q to the 441th K of SEQ ID NO: 7 and a polynucleotide comprising a base sequence encoding a light chain consisting of the amino acid sequence ranging from the 1st D to the 212th C of SEQ ID NO: 8;

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding a heavy chain consisting of the amino acid sequence ranging from the 1st Q to the 441th K of SEQ ID NO: 7 and an expression vector comprising a polynucleotide comprising a base sequence encoding a light chain consisting of the amino acid sequence ranging from the 1st D to the 212th C of SEQ ID NO: 8

(c) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding a heavy chain consisting of the amino acid sequence ranging from the 1st Q to the 441th K of SEQ ID NO: 7; and

(d) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding a light chain consisting of the amino acid sequence ranging from the 1st D to the 212th C of SEQ ID NO: 8.

19. An antibody drug conjugate comprising an antibody conjugated to monomethyl auristatin E (MMAE), wherein the antibody comprises the heavy chain consisting of the amino acid sequence ranging from the 1st Q to the 440th G of SEQ ID NO: 7 wherein the 1st Q is modified to pyroglutamate and the light chain consisting of the amino acid sequence ranging from the 1st D to the 212th C of SEQ ID NO: 8.

Claims

1. An antibody drug conjugate comprising:

an anti-CD37 antibody or antigen binding fragment thereof, conjugated to monomethyl auristatin E (MMAE) via a linker, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising CDR-H1 consisting of the amino acid sequence ranging from 31 to 35 of SEQ ID NO:7, CDR-H2 consisting of the amino acid sequence ranging from 50 to 65 of SEQ ID No: 7, and CDR-H3 consisting of the amino acid sequence ranging from 98 to 104 of SEQ ID NO: 7 and a light chain variable region comprising CDR-L1 consisting of the amino acid sequence ranging from 24 to 34 of SEQ ID NO: 8, CDR-L2 consisting of the amino acid sequence ranging from 50 to 56 of SEQ ID No: 8, and CDR-L3 consisting of the amino acid sequence ranging from 89 to 95 of SEQ ID NO: 8.

2. The antibody drug conjugate of claim 1, wherein the antibody or antigen binding fragment thereof comprises the heavy chain variable region consisting of the amino acid sequence ranging from residue 1 to residue 115 of SEQ ID NO: 7 and the light chain variable region consisting of the amino acid sequence ranging from residue 1 to residue 106 of SEQ ID NO: 8.

3. The antibody drug conjugate of claims 1 or 2, wherein the antibody comprises the heavy chain consisting of the amino acid sequence ranging from residue 1 to residue 441 of SEQ ID NO: 7 and the light chain consisting of the amino acid sequence ranging from residue 1 to residue 212 of SEQ ID NO: 8.

4. An antibody drug conjugate comprising an anti-CD37 antibody or antigen binding fragment thereof conjugated to monomethyl auristatin E (MMAE) via a linker, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of the heavy chain variable region of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under American Type Culture Collection (ATCC) Accession No. PTA-120464, and a light chain variable region comprising the amino acid sequence of the light chain variable region of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC Accession No. PTA-120464.

5. The antibody drug conjugate of claim 4, wherein the antibody comprises a heavy chain consisting of the amino acid sequence of the heavy chain of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC. Accession No. PTA-120464, and a light chain consisting of the amino acid sequence of the light chain of an antibody produced by a Chinese Hamster Ovary (CHO) deposited under ATCC. Accession No. PTA-120464.

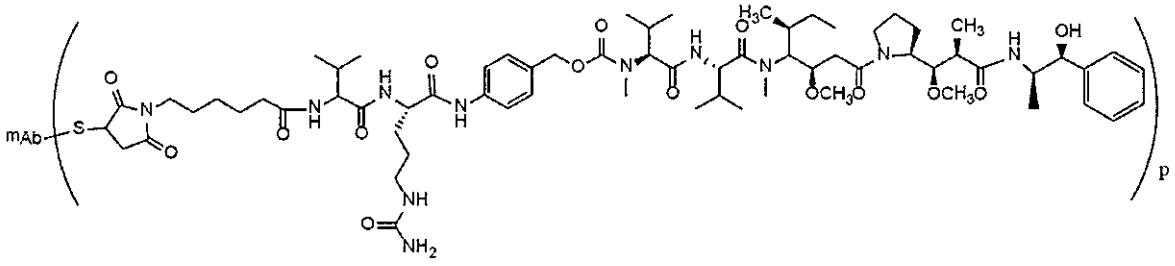
6. The antibody drug conjugate of claims 1, 2 and 4, wherein the antigen binding fragment thereof is an Fab, $F(ab')_2$, Fv or scFv fragment.

7. The antibody drug conjugate of any one of claims 1 to 6, wherein the antibody or antigen binding fragment thereof is a fully human antibody or antigen binding fragment thereof.

8. The antibody drug conjugate of any one of claims 1 to 7, wherein the antibody or antigen binding fragment thereof is recombinantly produced.

9. The antibody drug conjugate of claim 1, wherein the linker is Val-Cit linker.

10. The antibody drug conjugate of claim 1, wherein the antibody drug conjugate has the following structure:




wherein mAb represents an antibody or antigen binding fragment thereof and p is from 1 to 10.

11. The antibody drug conjugate of claim 10, wherein the antibody or antigen binding fragment thereof comprises the heavy chain variable region consisting of the amino acid

sequence ranging from residue 1 to residue 115 of SEQ ID NO: 7 and the light chain variable region consisting of the amino acid sequence ranging from residue 1 to residue 106 of SEQ ID NO: 8.

12. The antibody drug conjugate of claim 11, wherein the antibody comprises the heavy chain consisting of the amino acid sequence ranging from residue 1 to residue 441 of SEQ ID NO: 7 and the light chain consisting of the amino acid sequence ranging from residue 1 to residue 212 of SEQ ID NO: 8.

13. The antibody drug conjugate of any one of claims 1 to 12, wherein the antibody or antigen binding fragment thereof undergoes post-translational modifications.

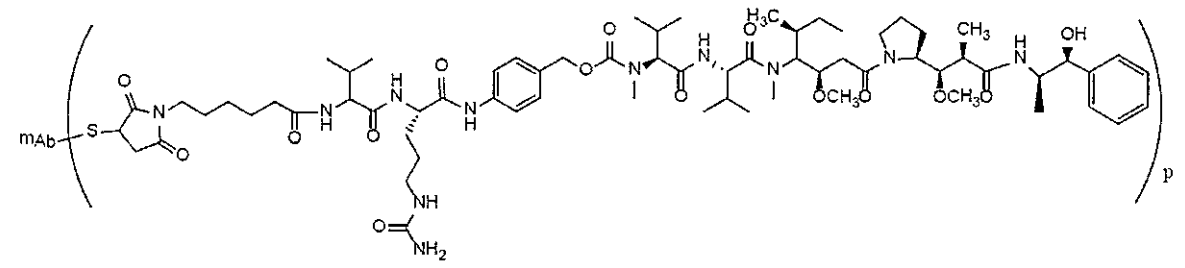
14. The antibody drug conjugate of any one of claims 1 to 12, wherein residue 1 of the heavy chain variable region is a pyroglutamate.

15. The antibody drug conjugate of claim 1, wherein the antibody or antigen binding fragment thereof comprises the heavy chain variable region consisting of the amino acid sequence ranging from residue 1 to residue 115 of SEQ ID NO: 7 wherein residue 1 is pyroglutamate and the light chain variable region consisting of the amino acid sequence ranging from residue 1 to residue 106 of SEQ ID NO: 8.

16. The antibody drug conjugate of claim 1, wherein the antibody comprises the heavy chain consisting of the amino acid sequence ranging from residue 1 to residue 440 of SEQ ID NO: 7 wherein residue 1 is pyroglutamate and the light chain consisting of the amino acid sequence ranging from residue 1 to residue 212 of SEQ ID NO: 8.

17. The antibody drug conjugate of claim 4, wherein the linker is Val-Cit linker.

18. The antibody drug conjugate of claim 4, wherein the antibody drug conjugate has the following structure:

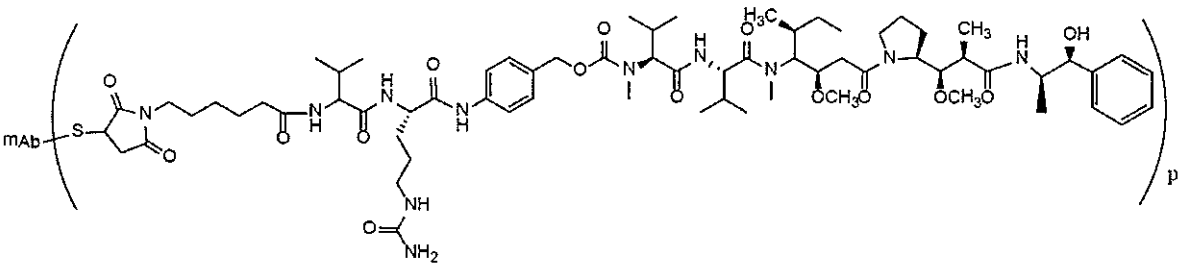


wherein mAb represents an antibody or antigen binding fragment thereof and p is from 1 to 10.

19. The antibody drug conjugate of claim 18, wherein the antibody comprises a heavy chain consisting of the amino acid sequence of the heavy chain of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC. Accession No. PTA-120464, and a light chain consisting of the amino acid sequence of the light chain of an antibody produced by a Chinese Hamster Ovary (CHO) deposited under ATCC. Accession No. PTA-120464.

20. The antibody drug conjugate of claim 15, wherein the linker is Val- Cit linker.

21. The antibody drug conjugate of claim 15, wherein the antibody drug conjugate has the following structure:



wherein mAb represents an antibody or antigen binding fragment thereof and p is from 1 to 10.

22. The antibody drug conjugate of claim 21, wherein the antibody comprises the heavy chain consisting of the amino acid sequence ranging from residue 1 to residue 440 of SEQ

ID NO: 7 wherein residue 1 is pyroglutamate and the light chain consisting of the amino acid sequence ranging from residue 1 to residue 212 of SEQ ID NO: 8.

23. A polynucleotide comprising a sequence encoding the heavy chain variable region of the anti-CD37 antibody or the antigen binding fragment thereof of any one of claims 1 to 2.

24. A polynucleotide comprising a sequence encoding the light chain variable region of the anti-CD37 antibody or the antigen binding fragment thereof of any one of claims 1 to 2.

25. An expression vector comprising the polynucleotide of claim 23 and/or 24.

26. A host cell selected from the group consisting of:

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-CD37 antibody or the antigen binding fragment thereof of any one of claims 1 to 2 and a polynucleotide comprising a base sequence encoding the light chain variable region of the antibody or the antigen binding fragment thereof.

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-CD37 antibody or the antigen binding fragment thereof of any one of claims 1 to 2 and an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain variable region of the antibody or the antigen binding fragment thereof;

(c) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-CD37 antibody or the antigen binding fragment thereof of any one of claims 1 to 2; and

(d) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain variable region of the anti-CD37 antibody or the antigen binding fragment thereof of any one of claims 1 to 2.

27. A method of producing an antibody drug conjugate, wherein the method comprises:

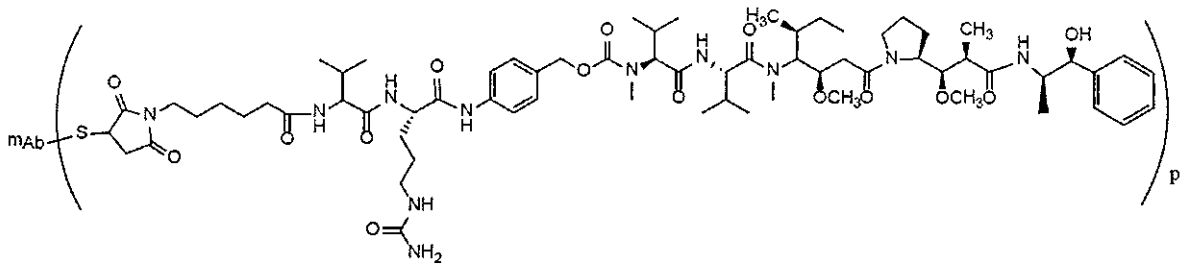
a) culturing the host cell of claim 26 under conditions suitable to allow expression of an anti-CD37 antibody or antigen binding fragment thereof; and

b) conjugating the antibody or antigen binding fragment thereof to monomethyl auristatin E (MMAE) via a linker.

28. An anti-CD37 antibody drug conjugate produced by the method of claim 27.

29. The antibody drug conjugate of claim 28, wherein the linker is Val- Cit linker.

30. The antibody drug conjugate of claim 28, wherein the antibody drug conjugate has the following structure:




wherein mAb represents an antibody or antigen binding fragment thereof and p is from 1 to 10.

31. A host cell selected from the group consisting of:

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-CD37 antibody of claim 3 and a polynucleotide comprising a base sequence encoding the light chain of the antibody;

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-CD37 antibody of claim 3 and an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the antibody;

(c) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-CD37 antibody of claim 3; and

(d) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the anti-CD37 antibody of claim 3.

32. A method of producing an antibody drug conjugate, wherein the method comprises:

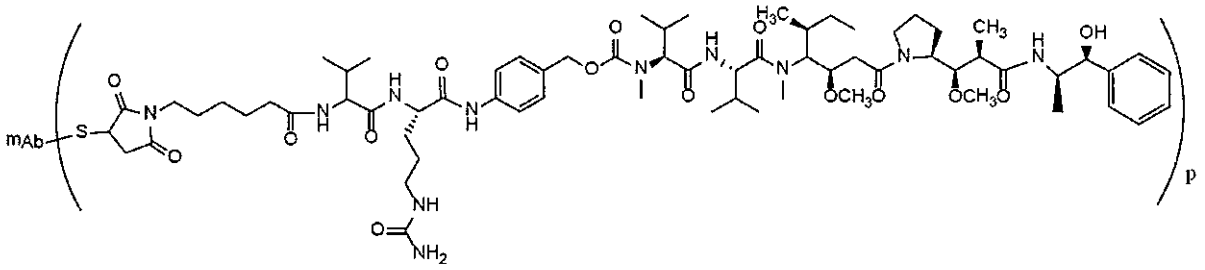
a) culturing the host cell of claim 31 under conditions suitable to allow expression of an anti-CD37 antibody; and

b) conjugating the antibody to monomethyl auristatin E (MMAE) via a linker.

33. An anti-CD37 antibody drug conjugate produced by the method of claim 32.

34. The antibody drug conjugate of claim 33, wherein the linker is Val- Cit linker.

35. The antibody drug conjugate of claim 33, wherein the antibody drug conjugate has the following structure:




wherein mAb represents an antibody and p is from 1 to 10.

36. A pharmaceutical composition that comprises the antibody drug conjugate of claims 1 to 22, 28 to 30 and 33 to 35 in a human unit dose form.

37. A pharmaceutical composition that comprises the antibody drug conjugate of claim 12 and the antibody drug conjugate of claim 22 in a human unit dose form.

38. The pharmaceutical composition of claims 36 or 37, wherein the composition is for cancer treatment.

39. The pharmaceutical composition of claim 38, wherein the cancer is Non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), or Multiple Myeloma (MM).

40. The pharmaceutical composition of claims 36 or 37, wherein the composition is for administration in combination with radiation or a chemotherapeutic agent.

41. The pharmaceutical composition of claims 36 or 37 comprising the antibody drug conjugate of claim 1 and a chemotherapeutic agent in a human unit dose form.

42. The pharmaceutical composition of claims 37 comprising the antibody drug conjugate of claim 12, the antibody drug conjugate of claim 22 and a chemotherapeutic agent in a human unit dose form.

43. The antibody drug conjugate of any of claims 1 to 22, 28 to 30 and 33 to 35 for use in the manufacture of a pharmaceutical composition for treating cancer in a subject.

44. The antibody drug conjugate of any of claims 1 to 22, 28 to 30 and 33 to 35 for use in a method of treating a cancer in a subject.

45. The antibody drug conjugate according to claim 43 or claim 44, wherein the antibody drug conjugate is for administration to a subject in an effective amount in combination with radiation.

46. The antibody drug conjugate according to claim 43 or claim 44, wherein the antibody drug conjugate is for administration to a subject in an effective amount in combination with chemotherapeutic agent.