

Claims

1. An antibody drug conjugate, which has the formula of Ab-(L-D)_n, wherein:

- (a) Ab is an antibody or a functional fragment thereof that specifically binds to MSLN;
- (b) L is a linker or does not exist;
- (c) D is a therapeutic agent; and
- (d) n is 1, 2, 3, 4, 5, 6, 7, or 8,

wherein the antibody that specifically binds to MSLN is a humanized antibody and Ab comprises a heavy chain variable region and a light chain variable region, wherein

(i) the heavy chain variable region comprises VH CDR1, VH CDR2, and VH CDR3 having an amino acid sequence as set forth in SEQ ID NO: 1, 2 and 3, respectively; and

(ii) the light chain variable region comprises VL CDR1, VL CDR2, and VL CDR3 having an amino acid sequence as set forth in SEQ ID NO: 4, 5 and 6, respectively.

2. The antibody drug conjugate according to Claim 1, wherein

(i) the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NO: 7 or a sequence having at least 90% sequence identity thereto; and

(ii) the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NO: 8 or a sequence having at least 90% sequence identity thereto

or wherein

(i) the heavy chain comprises an amino acid sequence as set forth in SEQ ID NO: 10 or a sequence having at least 90% sequence identity thereto; and

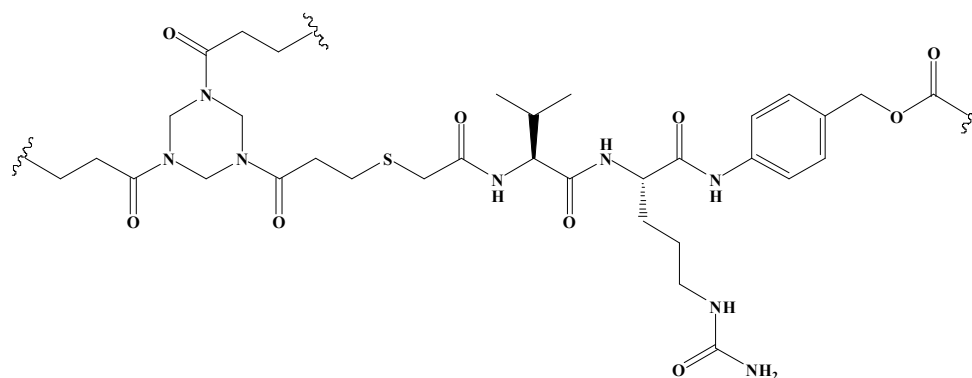
(ii) the light chain comprises an amino acid sequence as set forth in SEQ ID NO: 8 or a sequence having at least 90% sequence identity thereto.

3. The antibody drug conjugate according to any one of claims 1 to 2, wherein the antibody is a bispecific antibody.

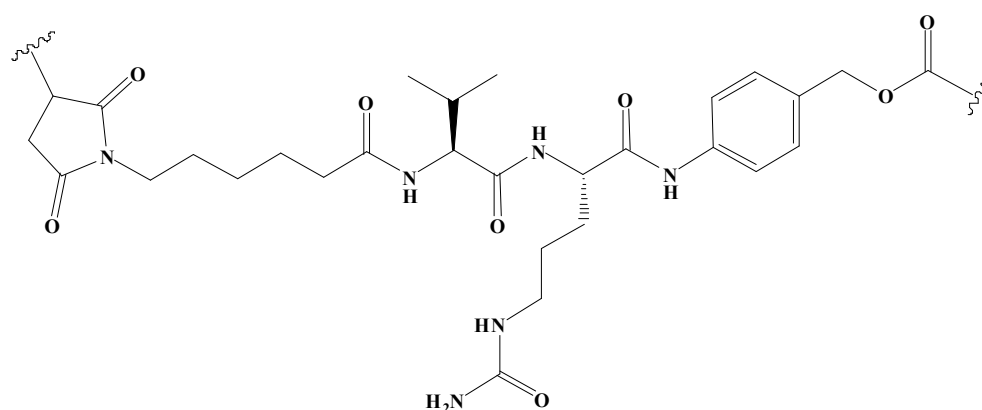
4. The antibody drug conjugate according to any one of claims 1 to 3, wherein the therapeutic agent is a dolastatin peptide, preferably MMAD, MMAE or MMAF, more preferably MMAE.

5. The antibody drug conjugate according to any one of claims 1 to 4, wherein L and Ab are linked by a thiol group on the antibody.

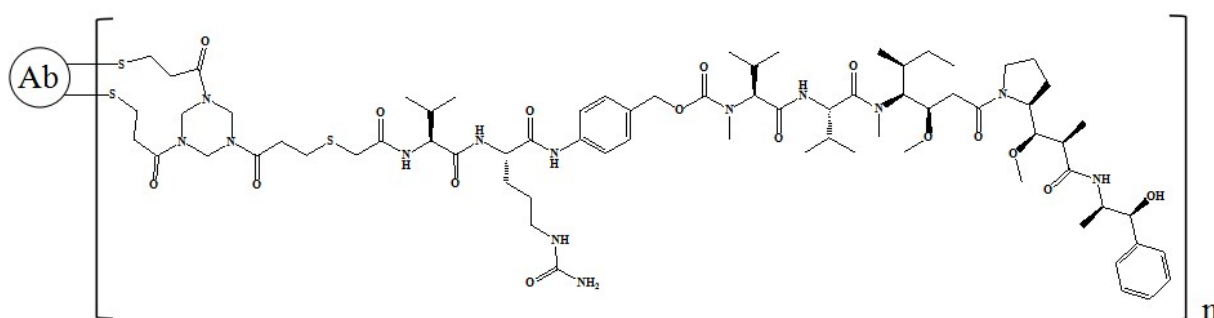
6. The antibody drug conjugate according to any one of claims 1 to 5, wherein the L has a structure as shown by the following formula:

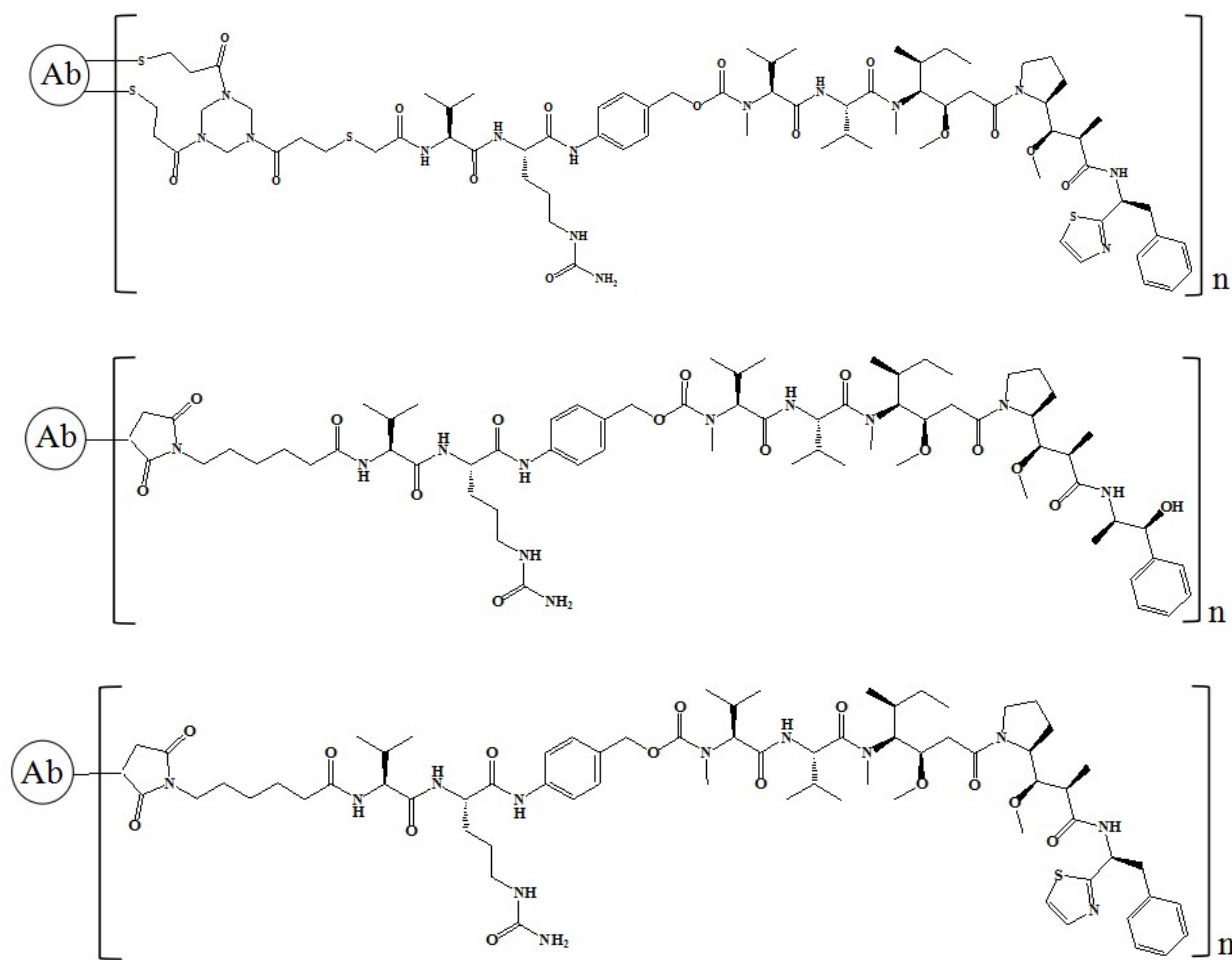


structure as shown by the following formula:



7. The antibody drug conjugate according to any one of claims 1 to 6, which has a structure as shown in any one of the following formulas:





8. A humanized antibody or a functional fragment thereof capable of specifically binding to mesothelin, wherein the antibody or the functional fragment thereof comprises a heavy chain variable and a light chain variable region , wherein

(i) the heavy chain variable region comprises VH CDR1, VH CDR2, and VH CDR3 having an amino acid sequence as set forth in SEQ ID NO: 1, 2 and 3, respectively; and

(ii) the light chain variable region comprises VL CDR1, VL CDR2, and VL CDR3 having an amino acid sequence as set forth in SEQ ID NO: 4, 5 and 6, respectively.

9. The antibody or functional fragment thereof according to claim 8, wherein

(i) the heavy chain variable region comprises an amino acid sequence as set forth in SEQ ID NO: 7 or a sequence having at least 90% sequence identity thereto;

(ii) the light chain variable region comprises an amino acid sequence as set forth in SEQ ID NO: 8 or a sequence having at least 90% sequence identity thereto;

or wherein

(i) the heavy chain comprises an amino acid sequence as set forth in SEQ ID NO: 10 or a sequence having at least 90% sequence identity thereto; and

(ii) the light chain comprises an amino acid sequence as set forth in SEQ ID NO: 9 or a sequence having at least 90% sequence identity thereto.

10. The antibody or functional fragment thereof according to any one of claims 8 to 9, wherein the antibody is a bispecific antibody.

11. An isolated polynucleotide, which encodes the antibody or functional fragment thereof according to any one of claims 8 to 10.

12. An expression vector, which comprises the polynucleotide according to claim 11, the polynucleotide being operably linked to a regulatory sequence allowing the expression of a polypeptide encoded thereby in a host cell or a cell-free expression system.

13. A pharmaceutical composition, which comprises the conjugate according to any one of claims 1 to 7 or the antibody or functional fragment thereof according to any one of claims 8 to 10, and a pharmaceutically acceptable carrier.

14. Use of the conjugate according to any one of claims 1 to 7, the antibody or functional fragment thereof according to any one of claims 8 to 10, the polynucleotide according to claim 11, the expression vector according to claim 12 or the pharmaceutical composition according to claim 13, in manufacture of a medicament for the treatment or prevention of a mesothelin-positive cancer.