

CLAIMS

1. A bispecific antibody that binds to TSPAN8 and CD3, comprising:
 - (a) a Fab region of an anti-TSPAN8 antibody consisting of: a heavy chain fragment comprising a heavy chain variable region of the anti-TSPAN8 antibody; and a light chain comprising a light chain variable region of the anti-TSPAN8 antibody;
 - (b) an anti-CD3-scFv region comprising a heavy chain variable region and a light chain variable region of an anti-CD3 antibody; and
 - (c) a Fc region consisting of a first Fc polypeptide linked to the heavy chain fragment of the Fab region (a) and a second Fc polypeptide linked to the anti-CD3-scFv region (b).
2. The bispecific antibody according to claim 1, wherein
 - the heavy chain variable region of the anti-TSPAN8 antibody comprises a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 6, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 66 of SEQ ID NO: 6, and a CDR3 consisting of an amino acid sequence from amino acid positions 99 to 110 of SEQ ID NO: 6, and the light chain variable region of the anti-TSPAN8 antibody comprises a CDR1 consisting of an amino acid sequence from amino acid positions 24 to 34 of SEQ ID NO: 8, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 56 of SEQ ID NO: 8, and a CDR3 consisting of an amino acid sequence from amino acid positions 89 to 96 of SEQ ID NO: 8; or
 - the heavy chain variable region of the anti-TSPAN8 antibody comprises a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 10, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 66 of SEQ ID NO: 10, and a CDR3 consisting of an amino acid sequence from amino acid positions 99 to 110 of SEQ ID NO: 10, and the light chain variable region of the anti-TSPAN8 antibody comprises a CDR1 consisting of an amino acid sequence from amino acid positions 24 to 34 of SEQ ID NO: 12, a CDR2 consisting of an amino acid sequence

from amino acid positions 50 to 56 of SEQ ID NO: 12, and a CDR3 consisting of an amino acid sequence from amino acid positions 89 to 96 of SEQ ID NO: 12.

3. The bispecific antibody according to claim 1, wherein

the heavy chain variable region of the anti-TSPAN8 antibody consists of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 6, and the light chain variable region of the anti-TSPAN8 antibody consists of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 8; or

the heavy chain variable region of the anti-TSPAN8 antibody consists of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 10, and the light chain variable region of the anti-TSPAN8 antibody consists of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 12.

4. The bispecific antibody according to claim 1, wherein

the Fab region of the anti-TSPAN8 antibody consists of a heavy chain fragment consisting of an amino acid sequence from amino acid positions 1 to 219 of SEQ ID NO: 6 and a light chain consisting of an amino acid sequence of SEQ ID NO: 8, or

the Fab region of the anti-TSPAN8 antibody consists of a heavy chain fragment consisting of an amino acid sequence from amino acid positions 1 to 219 of SEQ ID NO: 10 and a light chain consisting of an amino acid sequence of SEQ ID NO: 12.

5. The bispecific antibody according to any one of claims 1 to 4,

wherein the heavy chain variable region of the anti-CD3 antibody comprises a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 14, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 68 of SEQ ID NO: 14, and a CDR3 consisting of an amino acid sequence from amino acid positions 101 to 114 of SEQ ID NO: 14, and the light chain variable region of the anti-CD3 antibody comprises a CDR1 consisting of an amino acid sequence from amino acid positions 168 to 181 of SEQ ID NO: 14, a CDR2 consisting of an amino acid sequence from amino acid positions 197 to 203 of SEQ ID NO: 14, and a CDR3 consisting of an amino acid sequence from amino acid positions 236 to 244 of SEQ ID NO: 14.

6. The bispecific antibody according to any one of claims 1 to 4,

wherein the heavy chain variable region of the anti-CD3 antibody consists of an amino acid sequence from amino acid positions 1 to 125 of SEQ ID NO: 14, and the light chain variable region of the anti-CD3 antibody consists of an amino acid sequence from amino acid positions 146 to 254 of SEQ ID NO: 14.

7. The bispecific antibody according to any one of claims 1 to 4, wherein the anti-CD3-scFv region consists of an amino acid sequence from amino acid positions 1 to 254 of SEQ ID NO: 14.

8. The bispecific antibody according to claim 1, wherein

the bispecific antibody comprises: a heavy chain of an anti-TSPAN8 antibody in which a heavy chain fragment of the anti-TSPAN8 antibody comprising a heavy chain variable region comprising a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 6, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 66 of SEQ ID NO: 6, and a CDR3 consisting of an amino acid sequence from amino acid positions 99 to 110 of SEQ ID NO: 6 is linked to a first Fc polypeptide; a light chain of an anti-TSPAN8 antibody comprising a light chain variable region comprising a CDR1 consisting of an amino acid sequence from amino acid positions 24 to 34 of SEQ ID NO: 8, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 56 of SEQ ID NO: 8, and a CDR3 consisting of an amino acid sequence from amino acid positions 89 to 96 of SEQ ID NO: 8; and a polypeptide in which an anti-CD3-scFv region comprising a heavy chain variable region of an anti-CD3 antibody comprising a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 14, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 68 of SEQ ID NO: 14, and a CDR3 consisting of an amino acid sequence from amino acid positions 101 to 114 of SEQ ID NO: 14, and a light chain variable region of an anti-CD3 antibody comprising a CDR1 consisting of an amino acid sequence from amino acid positions 168 to 181 of SEQ ID NO: 14, a CDR2 consisting of an amino acid sequence from amino acid positions 197 to 203 of SEQ ID NO: 14, and a CDR3 consisting of an amino

acid sequence from amino acid positions 236 to 244 of SEQ ID NO: 14 is linked to a second Fc polypeptide, or

the bispecific antibody comprises: a heavy chain of an anti-TSPAN8 antibody in which a heavy chain fragment of the anti-TSPAN8 antibody comprising a heavy chain variable region comprising a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 10, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 66 of SEQ ID NO: 10, and a CDR3 consisting of an amino acid sequence from amino acid positions 99 to 110 of SEQ ID NO: 10 is linked to a first Fc polypeptide; a light chain of an anti-TSPAN8 antibody comprising a light chain variable region comprising a CDR1 consisting of an amino acid sequence from amino acid positions 24 to 34 of SEQ ID NO: 12, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 56 of SEQ ID NO: 12, and a CDR3 consisting of an amino acid sequence from amino acid positions 89 to 96 of SEQ ID NO: 12; and a polypeptide in which an anti-CD3-scFv region comprising a heavy chain variable region of an anti-CD3 antibody comprising a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 14, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 68 of SEQ ID NO: 14, and a CDR3 consisting of an amino acid sequence from amino acid positions 101 to 114 of SEQ ID NO: 14, and a light chain variable region of an anti-CD3 antibody comprising a CDR1 consisting of an amino acid sequence from amino acid positions 168 to 181 of SEQ ID NO: 14, a CDR2 consisting of an amino acid sequence from amino acid positions 197 to 203 of SEQ ID NO: 14, and a CDR3 consisting of an amino acid sequence from amino acid positions 236 to 244 of SEQ ID NO: 14 is linked to a second Fc polypeptide.

9. The bispecific antibody according to claim 1, wherein

the bispecific antibody comprises: a heavy chain of an anti-TSPAN8 antibody in which a heavy chain fragment of the anti-TSPAN8 antibody comprising a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 6 is linked to a first Fc polypeptide, a light chain of an anti-TSPAN8 antibody

comprising a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 8, and a polypeptide in which an anti-CD3-scFv region comprising a heavy chain variable region of an anti-CD3 antibody consisting of an amino acid sequence from amino acid positions 1 to 125 of SEQ ID NO: 14 and a light chain variable region of an anti-CD3 antibody consisting of an amino acid sequence from amino acid positions 146 to 254 of SEQ ID NO: 14 is linked to a second Fc polypeptide, or

the bispecific antibody comprises: a heavy chain of an anti-TSPAN8 antibody in which a heavy chain fragment of the anti-TSPAN8 antibody comprising a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 10 is linked to a first Fc polypeptide, a light chain of the anti-TSPAN8 antibody comprising a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 12, and a polypeptide in which an anti-CD3-scFv region comprising a heavy chain variable region of an anti-CD3 antibody consisting of an amino acid sequence from amino acid positions 1 to 125 of SEQ ID NO: 14 and a light chain variable region of an anti-CD3 antibody consisting of an amino acid sequence from amino acid positions 146 to 254 of SEQ ID NO: 14 is linked to a second Fc polypeptide.

10. The bispecific antibody according to any one of claims 1 to 9, comprising a Fc region containing LALA mutation (L234A and L235A (wherein positions of mutation are amino acid positions in human Igγ1 constant region according to EU index)).

11. The bispecific antibody according to any one of claims 1 to 10, comprising a Fc region containing N297G mutation (wherein a position of mutation is an amino acid position in human Igγ1 constant region according to EU index).

12. The bispecific antibody according to any one of claims 1 to 11, comprising a Fc region containing knobs-into-holes mutation.

13. The bispecific antibody according to any one of claims 1 to 12, comprising a Fc region containing LALA mutation, N297G mutation and knobs-into-holes mutation.

14. The bispecific antibody according to claims 12 or 13, wherein the knobs-into-holes mutation is T366W mutation in one Fc polypeptide included in the Fc region, and T366S,

L368A and Y407V mutation in another Fc polypeptide included in the Fc region (wherein positions of mutation are amino acid positions in human Igγ1 constant region according to EU index).

15. The bispecific antibody according to any one of claims 1 to 14, comprising a Fc region in which the first Fc polypeptide consists of an amino acid sequence from amino acids 235 to 451 of SEQ ID NO: 6 and the second Fc polypeptide consists of an amino acid sequence from amino acids 270 to 486 of SEQ ID NO: 14.

16. The bispecific antibody according to any one of claims 1 to 15, wherein the heavy chain fragment of the anti-TSPAN8 antibody and the first Fc polypeptide are linked through a hinge region, and the anti-CD3-scFv region and the second Fc polypeptide are linked through a hinge region.

17. The bispecific antibody according to claim 1, comprising: a heavy chain of the anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 6 in which the heavy chain fragment of the anti-TSPAN8 antibody is linked to the first Fc polypeptide; a light chain of the anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 8; and a polypeptide consisting of an amino acid sequence of SEQ ID NO: 14 in which an anti-CD3-scFv region is linked to the second polypeptide.

18. The bispecific antibody according to any one of claims 2 to 17, post-translationally modified.

19. The bispecific antibody according to claim 18, wherein the post-translational modification is pyroglutamylation at a N-terminal of the heavy chain variable region and/or lysine deletion at a heavy chain C-terminal.

20. A polynucleotide selected from the group consisting of the following (a) to (e):

(a) a polynucleotide comprising a nucleotide sequence encoding a heavy chain of an anti-TSPAN8 antibody in which a heavy chain fragment of the anti-TSPAN8 antibody comprising a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 6 is linked to a first Fc polypeptide;

(b) a polynucleotide comprising a nucleotide sequence encoding a light chain of an

anti-TSPAN8 antibody comprising a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 8;

(c) a polynucleotide comprising a nucleotide sequence encoding a heavy chain of an anti-TSPAN8 antibody in which a heavy chain fragment of the anti-TSPAN8 antibody comprising a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 10 is linked to a first Fc polypeptide;

(d) a polynucleotide comprising a nucleotide sequence encoding a light chain of an anti-TSPAN8 antibody comprising a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 12;

(e) a polynucleotide comprising a nucleotide sequence encoding a polypeptide in which an anti-CD3-scFv region comprising a heavy chain variable region of an anti-CD3 antibody consisting of an amino acid sequence from amino acid positions 1 to 125 of SEQ ID NO: 14, and a light chain variable region of an anti-CD3 antibody consisting of an amino acid sequence from amino acid positions 146 to 254 of SEQ ID NO: 14 is linked to a second Fc polypeptide.

21. A polynucleotide selected from the group consisting of the following (a) to (c):

(a) a polynucleotide comprising a nucleotide sequence encoding a heavy chain of an anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 6 in which a heavy chain fragment of the anti-TSPAN8 antibody is linked to a first Fc polypeptide;

(b) a polynucleotide comprising a nucleotide sequence encoding a light chain of an anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 8; and

(c) a polynucleotide comprising a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence of SEQ ID NO: 14 in which an anti-CD3-scFv region is linked to a second Fc polypeptide.

22. An expression vector comprising the polynucleotide according to claim 20 or 21.

23. A host cell transformed with the expression vector according to claim 22.

24. A host cell comprising: a polynucleotide comprising a nucleotide sequence encoding a heavy chain of an anti-TSPAN8 antibody in which a heavy chain fragment of the

anti-TSPAN8 antibody comprising a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 6 is linked to a first Fc polypeptide; a polynucleotide comprising a nucleotide sequence encoding a light chain of an anti-TSPAN8 antibody comprising a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 8; and a polynucleotide comprising a nucleotide sequence encoding a polypeptide in which an anti-CD3-scFv region comprising a heavy chain variable region of an anti-CD3 antibody consisting of an amino acid sequence from amino acid positions 1 to 125 of SEQ ID NO: 14, and a light chain variable region of an anti-CD3 antibody consisting of an amino acid sequence from amino acid positions 146 to 254 of SEQ ID NO: 14 is linked to a second Fc polypeptide.

25. A host cell comprising: a polynucleotide comprising a nucleotide sequence encoding a heavy chain of an anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 6 in which a heavy chain fragment of the anti-TSPAN8 antibody is linked to a first Fc polypeptide; a polynucleotide comprising a nucleotide sequence encoding a light chain of an anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 8; and a polynucleotide comprising a nucleotide sequence encoding a polypeptide consisting of an amino acid sequence of SEQ ID NO: 14 in which an anti-CD3-scFv region is linked to a second Fc polypeptide.

26. A method for producing a bispecific antibody that binds to TSPAN8 and CD3, comprising a step of culturing the host cell according to any one of claims 23 to 25.

27. A pharmaceutical composition comprising:
the bispecific antibody according to any one of claims 1 to 19, and
a pharmaceutically acceptable excipient.

28. The bispecific antibody according to any one of claims 1 to 19, for use in treating cancer.

29. The pharmaceutical composition according to claim 27, for treating cancer.

~~30. A method for treating cancer, comprising a step of administering, to a subject, a therapeutically effective amount of the bispecific antibody according to any one of claims 1 to 19.~~

~~301.~~ Use of the bispecific antibody according to any one of claims 1 to 19, in production of a pharmaceutical composition for use in treating cancer.

~~3231.~~ An anti-TSPAN8 antibody or an antigen-binding fragment thereof that selectively binds to a human TSPAN8-expressing cancer cell.

~~3332.~~ An anti-TSPAN8 antibody or an antigen-binding fragment thereof that binds to at least one amino acid present in the human TSPAN8 region from amino acid positions 126 to 155 of SEQ ID NO: 2.

~~3433.~~ The anti-TSPAN8 antibody or the antigen-binding fragment thereof according to claim ~~3332~~, which binds to at least the amino acid at amino acid position 131 of SEQ ID NO: 2 present in the human TSPAN8 region.

~~3534.~~ An anti-TSPAN8 antibody or an antigen-binding fragment thereof selected from the following (a) and (b):

(a) an anti-TSPAN8 antibody or an antigen-binding fragment thereof, comprising a heavy chain variable region comprising a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 4, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 66 of SEQ ID NO: 4, and a CDR3 consisting of an amino acid sequence from amino acid positions 99 to 110 of SEQ ID NO. 4, and a light chain variable region comprising a CDR1 consisting of an amino acid sequence from amino acid positions 24 to 34 of SEQ ID NO: 8, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 56 of SEQ ID NO: 8, and a CDR3 consisting of an amino acid sequence from amino acid positions 89 to 96 of SEQ ID NO. 8; and

(b) an anti-TSPAN8 antibody or an antigen-binding fragment thereof, comprising a heavy chain variable region comprising a CDR1 consisting of an amino acid sequence from amino acid positions 31 to 35 of SEQ ID NO: 10, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 66 of SEQ ID NO: 10, and a CDR3 consisting of

an amino acid sequence from amino acid positions 99 to 110 of SEQ ID NO. 10, and a light chain variable region comprising a CDR1 consisting of an amino acid sequence from amino acid positions 24 to 34 of SEQ ID NO: 12, a CDR2 consisting of an amino acid sequence from amino acid positions 50 to 56 of SEQ ID NO: 12, and a CDR3 consisting of an amino acid sequence from amino acid positions 89 to 96 of SEQ ID NO. 12.

3635. The anti-TSPAN8 antibody or the antigen-binding fragment thereof according to claim 3534, selected from the following (a) and (b):

(a) an anti-TSPAN8 antibody or an antigen-binding fragment thereof comprising a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 4, and a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 8; and

(b) an anti-TSPAN8 antibody or an antigen-binding fragment thereof comprising a heavy chain variable region consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 10, and a light chain variable region consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 12.

3736. The anti-TSPAN8 antibody according to claim 3534, selected from the following (a) and (b):

(a) an anti-TSPAN8 antibody comprising a heavy chain consisting of an amino acid sequence of SEQ ID NO: 4 and a light chain consisting of an amino acid sequence of SEQ ID NO: 8; and

(b) an anti-TSPAN8 antibody comprising a heavy chain consisting of an amino acid sequence of SEQ ID NO: 10 and a light chain consisting of an amino acid sequence of SEQ ID NO: 12.

3837. An anti-TSPAN8 antibody or an antigen-binding fragment thereof that competes with the anti-TSPAN8 antibody or the antigen-binding fragment thereof according to any one of claims 33-32 to 37-36 in the binding to the human TSPAN8-expressing cancer cell.

~~3938~~. The anti-TSPAN8 antibody or the antigen-binding fragment thereof according to any one of claims ~~32-31~~ to ~~3837~~, linked to an antibody to a surface antigen of T cell or NK cell, or an antigen-binding fragment thereof.

~~4039~~. The anti-TSPAN8 antibody or the antigen-binding fragment thereof according to claim ~~3938~~, wherein the surface antigen of T cell is CD3.

~~4140~~. The anti-TSPAN8 antibody or the antigen-binding fragment thereof according to claim ~~4039~~, wherein the antigen-binding fragment to the surface antigen of T cell is scFv of an anti-CD3 antibody.

~~4241~~. The anti-TSPAN8 antibody or the antigen-binding fragment thereof according to any one of claims ~~3231~~ to ~~4140~~, post-translationally modified.

~~4342~~. The anti-TSPAN8 antibody or the antigen-binding fragment thereof according to claim ~~4241~~, wherein the post-translational modification is pyroglutamylation at a N-terminal of a heavy chain variable region and/or lysine deletion at a heavy chain C-terminal.

~~4443~~. A fusion or complex of the anti-TSPAN8 antibody or the antigen-binding fragment thereof according to any one of claims ~~32-31~~ to ~~4342~~, or a cell on a surface of which the anti-TSPAN8 or the antigen-binding fragment thereof according to any one of claims ~~32-31~~ to ~~43-42~~ is expressed.

~~4544~~. A polynucleotide selected from the group consisting of the following (a) to (d):

(a) a polynucleotide comprising a nucleotide sequence encoding a heavy chain variable region of an anti-TSPAN8 antibody consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 4;

(b) a polynucleotide comprising a nucleotide sequence encoding a light chain variable region of an anti-TSPAN8 antibody consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 8;

(c) a polynucleotide comprising a nucleotide sequence encoding a heavy chain variable region of an anti-TSPAN8 antibody consisting of an amino acid sequence from amino acid positions 1 to 121 of SEQ ID NO: 10; and

(d) a polynucleotide comprising a nucleotide sequence encoding a light chain

variable region of an anti-TSPAN8 antibody consisting of an amino acid sequence from amino acid positions 1 to 107 of SEQ ID NO: 12.

~~4645~~. A polynucleotide selected from the group consisting of the following (a) to (d):

(a) a polynucleotide comprising a nucleotide sequence encoding a heavy chain of an anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 4;

(b) a polynucleotide comprising a nucleotide sequence encoding a light chain of an anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 8;

(c) a polynucleotide comprising a nucleotide sequence encoding a heavy chain of an anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 10; and

(d) a polynucleotide comprising a nucleotide sequence encoding a light chain of an anti-TSPAN8 antibody consisting of an amino acid sequence of SEQ ID NO: 12.

~~4746~~. An expression vector, comprising the polynucleotide according to claim ~~4544~~ or ~~4645~~.

~~4847~~. A host cell transformed with the expression vector according to claim ~~4746~~.

~~4948~~. A host cell selected from the following (a) and (b):

(a) a host cell comprising the polynucleotide comprising a nucleotide sequence encoding a heavy chain variable region of an anti-TSPAN8 antibody according to claim ~~4544~~, and the polynucleotide comprising a nucleotide sequence encoding a light chain variable region of an anti-TSPAN8 antibody according to claim ~~4544~~; and

(b) a host cell comprising the polynucleotide comprising a nucleotide sequence encoding a heavy chain of an anti-TSPAN8 antibody according to claim ~~4645~~, and the polynucleotide comprising a nucleotide sequence encoding a light chain of an anti-TSPAN8 antibody according to claim ~~4645~~.

~~5049~~. A method for producing an anti-TSPAN8 antibody or an antigen-binding fragment thereof, comprising a step of culturing the host cell according to claim ~~4847~~ or ~~4948~~.

~~5150~~. The anti-TSPAN8 antibody or the antigen-binding fragment thereof according to any one of claims ~~3231~~ to ~~4342~~, or the fusion, the complex, or the cell according to claim ~~4443~~, for use in treating cancer.

~~52~~51. A pharmaceutical composition comprising:

the anti-TSPAN8 antibody or the antigen-binding fragment thereof according to any one of claims ~~32-31~~ to ~~43~~42, or

the fusion, the complex, or the cell according to claim ~~44~~43, and

a pharmaceutically acceptable excipient.

~~53~~52. The pharmaceutical composition according to claim ~~52~~51, for treating cancer.

~~54. — A method for treating cancer, comprising a step of administering, to a subject, a therapeutically effective amount of the anti-TSPAN8 antibody or the antigen-binding fragment thereof according to any one of claims 32 to 43, or a step of administering, to a subject, a therapeutically effective amount of the fusion, the complex, or the cell according to claim 44.~~

~~55~~53. Use of the anti-TSPAN8 antibody or the antigen-binding fragment thereof according to any one of claims ~~32-31~~ to ~~43~~42, or use of the fusion, the complex, or the cell according to claim ~~44~~43, in production of a pharmaceutical composition for treating cancer.