

Claims

1. An anti-human Fn14 antibody or an antigen-binding fragment thereof comprising:
 a heavy chain variable region comprising CDR1 consisting of the amino acid
 sequence of amino acid numbers 31 to 35 of SEQ ID NO: 2, CDR2 consisting of the amino
 acid sequence of amino acid numbers 50 to 65 of SEQ ID NO: 2, and CDR3 consisting of
 the amino acid sequence of amino acid numbers 98 to 114 of SEQ ID NO: 2; and
 a light chain variable region comprising CDR1 consisting of the amino acid
 sequence of amino acid numbers 24 to 40 of SEQ ID NO: 4, CDR2 consisting of the amino
 acid sequence of amino acid numbers 56 to 62 of SEQ ID NO: 4, and CDR3 consisting of
 the amino acid sequence of amino acid numbers 95 to 103 of SEQ ID NO: 4.

2. The anti-human Fn14 antibody or the antigen-binding fragment thereof according
 to claim 1, selected from the following (1) and (2):

(1) an anti-human Fn14 antibody or an antigen-binding fragment thereof
 comprising a heavy chain variable region consisting of the amino acid sequence of amino
 acid numbers 1 to 125 of SEQ ID NO: 2 and a light chain variable region consisting of the
 amino acid sequence of amino acid numbers 1 to 114 of SEQ ID NO: 4; and

(2) an antibody or an antigen-binding fragment thereof formed by posttranslational
 modification of the anti-human Fn14 antibody or the antigen-binding fragment thereof of
 (1).

3. The anti-human Fn14 antibody or the antigen-binding fragment thereof according
 to claim 2, comprising:

a heavy chain variable region consisting of the amino acid sequence of amino acid
 numbers 1 to 125 of SEQ ID NO: 2; and

a light chain variable region consisting of the amino acid sequence of amino acid
 numbers 1 to 114 of SEQ ID NO: 4.

4. The anti-human Fn14 antibody or the antigen-binding fragment thereof according
 to claim 2, wherein the posttranslational modification is pyroglutamylation at the N
 terminal of the heavy chain variable region and/or deletion of lysine at the C terminal of
 the heavy chain.

5. The anti-human Fn14 antibody or the antigen-binding fragment thereof according
 to claim 2, comprising:

a heavy chain variable region consisting of the amino acid sequence of amino acid

numbers 1 to 125 of SEQ ID NO: 2, in which glutamine of amino acid number 1 of SEQ ID NO: 2 is modified to pyroglutamic acid; and

a light chain variable region consisting of the amino acid sequence of amino acid numbers 1 to 114 of SEQ ID NO: 4.

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6. The anti-human Fn14 antibody according to claim 2, selected from the following (31) and (24):

(31) an anti-human Fn14 antibody comprising a heavy chain consisting of the amino acid sequence represented by SEQ ID NO: 2 and a light chain consisting of the amino acid sequence represented by SEQ ID NO: 4; and

10

(42) an anti-human Fn14 antibody formed by posttranslational modification of the antibody of (31).

7. The anti-human Fn14 antibody according to claim 6, comprising:

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a heavy chain consisting of the amino acid sequence represented by SEQ ID NO: 2; and

a light chain consisting of the amino acid sequence represented by SEQ ID NO: 4

8. The anti-human Fn14 antibody according to claim 6, wherein the posttranslational modification is pyroglutamylation at the N terminal of the heavy chain and/or deletion of lysine at the C terminal of the heavy chain.

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9. The anti-human Fn14 antibody according to claim 8, comprising:

a heavy chain consisting of the amino acid sequence of amino acid numbers 1 to 454 of SEQ ID NO: 2, in which glutamine of amino acid number 1 of SEQ ID NO: 2 is modified to pyroglutamic acid; and

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a light chain consisting of the amino acid sequence represented by SEQ ID NO: 4.

10. The antigen-binding fragment according to any one of claims 1 to 5, which is a single chain variable region fragment, Fab, Fab', or F(ab')₂.

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11. A polynucleotide comprising:

a base sequence encoding the heavy chain variable region of the anti-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3.

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12. A polynucleotide comprising:

a base sequence encoding the light chain variable region of the anti-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3.

13. An expression vector comprising:
the polynucleotide according to claim 11 and/or 12.

14. A host cell 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 the heavy chain variable region of the anti-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3 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-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3, 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-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3; 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-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3.

15. A host cell selected from the group consisting of the following (~~ea~~) to (~~dh~~):

(~~ea~~) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Fn14 antibody according to claim 7 and a polynucleotide comprising a base sequence encoding the light chain of the antibody;

(~~fb~~) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Fn14 antibody according to claim 7, and an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the antibody;

(~~gc~~) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Fn14 antibody according to claim 7; and

(~~hd~~) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the anti-human Fn14 antibody according to claim 7.

16. A method for producing an anti-human Fn14 antibody or an antigen-

binding fragment thereof, the method comprising:

a step of culturing a host cell selected from the group consisting of the following (A) to (C) to express an anti-human Fn14 antibody or an antigen-binding fragment thereof:

(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-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3 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-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3, 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; and

(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-human Fn14 antibody or the antigen-binding fragment thereof according to claim 3, and a host cell transformed with 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.

17. A method for producing an anti-human Fn14 antibody comprising:

a step of culturing a host cell selected from the group consisting of the following (~~DA~~) to (~~FC~~) to express an anti-human Fn14 antibody:

(~~DA~~) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Fn14 antibody according to claim 7 and a polynucleotide comprising a base sequence encoding the light chain of the antibody;

(~~EB~~) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Fn14 antibody according to claim 7, and an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the antibody; and

(~~FC~~) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Fn14 antibody according to claim 7, and a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the anti-human Fn14 antibody.

~~18. An anti-human Fn14 antibody or an antigen-binding fragment thereof~~

produced by the method according to claim 16.

19. — An anti-human Fn14 antibody produced by the method according to claim 17.

5 ~~18~~20. A pharmaceutical composition comprising:
 the anti-human Fn14 antibody or the antigen-binding fragment thereof according
 to any one of claims 1 to 10, ~~18~~, and ~~19~~; and
 a pharmaceutically acceptable excipient.

10 ~~21~~19. A pharmaceutical composition comprising:
 the anti-human Fn14 antibody or the antigen-binding fragment thereof according
 to claim 3;
 the anti-human Fn14 antibody or the antigen-binding fragment thereof according
 to claim 5; and
 a pharmaceutically acceptable excipient.

20 ~~22~~20. A pharmaceutical composition comprising:
 the anti-human Fn14 antibody according to claim 7;
 the anti-human Fn14 antibody according to claim 9; and
 a pharmaceutically acceptable excipient.

25 ~~23~~21. The pharmaceutical composition according to any one of claims ~~20~~18 to ~~22~~20,
 which is a pharmaceutical composition for preventing or treating cancer cachexia.

30 ~~24~~22. The anti-human Fn14 antibody or the antigen-binding fragment thereof according
 to any one of claims 1 to 10, ~~18~~, and ~~19~~, for use in the prevention or treatment of ~~cancer or~~
 cancer cachexia.

35 ~~25~~23. Use of the anti-human Fn14 antibody or the antigen-binding fragment thereof
 according to any one of claims 1 to 10, ~~18~~, and ~~19~~ in the manufacture of a medicament for
 the prevention or treatment of ~~cancer or~~
 cancer cachexia.

40 ~~26~~24. The use according to claim ~~25~~23, wherein the medicament is to be used in
 combination with an anticancer agent.

45 ~~27~~25. The use according to claim ~~26~~24, wherein the anticancer agent is gemcitabine.

2826. A pharmaceutical composition for preventing or treating cancer or cancer cachexia, comprising:

the anti-human Fn14 antibody or the antigen-binding fragment thereof according to any one of claims 1 to 10, ~~18, and 19~~ as an active ingredient,

wherein the pharmaceutical composition is to be used in combination with an anticancer agent.

~~29. A pharmaceutical composition for preventing or treating cancer or cancer cachexia, comprising:~~

~~an anticancer agent,~~

~~wherein the pharmaceutical composition is to be used in combination with the anti-human Fn14 antibody or the antigen-binding fragment thereof according to any one of claims 1 to 10, 18, and 19.~~

~~30. The use of an anticancer agent in the manufacture of a medicament for the treatment of cancer or cancer cachexia,~~

~~wherein the medicament is to be used in combination with the anti-human Fn14 antibody or the antigen-binding fragment thereof according to any one of claims 1 to 10, 18, and 19.~~

~~31. The use of claim 30, wherein the anticancer agent is gemcitabine.~~