

Claims

1. An anti-hGDF15 antibody, wherein the antibody binds to an epitope of hGDF15 comprising the amino acid
5 sequence of DHCPLGPGRCCRLH (SEQ ID NO: 3).

2. The antibody of claim 1, wherein the antibody comprises

a heavy chain variable region that contains
10 CDR1 contained in a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 4, or CDR1 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR1 contained in the heavy chain variable region comprising the amino
15 acid sequence of SEQ ID NO: 4 by having amino acid modification of one to three amino acid residues,

CDR2 contained in a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 4, or CDR2 consisting of an amino acid sequence that differs
20 from the amino acid sequence of the CDR2 contained in the heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 4 by having amino acid modification of one to three amino acid residues, and

CDR3 contained in a heavy chain variable region
25 comprising the amino acid sequence of SEQ ID NO: 4, or CDR3 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR3 contained in the heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 4 by having amino acid
30 modification of one to three amino acid residues; and a light chain variable region that contains

CDR1 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 5, or

CDR1 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR1 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 5 by having amino acid modification of one to three amino acid residues,

CDR2 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 5, or CDR2 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR2 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 5 by having amino acid modification of one to three amino acid residues, and

CDR3 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 5, or CDR3 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR3 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 5 by having amino acid modification of one to three amino acid residues.

3. The antibody of claim 1 or 2, wherein the antibody comprises

a heavy chain variable region that contains

CDR1 comprising the amino acid sequence of SEQ ID NO: 18 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 18 by having amino acid modification of one to three amino acid residues,

CDR2 comprising the amino acid sequence of SEQ ID NO: 19 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 19 by having amino acid modification of one to three amino acid residues, and

CDR3 comprising the amino acid sequence of SEQ ID NO: 20 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 20 by having amino acid modification of one to three amino acid residues; and

a light chain variable region that contains

CDR1 comprising the amino acid sequence of SEQ ID NO: 21 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 21 by having amino acid modification of one to three amino acid residues,

CDR2 comprising the amino acid sequence of SEQ ID NO: 22 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 22 by having amino acid modification of one to three amino acid residues, and

CDR3 comprising the amino acid sequence of SEQ ID NO: 23 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 23 by having amino acid modification of one to three amino acid residues.

4. The antibody of any one of claims 1 to 3, wherein the antibody comprises

a heavy chain variable region that contains

CDR1 comprising the amino acid sequence of SEQ ID NO: 18,

CDR2 comprising the amino acid sequence of SEQ ID NO: 19, and

CDR3 comprising the amino acid sequence of SEQ ID NO: 20, and

a light chain variable region that contains

CDR1 comprising the amino acid sequence of SEQ ID NO: 21,

CDR2 comprising the amino acid sequence of SEQ ID NO: 22, and

CDR3 comprising the amino acid sequence of SEQ ID NO: 23.

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5. The antibody of any one of claims 1 to 4, wherein the antibody comprises CDR1, CDR2, and CDR3 contained in a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 4, and CDR1, CDR2, and CDR3
10 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 5.

6. The antibody of claim 1, wherein the antibody comprises

15 a heavy chain variable region that contains

CDR1 contained in a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 133, or CDR1 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR1
20 contained in the heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 133 by having amino acid modification of one to three amino acid residues,

CDR2 contained in a heavy chain variable region
25 comprising the amino acid sequence of SEQ ID NO: 133, or CDR2 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR2 contained in the heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 133
30 by having amino acid modification of one to three amino acid residues, and

CDR3 contained in a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 133,

or CDR3 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR3 contained in the heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 133 by having amino acid modification of one to three amino acid residues; and
a light chain variable region that contains

CDR1 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 134,
or CDR1 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR1 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 134 by having amino acid modification of one to three amino acid residues,

CDR2 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 134,
or CDR2 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR2 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 134 by having amino acid modification of one to three amino acid residues, and

CDR3 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 134,
or CDR3 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR3 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 134 by having amino acid modification of one to three amino acid residues.

7. The antibody of claim 1 or 6, wherein the antibody comprises

a heavy chain variable region that contains

5 CDR1 comprising the amino acid sequence of SEQ ID NO: 137 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 137 by having amino acid modification of one to three amino acid residues,

10 CDR2 comprising the amino acid sequence of SEQ ID NO: 138 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 138 by having amino acid modification of one to three amino acid residues, and

15 CDR3 comprising the amino acid sequence of SEQ ID NO: 139 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 139 by having amino acid modification of one to three amino acid residues; and

a light chain variable region that contains

20 CDR1 comprising the amino acid sequence of SEQ ID NO: 140 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 140 by having amino acid modification of one to three amino acid residues,

25 CDR2 comprising the amino acid sequence of SEQ ID NO: 141 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 141 by having amino acid modification of one to three amino acid residues, and

30 CDR3 comprising the amino acid sequence of SEQ ID NO: 142 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 142 by having

amino acid modification of one to three amino acid residues.

8. The antibody of any one of claims 1, 6 and 7,
5 wherein the antibody comprises

a heavy chain variable region that contains

CDR1 comprising the amino acid sequence of SEQ ID
NO: 137,

10 CDR2 comprising the amino acid sequence of SEQ ID
NO: 138, and

CDR3 comprising the amino acid sequence of SEQ ID
NO: 139, and

a light chain variable region that contains

15 CDR1 comprising the amino acid sequence of SEQ ID
NO: 140,

CDR2 comprising the amino acid sequence of SEQ ID
NO: 141, and

CDR3 comprising the amino acid sequence of SEQ ID
NO: 142.

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9. The antibody of any one of claims 1 and 6 to 8,
wherein the antibody comprises CDR1, CDR2, and CDR3
contained in a heavy chain variable region comprising the
amino acid sequence of SEQ ID NO: 133, and CDR1, CDR2, and
25 CDR3 contained in a light chain variable region comprising
the amino acid sequence of SEQ ID NO: 134.

10. The antibody of claim 1, wherein the antibody
comprises

30 a heavy chain variable region that contains

CDR1 contained in a heavy chain variable region
comprising the amino acid sequence of SEQ ID NO: 135,
or CDR1 consisting of an amino acid sequence that

differs from the amino acid sequence of the CDR1 contained in the heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 135 by having amino acid modification of one to three amino acid residues,

CDR2 contained in a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 135, or CDR2 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR2 contained in the heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 135 by having amino acid modification of one to three amino acid residues, and

CDR3 contained in a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 135, or CDR3 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR3 contained in the heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 135 by having amino acid modification of one to three amino acid residues; and

a light chain variable region that contains

CDR1 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 136, or CDR1 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR1 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 136 by having amino acid modification of one to three amino acid residues,

CDR2 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 136, or CDR2 consisting of an amino acid sequence that

differs from the amino acid sequence of the CDR2 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 136 by having amino acid modification of one to three amino acid residues, and

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CDR3 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 136, or CDR3 consisting of an amino acid sequence that differs from the amino acid sequence of the CDR3 contained in the light chain variable region comprising the amino acid sequence of SEQ ID NO: 136 by having amino acid modification of one to three amino acid residues.

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11. The antibody of claim 1 or 10, wherein the antibody comprises

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a heavy chain variable region that contains

CDR1 comprising the amino acid sequence of SEQ ID NO: 143 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 143 by having amino acid modification of one to three amino acid residues,

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CDR2 comprising the amino acid sequence of SEQ ID NO: 144 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 144 by having amino acid modification of one to three amino acid residues, and

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CDR3 comprising the amino acid sequence of SEQ ID NO: 145 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 145 by having amino acid modification of one to three amino acid residues; and

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a light chain variable region that contains

CDR1 comprising the amino acid sequence of SEQ ID NO: 146 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 146 by having amino acid modification of one to three amino acid residues,

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CDR2 comprising the amino acid sequence of SEQ ID NO: 147 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 147 by having amino acid modification of one to three amino acid residues, and

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CDR3 comprising the amino acid sequence of SEQ ID NO: 148 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 148 by having amino acid modification of one to three amino acid residues.

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12. The antibody of any one of claims 1, 10 and 11, wherein the antibody comprises

a heavy chain variable region that contains

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CDR1 comprising the amino acid sequence of SEQ ID NO: 143,

CDR2 comprising the amino acid sequence of SEQ ID NO: 144, and

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CDR3 comprising the amino acid sequence of SEQ ID NO: 145, and

a light chain variable region that contains

CDR1 comprising the amino acid sequence of SEQ ID NO: 146,

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CDR2 comprising the amino acid sequence of SEQ ID NO: 147, and

CDR3 comprising the amino acid sequence of SEQ ID NO: 148.

13. The antibody of any one of claims 1 and 10 to 12, wherein the antibody comprises CDR1, CDR2, and CDR3 contained in a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 135, and CDR1, CDR2, and
5 CDR3 contained in a light chain variable region comprising the amino acid sequence of SEQ ID NO: 136.

14. The antibody of any one of claims 1 to 13, wherein the antibody comprises
10 a heavy chain variable region comprising an amino acid sequence having 90% or more sequence identity to the amino acid sequence of SEQ ID NO: 8, or the amino acid sequence of SEQ ID NO: 8 or an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 8 by having amino
15 acid modification of 1 to 20 amino acid residues; and
a light chain variable region comprising an amino acid sequence having 90% or more sequence identity to the amino acid sequence of SEQ ID NO: 9, or the amino acid sequence of SEQ ID NO: 9 or an amino acid sequence that differs from
20 the amino acid sequence of SEQ ID NO: 9 by having amino acid modification of 1 to 20 amino acid residues.

15. The antibody of any one of claims 1 to 14, wherein the antibody comprises a heavy chain variable
25 region comprising the amino acid sequence of SEQ ID NO: 8 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 9.

16. An anti-hGDF15 antibody, wherein the antibody
30 competes for binding to hGDF15 with the antibody of any one of claims 1 to 15.

17. The antibody of claim 16, wherein the antibody competes for binding to hGDF15 with an anti-hGDF15 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 8 and a light chain
5 variable region comprising the amino acid sequence of SEQ ID NO: 9.

18. A polynucleotide encoding the antibody of any one of claims 1 to 17.

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19. An expression vector comprising the polynucleotide of claim 18.

20. A transformed cell comprising the polynucleotide
15 of claim 18.

21. A pharmaceutical composition comprising the antibody of any one of claims 1 to 17.

20 22. The pharmaceutical composition of claim 21,
| ~~wherein the pharmaceutical composition is for use in~~
| treating a disease or symptom associated with GDF15.

| 23. The pharmaceutical composition for use of claim
25 22, wherein the disease or symptom associated with GDF15 is cancer.

| 24. The pharmaceutical composition for use of claim
22, wherein the disease or symptom associated with GDF15 is
30 cachexia.

| 25. The pharmaceutical composition for use of claim
24, wherein the cachexia is cancer cachexia.

26. The pharmaceutical composition of claim 21,
~~wherein the pharmaceutical composition is for use in~~
decreasing blood GDF15 concentration.

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27. Use of the antibody of any one of claims 1 to 17
in the manufacture of a medicament for treating a disease
or symptom associated with GDF15.

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28. The use of claim 27, wherein the disease or
symptom associated with GDF15 is cancer.

29. The use of claim 27, wherein the disease or
symptom associated with GDF15 is cachexia.

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30. The use of claim 29, wherein the cachexia is
cancer cachexia.

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31. Use of the antibody of any one of claims 1 to 17
in the manufacture of a medicament for decreasing blood
GDF15 concentration.