CLAIMS

1. An antibody or an antibody fragment thereof which binds to FGF23, wherein the antibody comprises a heavy chain variable region (hereinafter, described as VH) comprising the amino acid sequence represented by SEQ ID NO: 1 and a light chain variable region (hereinafter, described as VL) comprising the amino acid sequence represented by SEQ ID NO: 2, and wherein at least the amino acid residue at position 100 or the amino acid residue at position 105 of the amino acid sequence represented by SEQ ID NO: 1 in the VH is substituted with another amino acid residue.

2. The antibody or the antibody fragment thereof according to claim 1, wherein the amino acid residue at position 100 of the amino acid sequence represented by SEQ ID NO: 1 in the VH is substituted with one amino acid residue selected from alanine residue, asparagine residue, glycine residue, tyrosine residue, arginine residue, aspartic acid residue, histidine residue, tryptophan residue, and methionine residue.

3. The antibody or the antibody fragment thereof according to claim 1 or 2, wherein the amino acid residue at position 100 of the amino acid sequence represented by SEQ ID NO: 1 in the VH is substituted with alanine residue or tyrosine residue.

4. The antibody or the antibody fragment thereof according to any one of claims 1 to 3, wherein the amino acid residue at position 105 of the amino acid sequence represented by SEQ ID NO: 1 in the VH is substituted with one amino acid residue selected from alanine residue, phenylalanine residue, glycine residue, histidine residue, isoleucine residue, lysine residue, leucine residue, methionine residue, proline residue, glutamine residue, arginine residue, valine residue, tryptophan residue, tyrosine residue, threonine residue, asparagine residue, and serine residue.

5. The antibody or the antibody fragment thereof according to any one of claims 1 to 4, wherein the antibody further comprises one substitution selected from the following (a1) to (a4):

(a1) at least one substitution selected from substitution of the amino acid residue at position 50 with leucine residue, substitution of the amino acid residue at position 54 with

tryptophan residue, substitution of the amino acid residue at position 55 with histidine residue, substitution of the amino acid residue at position 57 with threonine residue, and substitution of the amino acid residue at position 58 with phenylalanine residue in the amino acid sequence represented by SEQ ID NO: 1 in the VH,

(a2) at least one substitution selected from substitution of the amino acid residue at position 91 with methionine residue or leucine residue, substitution of the amino acid residue at position 92 with tyrosine residue, substitution of the amino acid residue at position 94 with aspartic acid residue, and substitution of the amino acid residue at position 96 with asparagine residue or aspartic acid residue in the amino acid sequence represented by SEQ ID NO: 2 in the VL,

(a3) at least one substitution selected from substitution of the amino acid residue at position 28 with aspartic acid residue, substitution of the amino acid residue at position 29 with valine residue, substitution of the amino acid residue at position 31 with threonine residue, and substitution of the amino acid residue at position 34 with leucine residue in the amino acid sequence represented by SEQ ID NO: 2 in the VL, and

(a4) at least one substitution selected from substitution of the amino acid residue at position 92 with tyrosine residue or tryptophan residue, substitution of the amino acid residue at position 94 with aspartic acid residue, and substitution of the amino acid residue at position 96 with aspartic acid residue in the amino acid sequence represented by SEQ ID NO: 2 in the VL.

6. The antibody or the antibody fragment thereof according to any one of claims 1 to 5, wherein the antibody is one selected from the following (c1) to (c10):

(c1) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 39 and a VL comprising the amino acid sequence represented by SEQ ID NO: 2,

(c2) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 47 and a VL comprising the amino acid sequence represented by SEQ ID NO: 2,

(c3) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 3 and a VL comprising the amino acid sequence represented by SEQ ID NO: 44,

(c4) an antibody comprising a VH comprising the amino acid sequence represented

by SEQ ID NO: 6 and a VL comprising the amino acid sequence represented by SEQ ID NO: 44,

(c5) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 3 and a VL comprising the amino acid sequence represented by SEQ ID NO: 45,

(c6) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 6 and a VL comprising the amino acid sequence represented by SEQ ID NO: 45,

(c7) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 3 and a VL comprising the amino acid sequence represented by SEQ ID NO: 46,

(c8) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 6 and a VL comprising the amino acid sequence represented by SEQ ID NO: 46,

(c9) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 3 and a VL comprising the amino acid sequence represented by SEQ ID NO: 58, and

(c10) an antibody comprising a VH comprising the amino acid sequence represented by SEQ ID NO: 6 and a VL comprising the amino acid sequence represented by SEQ ID NO: 59.

7. The antibody or the antibody fragment thereof according to any one of claims 1 to 6, wherein a subclass of the antibody is IgG1, IgG2, IgG3 or IgG4.

8. The antibody or the antibody fragment thereof according to any one of claims 1 to 7, wherein an Fc region of the antibody is one selected from the following (d1) to (d5):

(d1) an Fc region comprising substitution of the amino acid residue at position 252 with tyrosine residue, substitution of the amino acid residue at position 254 with threonine residue, and substitution of the amino acid residue at position 256 with glutamic acid residue according to the EU index,

(d2) an Fc region comprising substitution of the amino acid residue at position 428 with leucine residue, and substitution of the amino acid residue at position 434 with serine residue according to the EU index,

(d3) an Fc region comprising substitution of the amino acid residue at position 308 with proline residue according to the EU index,

(d4) an Fc region comprising substitution of the amino acid residue at position 250 with glutamine residue, and substitution of the amino acid residue at position 428 with leucine residue according to the EU index, and

(d5) an Fc region comprising substitution of the amino acid residue at position 434 with alanine residue according to the EU index.

9. The antibody or the antibody fragment thereof according to any one of claims 1 to 8, wherein a heavy chain constant region of the antibody comprises the amino acid sequence represented by SEQ ID NO: 48, 49, 50, 51 or 52.

10. The antibody or the antibody fragment thereof according to any one of claims 1 to 9, wherein the antibody fragment is one selected from Fab, Fab', $(Fab')_2$, scFv, diabody, dsFv, and a peptide comprising CDR.

11. A nucleic acid comprising a nucleotide sequence that encodes the antibody or the antibody fragment thereof according to any one of claims 1 to 10.

12. A vector comprising the nucleic acid according to claim 11.

13. A transformant cell comprising the vector according to claim 12.

14. A method for producing the antibody or the antibody fragment thereof according to any one of claims 1 to 10, comprising:

culturing the transformant cell according to claim 13 in a medium, and

collecting the antibody or the antibody fragment thereof from a culture.

15. A composition comprising:

the antibody or the antibody fragment thereof according to any one of claims 1 to 10.

16. A therapeutic agent for a disease associated with human FGF23, comprising:

the antibody or the antibody fragment thereof according to any one of claims 1 to 10.

17. Use of the antibody or the antibody fragment thereof according to any one of claims 1 to 10 for the manufacture of a medicament for treating a disease associated with human FGF23.