Claims ~~【CLAIMS】~~

~~【Claim 1】~~

1. A fusion polypeptide, comprising

GDF15 (Growth/differentiation factor 15) or its functional variant, and

Fc region of an immunoglobulin,

w~~W~~herein,

the Fc region of the immunoglobulin is a single chain of ~~IgG1 Fc region or~~ human IgG4 Fc region, and is linked to the N-terminus of the GDF15 or its functional variant, via a flexible peptide linker,

the functional variant of GDF15 is a deletion variant in which at least one of 14 amino acids at positions 1 to 14 of the amino acid sequence of SEQ ID NO: 1 are deleted, the human IgG4 Fc region comprises the amino acid sequence of SEQ ID NO: 7, 8, or 9, and

the flexible peptide linker is represented by (GGGGS)n, wherein ~~(~~n is 1, 2, 3, 4, or 5~~)~~.

~~【Claim 2】~~

~~The fusion polypeptide according to claim 1, wherein the Fc region of the immunoglobulin is human IgG4 Fc region.~~

~~【Claim 3】~~

2. The fusion polypeptide according to claim 1~~2~~, wherein the human IgG4 Fc region

~~(1) comprises the amino acid sequence of SEQ ID NO: 5, or~~

~~(2)~~ further comprises the amino acid sequence of SEQ ID NO: 10 at the N-terminus of the amino acid sequence of SEQ ID NO: ~~5~~7, 8, or 9.

~~【Claim 4】~~

3. The fusion polypeptide according to claim 1~~3~~, wherein the human IgG4 Fc region

~~(1) comprises an amino acid sequence selected from SEQ ID NOs: 6 to 9, or~~

~~(2)~~ further comprises an amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 12 at the N-terminus of an amino acid sequence selected from SEQ ID NOs: ~~6~~7 to 9.

~~【Claim 5】~~

4. The fusion polypeptide according to claim 1, wherein the functional variant of GDF15 comprises the amino acid sequence of SEQ ID NO: 2.

~~【Claim 6】~~

5. The fusion polypeptide according to any one of claims 1 to 4~~5~~, wherein GDF15 or its functional variant linked to the Fc region of the immunoglobulin in the fusion polypeptide has at least 1.5 times increased in vivo half-life, compared to GDF15 or its functional variant which is not linked to Fc region of the immunoglobulin.

~~【Claim 7】~~

6. A fusion polypeptide dimer, comprising two fusion polypeptides of any one of claims 1 to 4~~5~~.

~~【Claim 8】~~

7. A nucleic acid molecule encoding the fusion polypeptide of any one of claims 1 to 4~~5~~.

~~【Claim 9】~~

8. A recombinant vector comprising the nucleic acid molecule of claim 7~~8~~.

~~【Claim 10】~~

9. A recombinant cell comprising the recombinant vector of claim 8~~9~~.

~~【Claim 11】~~

10. A method of preparation of the fusion polypeptide of claim 1, ~~wherein the fusion polypeptide comprises GDF15 or its functional variant and an Fc region of immunoglobulin,~~ the method comprising culturing the recombinant cell of claim 9~~10~~.

~~【Claim 12】~~

11. A method of enhancing in vivo stability of GDF15 or its functional variant, comprising linking a single chain of ~~IgG1 Fc region or~~human IgG4 Fc region to the N-terminus of GDF15 or its functional variant via a flexible peptide linker,

wherein the functional variant of GDF15 is a deletion variant in which at least one of 14 amino acids at positions 1 to 14 of the amino acid sequence of SEQ ID NO: 1 are deleted, the human IgG4 Fc region comprises the amino acid sequence of SEQ ID NO: 7, 8, or 9, and the flexible peptide linker is represented by (GGGGS)n ~~((SEQ ID NO: 13)n~~, wherein n is 1, 2, 3, 4, or 5~~)~~.

~~【Claim 13】~~

~~The method for enhancing in vivo stability of GDF15 or its functional variant according to claim 12, wherein the Fc region of the immunoglobulin is human IgG4 Fc region.~~

~~【Claim 14】~~

12. The method for enhancing in vivo stability of GDF15 or its functional variant according to claim 1~~3~~, wherein the human IgG4 Fc region

~~(1) comprises the amino acid sequence of SEQ ID NO: 5, or~~

~~(2)~~ further comprises the amino acid sequence of SEQ ID NO: 10 at the N-terminus of the amino acid sequence of SEQ ID NO: ~~5~~7, 8, or 9.

~~【Claim 15】~~

13. The method for enhancing in vivo stability of GDF15 or its functional variant according to claim 1~~4~~, wherein the human IgG4 Fc region

~~(1) comprises an amino acid sequence selected from SEQ ID NOs: 6 to 9, or~~

~~(2)~~ further comprises an amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 12 at the N-terminus of an amino acid sequence selected from SEQ ID NOs: 7~~6~~ to 9.

~~【Claim 16】~~

14. The method for enhancing in vivo stability of GDF15 or its functional variant according to claim 1~~2~~, wherein the functional variant of GDF15 comprises the amino acid sequence of SEQ ID NO: 2.

~~【Claim 17】~~

15. The method for enhancing in vivo stability of GDF15 or its functional variant according to any one of claims 1~~2~~ to 1~~6~~, wherein GDF15 or its functional variant linked to the Fc region of the immunoglobulin in the fusion polypeptide has at least 1.5 times increased in vivo half-life, compared to GDF15 or its functional variant which is not linked to Fc region of the immunoglobulin.

~~【Claim 18】~~

16. A composition for weight loss, comprising at least one selected from the group consisting of:

the fusion polypeptide of any one of claims 1 to 4~~5~~,

a fusion polypeptide dimer comprising two of the fusion polypeptides,

a nucleic acid molecule encoding the fusion polypeptide,

a recombinant vector comprising the nucleic acid molecule, and

a recombinant cell comprising the recombinant vector.

~~【Claim 19】~~

17. A composition for dietary control, comprising at least one selected from the group consisting of:

the fusion polypeptide of any one of claims 1 to 4~~5~~,

a fusion polypeptide dimer comprising two of the fusion polypeptides,

a nucleic acid molecule encoding the fusion polypeptide,

a recombinant vector comprising the nucleic acid molecule, and

a recombinant cell comprising the recombinant vector,

wherein the dietary control is decrease in size or amount of meal.

~~【Claim 20】~~

18. A pharmaceutical composition for prevention or treatment of metabolic disease, comprising at least one selected from the group consisting of:

the fusion polypeptide of any one of claims 1 to 5,

a fusion polypeptide dimer comprising two of the fusion polypeptides,

a nucleic acid molecule encoding the fusion polypeptide,

a recombinant vector comprising the nucleic acid molecule, and

a recombinant cell comprising the recombinant vector,

wherein the metabolic disease is obesity, diabetes, or nonalcoholic fatty liver disease.

~~【Claim 21】~~

19. The pharmaceutical composition according to claim 18~~20~~, wherein the metabolic disease is obesity~~, diabetes, or nonalcoholic fatty liver disease~~.