

Claims

1. A polypeptide comprising a contiguous amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 1, wherein the polypeptide comprises one of the following pairs of substitutions of the corresponding amino acids in SEQ ID NO: 1:

K91N and D93T/S or D93N and G95T/S;

wherein the polypeptide is suitable for use in the treatment or prevention of a metabolic disease, a metabolic-associated disease, a body weight disorder or a glucose metabolism disorder.

2. The polypeptide of claim 1, wherein the contiguous amino acid sequence is at least 95% identical to the amino acid sequence of SEQ ID NO: 1.

3. The polypeptide of claim 1, wherein the contiguous amino acid sequence is at least 97% identical to the amino acid sequence of SEQ ID NO: 1.

4. The polypeptide of any one of claims 1 to 3, wherein the polypeptide lacks the first three amino acids present at the N-terminus of SEQ ID NO: 1.

5. The polypeptide of any one of claims 1 to 4, comprising the amino acid sequence set forth in SEQ ID NO: 30.

6. The polypeptide of any one of claims 1 to 5, wherein the polypeptide is fused to a heterologous polypeptide.

7. The polypeptide of claim 6, wherein the heterologous polypeptide is serum albumin, maltose binding protein, or immunoglobulin Fc polypeptide, and wherein the heterologous polypeptide is conjugated to the N-terminus of the polypeptide or the C-terminus of the polypeptide.

8. A dimer comprising the polypeptide of any one of claims 1 to 7.

9. The dimer of claim 8, which is (a) a homodimer and/or (b) N-glycosylated.
10. The dimer of claim 8 or claim 9, which is a modified GDF15 N-glycosylated dimer, which is a homodimer having two polypeptides each comprising the same amino acid sequences, wherein the polypeptides contain at least one N-glycosylation site that is N-glycosylated.
11. The dimer of any one of claims 8 to 10, wherein said dimer comprises two polypeptides each consisting of the amino acid sequence set forth in SEQ ID NO: 30.
12. A nucleic acid molecule encoding the polypeptide of any one of claims 1 to 7 or the dimer of any one claims 8 to 11.
13. A vector comprising the nucleic acid molecule of claim 12, wherein the nucleic acid molecule is operably linked to an expression control element that confers expression of the nucleic acid molecule in vitro or in vivo.
14. The vector of claim 13, wherein the vector comprises a viral vector.
15. A host cell that expresses the polypeptide of any one of claims 1 to 7 or the dimer of any one of claims 8 to 11.
16. A pharmaceutical composition, comprising the polypeptide of any one of claims 1 to 7 or the dimer of any one of claims 8 to 11, and a pharmaceutically acceptable diluent, carrier or excipient.
17. A sterile container comprising the pharmaceutical composition of claim 16.
18. The sterile container of claim 17, wherein the sterile container is a syringe.
19. A method of making the polypeptide of any one of claims 1 to 7 or the dimer of any one of claims 8 to 11, the method comprising:
culturing a host cell expressing the polypeptide or dimer; and

purifying the expressed polypeptide or dimer.

20. The polypeptide of any one of claims 1 to 7 the dimer of any one of claims 8 to 11, or the pharmaceutical composition of claim 16, for use in a method of treating or preventing a metabolic disease, a metabolic-associated disease, a body weight disorder or a glucose metabolism disorder in a subject.

21. The polypeptide, dimer or pharmaceutical composition for use according to claim 20, wherein the glucose metabolism disorder is diabetes mellitus, hyperglycemia, hyperinsulinemia, glucose intolerance or metabolic syndrome.

22. The polypeptide, dimer or pharmaceutical composition for use according to claim 20 or claim 21, wherein the subject is human.

23. The polypeptide, dimer or pharmaceutical composition for use according to any one of claims 20 to 21, wherein the subject is obese.