Claims

1. A fusion protein comprising the polypeptide with structure A-B-C or C-B-A or A-B-C-B-C or A-B-C-B or A-C-B-C, wherein

A is a GLP-1R (glucagon-like peptide-1 receptor) agonist and

C is an FGF-21 (fibroblast growth factor 21) compound and

B is a linker comprising an Fc portion of an immunoglobulin comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, and SEQ ID NO: 85.

2. The fusion protein according to claim 1, wherein the FGF-21 compound is selected from the group of native FGF-21, FGF-21 mimetic and SEQ ID NO: 3.

3. The fusion protein according to claim 2, wherein the FGF-21 mimetic is selected from a protein having at least 80% amino acid sequence identity to the amino acid sequence shown in SEQ ID NO: 3 and having FGF-21 activity, a FGF-21 fusion protein and/or a FGF-21 conjugate.

4. The fusion protein according to claim 2, wherein the FGF-21 mimetic is selected from a protein having at least 90% amino acid sequence identity to the amino acid sequence shown in SEQ ID NO: 3 and having FGF-21 activity, a FGF-21 fusion protein and/or a FGF-21 conjugate.

5. The fusion protein according to claim 2, wherein the FGF-21 mimetic is selected from a protein having at least 96% amino acid sequence identity to the amino acid sequence shown in SEQ ID NO: 3 and having FGF-21 activity, a FGF-21 fusion protein and/or a FGF-21 conjugate.

6. The fusion protein according to claim 2, wherein the FGF-21 mimetic is selected from a FGF-21 mutein, a FGF-21-Fc fusion protein, a FGF-21-HSA fusion protein and/or a PEGylated FGF-21.

7. The fusion protein according to claim 1, wherein the GLP-1R agonist is selected from a bioactive GLP-1, a GLP-1 analogue or a GLP-1 substitute.

8. The fusion protein according to claim 7, wherein the GLP-1R agonist is selected from GLP-1(7-37), GLP-1(7-36)amide, exendin-4, liraglutide, CJC-1131, albugon, albiglutide, exenatide, exenatide-LAR, oxyntomodulin, or lixisenatide.

9. The fusion protein according to claim 1, wherein C is an FGF-21 mutein and A is exenatide, exendin-4 or lixisenatide.

10. The fusion protein according to claim 9, wherein C is an FGF-21 mutein comprising or consisting of SEQ ID NO: 102.

11. The fusion protein according to claim 10, wherein A is exenatide.

12. The fusion protein according to claim 11 for use as a medicament.

13. A pharmaceutical composition comprising the fusion protein of claim 1 together with a pharmaceutically acceptable excipient.

14. A pharmaceutical composition comprising the fusion protein of claim 1 together with a pharmaceutically acceptable excipient for use as a medicament.

15. Article of manufacture comprising

a) a pharmaceutical composition according to claim 13 and

b) a container or packaging material.

16. Use of a fusion protein of claim 1 for the manufacture of a medicament for treating a cardiovascular disease and/or diabetes mellitus and/or at least one metabolic syndrome which increases the risk of developing a cardiovascular disease and/or diabetes mellitus, wherein the metabolic syndrome is selected from dyslipidemia, fatty liver disease (FLD), dysglycemia, impaired glucose tolerance (IGT), and/or obesity.

17. The use of claim 16, wherein the diabetes mellitus is Type 2-diabetes.

18. Use of a fusion protein of claim 1 for the manufacture of a medicament for treating hyperlipidemia and/or hyperglycemia.

19. A nucleic acid encoding the fusion protein according to claim 1.

20. A vector comprising the nucleic acid of claim 19 suitable for expression of the encoded protein in a eukaryotic or prokaryotic host.

21. A cell stably or transiently carrying the vector of claim 20 and capable of expressing the fusion protein according to claim 1 under appropriate culture conditions.

22. A method of preparing the fusion protein of claim 1 comprising

a) cultivating a culture of cells of claim 21 under appropriate culture conditions for the fusion protein to be expressed in the cells, or

b) harvesting or purifying the fusion protein from a culture comprising cells of claim 21 that have been cultivated under appropriate conditions for the fusion protein to be expressed, or

c) cultivating the cells according to step a) and purifying the fusion protein according to step b).