

WHAT IS CLAIMED IS:

1. An isolated polypeptide comprising the amino acid sequence:
HAibEGS-(α MeF)TSDV-(α MeS)SX13LE-GEAA(α MeK)-
E(α MeF)IAX25-VVEGG
X13 is a lipid modified K, and
X25 is a lipid modified K.
2. The polypeptide of claim 1, wherein the peptide comprises a C-terminal amide.
3. The polypeptide of claim 1, wherein the two lipid modified K residues are the same or are different, and are selected from the group consisting of: K(ϵ -(PEG)₂-(PEG)₂- γ E-Lauroyl), K(ϵ -(PEG)₂-(PEG)₂- γ E-Myristoyl), K(ϵ -(PEG)₂-(PEG)₂- γ E-Palmitoyl), K(ϵ -(PEG)₂-(PEG)₂- γ E-Stearoyl), and any combination thereof.
4. The polypeptide of claim 1, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 405, SEQ ID NO: 408, SEQ ID NO: 409, or SEQ ID NO: 410.
5. A pharmaceutical composition comprising the polypeptide of claim 1 and a carrier.

6. The polypeptide according to any one of claims 1 to 4 or the composition according to claim 5 for use in therapy.

7. The polypeptide according to any one of claims 1 to 4 or the composition according to claim 5 for use as a medicament.

8. The polypeptide according to any one of claims 1 to 4 or the composition according to claim 5 for use in the treatment or prevention of a disease or condition caused or characterized by hypoglycemia or impaired insulin release, wherein an effective amount of the polypeptide or the composition is to be administered to a subject in need of treatment.

9. The polypeptide or composition for use according to claim 8, wherein the disease or condition is diabetes.

10. The polypeptide or composition for use according to claim 9, wherein the disease or condition is type-2 diabetes.

11. The polypeptide or composition for use according to claim 8, wherein the administration further improves glycemic control, provides body weight control, improves β -cell function and mass, reduces the rate of gastric acid secretion and gastric emptying, or any combination thereof.

12. The polypeptide or composition for use according to claim 8, wherein the polypeptide or the pharmaceutical composition is to be administered orally or by injection.

13. The polypeptide or composition for use according to claim 12, wherein the injection is to be administered subcutaneously or intravenously.

14. The polypeptide or composition for use according to claim 8, wherein the peptide or the pharmaceutical composition is to be administered once per day.

15. The polypeptide or composition for use according to claim 8, wherein the treatment further comprises one or more additional therapies to be administered.

16. The polypeptide or composition for use according to claim 15, wherein the additional therapy comprises blood sugar monitoring, diet modifications, exercise, insulin, a thiazolidinedione, a sulfonylurea, an incretin, metformin, a glyburide, a dipeptidyl peptidase 4 inhibitor, a bile acid sequestrant, or any combination thereof.

17. The polypeptide or composition for use according to claim 16, wherein the subject is human.

18. The use of the polypeptide of any one of claims 1 to 4 or the composition of claim 5 in the manufacture of a medicament for the treatment or prevention of a disease or condition caused or characterized by hypoglycemia or impaired insulin release, wherein an effective amount of the medicament is to be administered to a subject in need of treatment.

19. The use according to claim 18, wherein the disease or condition is diabetes.

20. The use according to claim 19, wherein the diabetes is type-2 diabetes.

21. The use according to claim 19, wherein the administration further improves glycemic control, provides body weight control, improves β -cell function and mass, reduces the rate of gastric acid secretion and gastric emptying, or any combination thereof.

22. The use according to claim 19, wherein the medicament is to be administered orally or by injection.

23. The use according to claim 22, wherein the injection is to be administered subcutaneously or intravenously.

24. The use according to claim 18, wherein the medicament is to be administered once per day.

25. The use according to claim 18, wherein the treatment further comprises one or more additional therapies to be administered.

26. The use according to claim 25, wherein the additional therapy comprises blood sugar monitoring, diet modifications, exercise, insulin, a thiazolidinedione, a sulfonylurea, an incretin, metformin, a glyburide, a dipeptidyl peptidase 4 inhibitor, a bile acid sequestrant, or any combination thereof.

27. The use according to claim 26, wherein the subject is human.