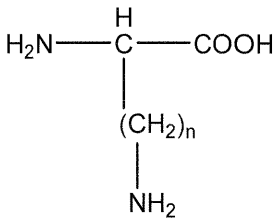
Claims:

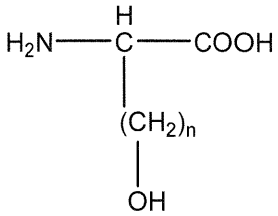
1. A glucagon peptide comprising the amino acid sequence of SEQ ID NO: 1 with up to ten amino acid modifications and comprising an amino acid which is acylated with a C4 to C30 fatty acid at position 10 of the glucagon peptide or alkylated with a C4 to C30 alkyl at position 10 of the glucagon peptide, and amino isobutyric acid (AIB) at position 16 of the glucagon peptide, wherein said glucagon peptide exhibits enhanced activity at the GLP-1 receptor as compared to native glucagon, or a pharmaceutically acceptable salt thereof.

2. The glucagon peptide of claim 1, wherein the amino acid at position 10 of the glucagon peptide is an acylated or alkylated amino acid of Formula I, Formula II, or Formula III, wherein Formula I is



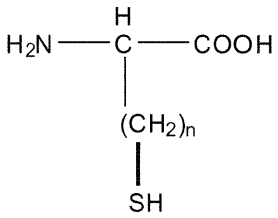
wherein n = 1 to 4;

Formula II is



wherein n = 1 to 4

and Formula III is



wherein n = 1 to 4.

3. The glucagon peptide of claim 2, wherein the amino acid at position 10 is Lys.

4. The glucagon peptide of any one of claims 1 to 3, further comprising a spacer between the amino acid at position 10 of the glucagon peptide and the acyl group or alkyl group.

5. The glucagon peptide of claim 4, wherein the spacer is 3 to 10 atoms in length.

6. The glucagon peptide of claim 5, wherein the spacer is an amino acid or dipeptide or tripeptide.

7. The glucagon peptide of claim 5 or 6, wherein the spacer comprises one or two negatively charged amino acids.

8. The glucagon peptide of any one of claims 1 to 7, wherein the acyl group is a C8 to C20 fatty acyl group.

9. The glucagon peptide of claim 8, wherein the acyl group is a C12 to C18 fatty acyl group.

10. The glucagon peptide of claim 9, wherein the acyl group is a C14 or C16 fatty acyl group.

11. The glucagon peptide of any one of claims 1 to 10, comprising an amino acid substitution at position 1, position 2, or positions 1 and 2, wherein the amino acid substitution(s) achieve dipeptidyl-peptidase IV (DPP-IV) protease resistance.

12. The glucagon peptide of claim 11, wherein the His at position 1 is substituted with an amino acid selected from the group consisting of: D-histidine, alpha, alpha-dimethyl imidiazole acetic acid (DMIA), N-methyl histidine, alpha-methyl histidine, imidazole acetic acid, desaminohistidine, hydroxyl-histidine, acetyl-histidine and homo-histidine.

13. The glucagon peptide of claim 11 or 12, wherein the Ser at position 2 is substituted with an amino acid selected from the group consisting of: D-serine, alanine, D-alanine, valine, glycine, N-methyl serine, N-methyl alanine, and amino isobutyric acid.

14. The glucagon peptide of claim 13, wherein the amino acid at position 2 is AIB.

15. The glucagon peptide of any one of claims 1 to 14, comprising one, two, or three charged amino acids C-terminal to the amino acid at position 27.

16. The glucagon peptide of claim 15, comprising a charged amino acid at position 28 or 29.

17. The glucagon peptide of claim 15 or 16, comprising a charged amino acid after position 29.

18. The glucagon peptide of any one of claims 15 to 17, wherein the charged amino acid is a negatively charged amino acid.

19. The glucagon peptide of claim 18, wherein the charged amino acid is an atypical or non-naturally occurring amino acid.

20. The glucagon peptide of any one of claims 15 to 17, wherein the charged amino acid is a positively charged amino acid.

21. The glucagon peptide of claim 20, wherein the positively charged amino acid is arginine, lysine, or histidine.

22. The glucagon peptide of claim 15 or 16, wherein the amino acid at position 28 is Asp, Asn, or Lys and the amino acid at position 29 is Gly or Thr.

23. The glucagon peptide of any one of claims 1 to 22, further comprising one or more modifications selected from the group consisting of: Gln at position 17, Ala at position 18, Glu at position 21, Ile at position 23, and Ala at position 24.

24. The glucagon peptide of any one of claims 1 to 23, comprising a C-terminal amide.

25. The glucagon peptide of any one of claims 1 to 24, wherein the glucagon peptide comprises a hydrophilic moiety, optionally PEG.

26. The glucagon peptide of claim 1, comprising up to 2, up to 3, up to 4, up to 5, up to 6, up to 7, up to 8 or up to 9 amino acid modifications.

27. The glucagon peptide of any one of claims 1 to 26, wherein the glucagon peptide exhibits a ratio of glucagon/GLP-1 activity of about 1:1, 1.5:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1 or 10:1, or about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, or 1:1.5.

28. The glucagon peptide of any one of claims 1 to 27, wherein the glucagon peptide exhibits (i) at least 10% of the activity of native glucagon at the glucagon receptor and at least 50% of the activity of native GLP-1 at the GLP-1 receptor, (ii) at least 40% of the activity of native glucagon at the glucagon receptor and at least 40% of the activity of native GLP-1 at the GLP-1 receptor, (iii) at least 60% of the activity of native glucagon at the glucagon receptor and at least 60% of the activity of native GLP-1 at the GLP-1 receptor, (iv) about 0.1-10% of the activity of native glucagon at the glucagon receptor and at least 20% of the activity of native GLP-1 at the GLP-1 receptor, or (v) about 1-10% of the activity of native glucagon at the glucagon receptor and at least 20% of the activity of native GLP-1 at the GLP-1 receptor.

29. A conjugate comprising a glucagon peptide of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, wherein the conjugate comprises the glucagon peptide linked to a conjugate moiety.

30. A dimer comprising a glucagon peptide of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, wherein the dimer comprises two glucagon peptides bound to one another through a linker.

31. A fusion peptide comprising a glucagon peptide of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, wherein the fusion peptide comprises a second peptide fused to a terminus of the glucagon peptide.

32. A pharmaceutical composition comprising a glucagon peptide of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, a conjugate of claim 29, a dimer of claim 30, or a fusion peptide of claim 31, and a pharmaceutically acceptable carrier.

33. The pharmaceutical composition of claim 32, further comprising another anti-diabetes or anti-obesity agent.

34. The pharmaceutical composition of claim 33, further comprising insulin, a sulfonylurea, tolbutamide, acetohexamide, tolazamide, chlorpropamide, glipizide, glyburide,

glimepiride, gliclazide, a meglitinide, repaglinide, nateglinide, a biguanide, metformin, phenformin, a thiazolidinedione, rosiglitazone, pioglitazone, troglitazone, a PPAR-γ inhibitor, an alpha glucosidase inhibitor, miglitol, acarbose, exenatide, pramlintide, a dipeptidyl peptidase-4 inhibitor, vildagliptin, sitagliptin, a sodium-dependent glucose transporter 1 inhibitor, a glucokinase activator, a glucagon receptor antagonist, a fructose 1,6-bisphosphatase inhibitor, an appetite suppressant, a phenethylamine type stimulant, phentermine, diethylpropion, phendimetrazine, benzphetamine, sibutramine, rimonabant, a cannabinoid receptor antagonist, oxyntomodulin, fluoxetine, topiramate and phentermine, bupropion and zonisamide, bupropion and naltrexone, a lipase inhibitor, orlistat, cetilistat, or GT 389-255.

35. Use of a glucagon peptide of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, a conjugate of claim 29, a dimer of claim 30, or a fusion peptide of claim 31 in the preparation of a medicament for treating diabetes .

36. Use of a glucagon peptide of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, a conjugate of claim 29, a dimer of claim 30, or a fusion peptide of claim 31 in the preparation of a medicament for reducing weight gain or inducing weight loss.

37. The use of claim 35 or 36, wherein the glucagon peptide, pharmaceutically acceptable salt, conjugate, dimer or fusion peptide is suitable for administering in combination with another anti-diabetes or anti-obesity agent.

38. The use of claim 37, wherein the glucagon peptide, pharmaceutically acceptable salt, conjugate, dimer or fusion peptide is suitable for administering in combination with one or more of insulin, a sulfonylurea, tolbutamide, acetohexamide, tolazamide, chlorpropamide, glipizide, glyburide, glimepiride, gliclazide, a meglitinide, repaglinide, nateglinide, a biguanide, metformin, phenformin, a thiazolidinedione, rosiglitazone, pioglitazone, troglitazone, a PPAR-γ inhibitor, an alpha glucosidase inhibitor, miglitol, acarbose, exenatide, pramlintide, a dipeptidyl peptidase-4 inhibitor, vildagliptin, sitagliptin, a sodium-dependent glucose transporter 1 inhibitor, a glucokinase activator, a glucagon receptor antagonist, a fructose 1,6-bisphosphatase inhibitor, an appetite suppressant, a phenethylamine type stimulant, phentermine, diethylpropion, phendimetrazine, benzphetamine, sibutramine, rimonabant, a cannabinoid receptor antagonist, oxyntomodulin,

fluoxetine, topiramate and phentermine, bupropion and zonisamide, bupropion and naltrexone, a lipase inhibitor, orlistat, cetilistat, or GT 389-255.

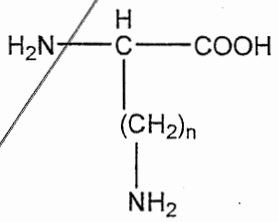
Claims:

1. A glucagon peptide comprising the amino acid sequence of SEQ ID NO: 1 with up to ten amino acid modifications and comprising an amino acid which is acylated or alkylated with a C4 to C30 fatty acid at position 10 of the glucagon peptide and an α, α-disubstituted amino acid at position 16 of the glucagon peptide, wherein said glucagon peptide exhibits enhanced activity at the GLP-1 receptor as compared to native glucagon, or a pharmaceutically acceptable salt thereof.

2. The glucagon peptide of claim 1, wherein the α, α-disubstituted amino acid is an amino acid disubstituted with the same or a different group selected from methyl, ethyl, propyl, n-butyl, cyclooctane, and cycloheptane.

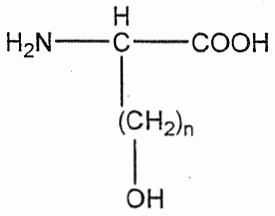
3. The glucagon peptide of claim 2, wherein the α, α-disubstituted amino acid is amino isobutyric acid (AIB).

4. The glucagon peptide of any one of claims 1 to 3, wherein the amino acid at position 10 of the glucagon peptide is an acylated or alkylated amino acid of Formula I, Formula II, or Formula III, wherein Formula I is



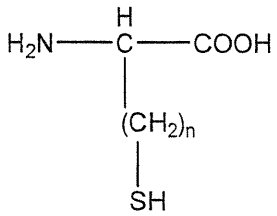
wherein n = 1 to 4;

Formula II is



wherein n = 1 to 4

and Formula III is



wherein n = 1 to 4.

5. The glucagon peptide of claim 4, wherein the amino acid at position 10 is Lys.

6. The glucagon peptide of any one of claims 1 to 5, further comprising a spacer between the amino acid at position 10 of the glucagon peptide and the acyl group or alkyl group.

7. The glucagon peptide of claim 6, wherein the spacer is 3 to 10 atoms in length.

8. The glucagon peptide of claim 7, wherein the spacer is an amino acid or dipeptide or tripeptide.

9. The glucagon peptide of claim 7 or 8, wherein the spacer comprises one or two negatively charged amino acids.

10. The glucagon peptide of any one of claims 1 to 9, wherein the acyl group is a C8 to C20 fatty acyl group.

11. The glucagon peptide of claim 10, wherein the acyl group is a C12 to C18 fatty acyl group.

12. The glucagon peptide of claim 11, wherein the acyl group is a C14 or C16 fatty acyl group.

13. The glucagon peptide of any one of claims 1 to 12, comprising an amino acid substitution at position 1, position 2, or positions 1 and 2, wherein the amino acid substitution(s) achieve dipeptidyl-peptidase IV (DPP-IV) protease resistance.

14. The glucagon peptide of claim 13, wherein the His at position 1 is substituted with an amino acid selected from the group consisting of: D-histidine, alpha, alpha-dimethyl imidiazole acetic acid (DMIA), N-methyl histidine, alpha-methyl histidine, imidazole acetic acid, desaminohistidine, hydroxyl-histidine, acetyl-histidine and homo-histidine.

15. The glucagon peptide of claim13 or 14, wherein the Ser at position 2 is substituted with an amino acid selected from the group consisting of: D-serine, alanine, D-alanine, valine, glycine, N-methyl serine, N-methyl alanine, and amino isobutyric acid.

16. The glucagon peptide of claim 15, wherein the amino acid at position 2 is AIB.

17. The glucagon peptide of any one of claims 1 to 16, comprising one, two, or three charged amino acids C-terminal to the amino acid at position 27.

18. The glucagon peptide of claim 17, comprising a charged amino acid at position 28 or 29.

19. The glucagon peptide of claim 17 or 18, comprising a charged amino acid after position 29.

20. The glucagon peptide of any one of claims 17 to 19, wherein the charged amino acid is a negatively charged amino acid.

21. The glucagon peptide of claim 20, wherein the charged amino acid is an atypical or non-naturally occurring amino acid.

22. The glucagon peptide of any one of claims 17 to 19, wherein the charged amino acid is a positively charged amino acid.

23. The glucagon peptide of claim 22, wherein the positively charged amino acid is arginine, lysine, or histidine.

24. The glucagon peptide of claim 17 or18, wherein the amino acid at position 28 is Asp, Asn, or Lys and the amino acid at position 29 is Gly or Thr.

25. The glucagon peptide of any one of claims 1 to 24, wherein the α, α-disubstituted amino acid at position 16 is AIB and the C4 to C30 fatty acid is a C14, C16 or C18 fatty acyl group covalently attached to a Lys at position 10.

26. The glucagon peptide of any one of claims 1 to 25, further comprising one or more modifications selected from the group consisting of: Gln at position 17, Ala at position 18, Glu at position 21, Ile at position 23, and Ala at position 24.

27. The glucagon peptide of any one of claims 1 to 26, comprising a C-terminal amide.

28. The glucagon peptide of any one of claims 1 to 27, wherein the glucagon peptide comprises a hydrophilic moiety, optionally PEG.

29. The glucagon peptide of claim 1, comprising up to 2, up to 3, up to 4, up to 5, up to 6, up to 7, up to 8 or up to 9 amino acid modifications.

30. The glucagon peptide of any one of claims 1 to 29, wherein the glucagon peptide exhibits a ratio of glucagon/GLP-1 activity of about 1:1, 1.5:1, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1 or 10:1, or about 1:10, 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, or 1:1.5.

31. The glucagon peptide of any one of claims 1 to 30, wherein the glucagon peptide exhibits (i) at least 10% of the activity of native glucagon at the glucagon receptor and at least 50% of the activity of native GLP-1 at the GLP-1 receptor, (ii) at least 40% of the activity of native glucagon at the glucagon receptor and at least 40% of the activity of native GLP-1 at the GLP-1 receptor, (iii) at least 60% of the activity of native glucagon at the glucagon receptor and at least 60% of the activity of native GLP-1 at the GLP-1 receptor, (iv) about 0.1-10% of the activity of native glucagon at the glucagon receptor and at least 20% of the activity of native GLP-1 at the GLP-1 receptor, or (v) about 1-10% of the activity of native glucagon at the glucagon receptor and at least 20% of the activity of native GLP-1 at the GLP-1 receptor.

32. A conjugate comprising a glucagon peptide of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, wherein the conjugate comprises the glucagon peptide linked to a conjugate moiety.

33. A dimer comprising a glucagon peptide of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, wherein the dimer comprises two glucagon peptides bound to one another through a linker.

34. A fusion peptide comprising a glucagon peptide of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, wherein the fusion peptide comprises a second peptide fused to a terminus of the glucagon peptide.

35. A pharmaceutical composition comprising a glucagon peptide of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, a conjugate of claim 32, a dimer of claim 33, or a fusion peptide of claim 34, and a pharmaceutically acceptable carrier.

36. The pharmaceutical composition of claim 35, further comprising another anti-diabetes or anti-obesity agent.

37. The pharmaceutical composition of claim 36, further comprising insulin, a sulfonylurea, tolbutamide, acetohexamide, tolazamide, chlorpropamide, glipizide, glyburide, glimepiride, gliclazide, a meglitinide, repaglinide, nateglinide, a biguanide, metformin, phenformin, a thiazolidinedione, rosiglitazone, pioglitazone, troglitazone, a PPAR-γ inhibitor, an alpha glucosidase inhibitor, miglitol, acarbose, exenatide, pramlintide, a dipeptidyl peptidase-4 inhibitor, vildagliptin, sitagliptin, a sodium-dependent glucose transporter 1 inhibitor, a glucokinase activator, a glucagon receptor antagonist, a fructose 1,6-bisphosphatase inhibitor, an appetite suppressant, a phenethylamine type stimulant, phentermine, diethylpropion, phendimetrazine, benzphetamine, sibutramine, rimonabant, a cannabinoid receptor antagonist, oxyntomodulin, fluoxetine, topiramate and phentermine, bupropion and zonisamide, bupropion and naltrexone, a lipase inhibitor, orlistat, cetilistat, or GT 389-255.

38. Use of a glucagon peptide of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, a conjugate of claim 32, a dimer of claim 33, or a fusion peptide of claim 34 in the preparation of a medicament for treating diabetes .

39. Use of a glucagon peptide of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, a conjugate of claim 32, a dimer of claim 33, or a fusion peptide of claim 34 in the preparation of a medicament for reducing weight gain or inducing weight loss.

40. The use of claim 38 or 39, wherein the glucagon peptide, pharmaceutically acceptable salt, conjugate, dimer or fusion peptide is suitable for administering in combination with another anti-diabetes or anti-obesity agent.

41. The use of claim 40, wherein the glucagon peptide, pharmaceutically acceptable salt, conjugate, dimer or fusion peptide is suitable for administering in combination with one or more of insulin, a sulfonylurea, tolbutamide, acetohexamide, tolazamide, chlorpropamide, glipizide, glyburide, glimepiride, gliclazide, a meglitinide, repaglinide, nateglinide, a biguanide, metformin,

phenformin, a thiazolidinedione, rosiglitazone, pioglitazone, troglitazone, a PPAR-γ inhibitor, an alpha glucosidase inhibitor, miglitol, acarbose, exenatide, pramlintide, a dipeptidyl peptidase-4 inhibitor, vildagliptin, sitagliptin, a sodium-dependent glucose transporter 1 inhibitor, a glucokinase activator, a glucagon receptor antagonist, a fructose 1,6-bisphosphatase inhibitor, an appetite suppressant, a phenethylamine type stimulant, phentermine, diethylpropion, phendimetrazine, benzphetamine, sibutramine, rimonabant, a cannabinoid receptor antagonist, oxyntomodulin, fluoxetine, topiramate and phentermine, bupropion and zonisamide, bupropion and naltrexone, a lipase inhibitor, orlistat, cetilistat, or GT 389-255.