

Claims

1. An agent comprising:

a) a peptide or a peptide analog comprising no more than 40 amino acid residues

5 selected from the group consisting of:

i) a peptide or peptide analog comprising or consisting of an amino acid sequence selected from the group consisting of KPLAEIDSIELSYGIK (SEQ ID NO: 136), VDTYDGGISVVYGLR (SEQ ID NO: 138), KCLAECDSELSYGIK (cyclic) (SEQ ID NO: 141),
 10 KPLAEDISELSYGIK (SEQ ID NO: 145), KPLAEIGDISELSYGIK (SEQ ID NO: 146), KPLAEIDSELTGYIK (SEQ ID NO: 149), KPLAEIDGISELSYGIK (SEQ ID NO: 150), KPLAEIGSELSYGIK (SEQ ID NO: 152), KGLAEIDSELSYGIK (SEQ ID NO: 153), KPLAGIDSIGLSYGIK (SEQ ID NO: 154); CLAEIDSC (cyclic) (SEQ ID NO: 142), CFKPLAEIDSIECSYGIK (cyclic) (SEQ ID NO: 143),
 15 KPLAEGDISELSYGIK (SEQ ID NO: 147), KPLAEISELSYGIK (SEQ ID NO: 148), KCLAEIDSELSYGIK (cyclic) (SEQ ID NO: 155), CFKPLAEIDSIEC (cyclic) (SEQ ID NO: 156), VDTYDGDGSSVVYGLR (SEQ ID NO: 139), VDVPEGDISLAYGLR (SEQ ID NO: 157),
 20 LDGLVRAYDNISPVG (SEQ ID NO: 158), GDPNGDISVVYGLR (SEQ ID NO: 159), VDVPNGDISLAYRLR (SEQ ID NO: 160), VDVPEGDISLAYRLR (SEQ ID NO: 161), V(beta-D)TYDGDISVVYGLR (SEQ ID NO: 167), VDTY(beta-D)GDISVVYGLR (SEQ ID NO: 168), and VDTYDG(beta-D)ISVVYGLR (SEQ ID NO: 169);

ii) a peptide or peptide analog consisting of the amino acid sequence GDPNDGRGDSVVYGLR (SEQ ID NO: 137); and

iii) a peptide or peptide analog comprising or consisting of the amino acid sequence KPLAEIDGIELTYGIK (SEQ ID NO: 151), wherein the
 30 peptide or peptide analog comprises no more than 25 amino acid residues;

b) a polynucleotide encoding upon expression, the peptide of a);

c) a vector comprising the polynucleotide of b); or

d) a cell comprising the polynucleotide of b), or the vector of c).

35

2. The agent according to claim 1, wherein the agent comprises no more than 26 amino acid residues.
3. The agent according to any one of the preceding claims, wherein the agent is
5 conjugated to a moiety, such as a moiety selected from the group consisting of polyethylene glycol (PEG), monosaccharides, fluorophores, chromophores, radioactive compounds, and cell-penetrating peptides.
4. The agent according to any one of the preceding claims, wherein the agent is further
10 modified such as being glycosylated or by PEGylation, amidation, esterification, acylation, acetylation and/or alkylation.
5. The agent according to any of the preceding claims, wherein the agent is fused to
15 another polypeptide, such as a polypeptide selected from the group consisting of glutathione-S-transferase (GST) and protein A, or to a tag.
6. The agent according to any of the preceding claims, wherein the agent is cyclic.
7. The agent according to any one of the preceding claims, wherein the agent comprises
20 a second or further active ingredient, such as an active ingredient is selected from the group consisting of insulin, glucagon-like peptide-1 (GLP-1), sulfonylurea, a dipeptidyl peptidase-4 (DPP4) inhibitor, an alpha-glucosidase inhibitor, a thiazolidinedione, a meglitinide and a sodium-glucose cotransporter-2 (SGLT2) inhibitor.
8. The agent according to any one of the preceding claims, for use as a medicament.
9. Use of an agent comprising:
 - a) a peptide or a peptide analog comprising no more than 40 amino acid residues
selected from the group consisting of:
30 (i) a peptide or peptide analog comprising or consisting of an amino acid sequence of the general formula:

$$\text{KX}_2\text{LAX}_5\text{X}_6\text{X}_7\text{X}_8\text{IX}_{10}\text{LX}_{12}\text{YGIIK}$$

(SEQ ID NO: 140)

 wherein:
 - 35 X_2 is C, P or G;
 - X_5 is E or G;
 - X_6 is C, D or I;

X₇ is D, I, S or G;

X₈ is S, D or G;

X₁₀ is E or G;

X₁₂ is S or T;

- 5 with the proviso that if X₁₂ is T, the peptide comprises no more than 25 amino acid residues;
- (ii) a peptide or peptide analog comprising or consisting of an amino acid sequence selected from the group consisting of VDTYDGGISVVYGLR (SEQ ID NO: 138), VDTYDGDISVVYGLR (SEQ ID NO: 1), VDTYDGDISVVYGL (SEQ ID NO: 3), VDTYDGDISVVYG (SEQ ID NO: 6), GDISVVYGLR (SEQ ID NO: 26), VDTYDGDIS (SEQ ID NO: 28), VDTYDGRGDSVVYGLR (SEQ ID NO: 67), VDVPNGDISLAYGLR (SEQ ID NO: 69), VDVPNGDISLAYGL (SEQ ID NO: 71) DVPNGDISLAYGLR (SEQ ID NO: 72), VDVPNGDISLAYG (SEQ ID NO: 74), PNGDISLAYGLR (SEQ ID NO: 81), VDVPNGDISLA (SEQ ID NO: 83), GDISLAYGLR (SEQ ID NO: 94), VDVPNGDIS (SEQ ID NO: 96), CLAEIDSC (cyclic) (SEQ ID NO: 142), CFKPLAEIDSIECSYGIK (cyclic) (SEQ ID NO: 143), KPLAEGDIELSYGIK (SEQ ID NO: 147), KPLAEIELSYGIK (SEQ ID NO: 148), KCLAEIDSCIELSYGIK (cyclic) (SEQ ID NO: 155) and CFKPLAEIDSIEC (cyclic) (SEQ ID NO: 156); and
- 10 (iii) a peptide or peptide analog consisting of the amino acid sequence GDPNDGRGDSVVYGLR (SEQ ID NO: 137);
- b) a polynucleotide encoding upon expression, the peptide of a);
- c) a vector comprising the polynucleotide of b); or
- 15 d) a cell comprising the polynucleotide of b), or the vector of c);
- 25 in the manufacture of a medicament for treatment of an endocrine disease and/or a metabolic disease in a mammal, such as a human, wherein the endocrine disease and/or a metabolic disease is selected from the group consisting of diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, malnutrition-related diabetes mellitus, specified diabetes mellitus, unspecified diabetes mellitus, disorders of glucose regulation and pancreatic internal secretion, insulin resistance syndrome, impaired glucose tolerance, hyperglycemia, hyperinsulinemia, and any combinations thereof.
- 30

10. The use according to claim 9, wherein the peptide or peptide analog of the general formula of SEQ ID NO: 140 comprises or consists of an amino acid sequence selected
- 35

from the group consisting of KPLAEIDSIELSYGIK (SEQ ID NO: 136), KCLAECDSIELSYGIK (cyclic) (SEQ ID NO: 141), KPLAEDISIELSYGIK (SEQ ID NO: 145), KPLAEIGDIELSYGIK (SEQ ID NO: 146), KPLAEIDSIELTYGIK (SEQ ID NO: 149), KPLAEIDGIELSYGIK (SEQ ID NO: 150), KPLAEIDGIELTYGIK (SEQ ID NO: 151), KPLAEIGSIELSYGIK (SEQ ID NO: 152), KGLAEIDSIELSYGIK (SEQ ID NO: 153), and KPLAGIDSIGLSYGIK (SEQ ID NO: 154).

11. The use according to any of claims 9 to 10, wherein the agent comprises no more than 26 amino acid residues.

12. The use according to any of claims 9 to 11, wherein the agent is cyclic.

13. The use according to any one of claims 9 to 12, wherein said agent comprises a second or further active ingredient, such as an active ingredient is selected from the group consisting of insulin, glucagon-like peptide-1 (GLP-1), sulfonylurea, a dipeptidyl peptidase-4 (DPP4) inhibitor, an alpha-glucosidase inhibitor, a thiazolidinedione, a meglitinide and a sodium-glucose cotransporter-2 (SGLT2) inhibitor.