【CLAIMS】

【Claim 1】

A pharmaceutical composition for treating or preventing metabolic syndromes comprising i) a peptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS: 13, 15, and 36 to 44 and ii) at least one compound or material having a therapeutic activity for metabolic syndrome.

【Claim 2】

The pharmaceutical composition of claim 1, wherein the peptide comprising the amino acid sequence as defined in claim 1 is a glucagon derivative capable of activating a glucagon receptor.

【Claim 3】

The pharmaceutical composition of claim 1, wherein the compound or material having a therapeutic activity for metabolic syndrome is selected from the group consisting of an insulinotropic peptide, a glucagon-like peptide-1 (GLP-1) receptor agonist, a leptin receptor agonist, a dipeptidyl peptidase-IV (DPP-IV) inhibitor, a Y5 receptor antagonist, a melanin-concentrating hormone (MCH) receptor antagonist, a Y2/4 receptor agonist, a melanocortin 3/4 (MC 3/4) receptor agonist, a gastric/pancreatic lipase inhibitor, an agonist of 5-hydroxytryptamine receptor 2C (5HT2C), a β3A receptor agonist, an amylin receptor agonist, a ghrelin antagonist, a ghrelin receptor antagonist, a peroxisome proliferator-activated receptor alpha (PPARα) agonist, a peroxisome proliferator-activated receptor delta (PPARδ) agonist, a Farnesoid X receptor (FXR) agonist, an acetyl-CoA carboxylase inhibitor, a peptide YY, cholecystokinin (CCK), xenin, glicentin, obestatin, secretin, nesfatin, insulin, and a glucose-dependent insulinotropic peptide (GIP).

【Claim 4】

The pharmaceutical composition of claim 3, wherein the insulinotropic peptide is selected from the group consisting of GLP-1, exendin-3, exendin-4, an agonist thereof, a

derivative thereof, a fragment thereof, a variant thereof, and a combination thereof.

【Claim 5】

The pharmaceutical composition of claim 4, wherein the insulinotropic peptide is an insulinotropic peptide derivative, in which the N-terminal histidine residue is substituted with one selected from the group consisting of desamino-histidyl, N-dimethyl-histidyl, β-hydroxy imidazopropionyl, 4-imidazoacetyl, and β-carboxy imidazopropionyl.

【Claim 6】

The pharmaceutical composition of claim 4, wherein the insulinotropic peptide is selected from the group consisting of a native exendin-4; an exendin-4 derivative in which the N-terminal amine group of exendin-4 is deleted; an exendin-4 derivative in which the N-terminal amine group of exendin-4 is substituted with a hydroxyl group; an exendin-4 derivative in which the N-terminal amine group of exendin-4 is modified with a dimethyl group; an exendin-4 derivative in which the α-carbon of the 1^{st} amino acid of exendin-4, histidine, is deleted; an exendin-4 derivative in which the 12^{th} amino acid of exendin-4, lysine, is substituted with serine, and an exendin-4 derivative in which the 12^{th} amino acid of exendin-4, lysine, is substituted with arginine.

【Claim 7】

The pharmaceutical composition of claim 3, wherein:

the peptide comprising the amino acid sequence as defined in claim 1is in the form of a long-acting conjugate, to which a biocompatible material capable of increasing *in vivo* half-life of the peptide is linked; and

the insulinotropic peptide is in the form of a long-acting conjugate, to which a biocompatible material capable of increasing *in vivo* half-life of the insulinotropic peptide is linked.

【Claim 8】

The pharmaceutical composition of claim 7, wherein the biocompatible material is

selected from the group consisting of polyethylene glycol, fatty acid, cholesterol, albumin and a fragment thereof, an albumin-binding material, a polymer of repeating units of a particular amino acid sequence, an antibody, an antibody fragment, an FcRn-binding material, *in vivo* connective tissue or a derivative thereof, a nucleotide, fibronectin, transferrin, a saccharide, and a polymer.

【Claim 9】

The pharmaceutical composition of claim 7, wherein the peptide comprising the amino acid sequence as defined in claim 1and the insulinotropic peptide are respectively linked to a biocompatible material by a linker selected from the group consisting of polyethylene glycol, polypropylene glycol, an ethylene glycol-propylene glycol copolymer, polyoxyethylated polyol, polyvinyl alcohol, a polysaccharide, dextran, polyvinyl ethyl ether, a biodegradable polymer including polylactic acid (PLA) or polylactic-glycolic acid (PLGA), lipid polymer, chitin, hyaluronic acid, fatty acid, a polymer, a low molecular weight compound, a nucleotide, and a combination thereof.

【Claim 10】

The pharmaceutical composition of claim 7,

wherein the biocompatible material is an FcRn-binding material, and

the peptide comprising the amino acid sequence as defined in claim 1and the insulinotropic peptide are respectively linked to a biocompatible material by a peptide linker or a non-peptide linker selected from the group consisting of polyethylene glycol, polypropylene glycol, an ethylene glycol-propylene glycol copolymer, polyoxyethylated polyol, polyvinyl alcohol, a polysaccharide, dextran, polyvinyl ethyl ether, a biodegradable polymer including polylactic acid (PLA) or polylactic-glycolic acid (PLGA), lipid polymer, chitin, hyaluronic acid, and a combination thereof.

【Claim 11】

The pharmaceutical composition of claim 10, wherein the FcRn-binding material is a polypeptide comprising an immunoglobulin Fc region.

【Claim 12】

The pharmaceutical composition of claim 11, wherein the immunoglobulin Fc region is aglycosylated.

【Claim 13】

The pharmaceutical composition of claim 11, wherein the immunoglobulin Fc region is selected from the group consisting of:

(a) a CH1 domain, a CH2 domain, a CH3 domain, and a CH4 domain;

(b) a CH1 domain and a CH2 domain;

(c) a CH1 domain and a CH3 domain;

(d) a CH2 domain and a CH3 domain;

(e) a combination between one or at least two domains among a CH1 domain, a CH2 domain, a CH3 domain, and a CH4 domain, and an immunoglobulin hinge region or a part of the hinge region; and

(f) a dimer between each domain of the heavy chain constant region and the light chain constant region.

【Claim 14】

The pharmaceutical composition of claim 11, wherein the polypeptide comprising the immunoglobulin Fc region is in the form of a dimer.

【Claim 15】

The pharmaceutical composition of claim 11, wherein the immunoglobulin Fc region is a native Fc derivative in which the region capable of forming a disulfide bond is deleted, a native Fc derivative in which a part of the amino acid(s) in the N-terminus is removed, a native Fc derivative in which a methionine is added to the N-terminus, a native Fc derivative in which a complement-binding site is deleted, or a native Fc derivative in which an antibody dependent cell mediated cytotoxicity (ADCC) site is deleted.

【Claim 16】

The pharmaceutical composition of claim 11, wherein the immunoglobulin Fc region is derived from an immunoglobulin selected from the group consisting of IgG, IgA, IgD, IgE, and IgM.

【Claim 17】

The pharmaceutical composition of claim 16, wherein the immunoglobulin Fc region is an IgG4 Fc region.

【Claim 18】

The pharmaceutical composition of claim 11, wherein the immunoglobulin Fc region is an aglycosylated Fc region derived from human IgG4.

【Claim 19】

The pharmaceutical composition of claim 10, wherein the non-peptide linker is linked to the cysteine residue of the peptide.

【Claim 20】

The pharmaceutical composition of claim 10, wherein both ends of the non-peptide linker are respectively linked to an amine group or a thiol group of the peptidewhich comprises the amino acid sequence as defined in claim 1 or an insulinotropic peptide, and a biocompatible material.

【Claim 21】

The pharmaceutical composition of claim 1, wherein the metabolic syndrome is selected from the group consisting of impaired glucose tolerance, hypercholesterolemia, dyslipidemia, obesity, diabetes, hypertension, nonalcoholic steatohepatitis (NASH), atherosclerosis caused by dyslipidemia, atherosclerosis, arteriosclerosis, coronary heart disease, and stroke.

【Claim 22】

An isolated peptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS: 13, 15, and 36 to 44.

【Claim 23】

The peptide of claim 22, wherein the C-terminus of the peptide is amidated.

【Claim 24】

The peptide of claim 22, wherein the peptide is a glucagon derivative capable of activating a glucagon receptor.

【Claim 25】

An isolated polynucleotide encoding the isolated peptide of any of claims 22 to 24.

【Claim 26】

A vector comprising the isolated polynucleotide of claim 25.

【Claim 27】

An isolated conjugate, wherein the isolated peptide of claim 22 and a biocompatible material capable of increasing *in vivo* half-life are linked.

【Claim 28】

The isolated conjugate of claim 27, wherein the biocompatible material is selected from the group consisting of polyethylene glycol, fatty acid, cholesterol, albumin and a fragment thereof, an albumin-binding material, a polymer of repeating units of a particular amino acid sequence, an antibody, an antibody fragment, an FcRn-binding material, *in vivo* connective tissue or a derivative thereof, a nucleotide, fibronectin, transferrin, a saccharide, and a polymer.

【Claim 29】

The isolated conjugate of claim 27, wherein the peptide is linked to a biocompatible material by a linker selected from the group consisting of polyethylene glycol, polypropylene glycol, an ethylene glycol-propylene glycol copolymer, polyoxyethylated polyol, polyvinyl alcohol, a polysaccharide, dextran, polyvinyl ethyl ether, a biodegradable polymer including polylactic acid (PLA) or polylactic-glycolic acid (PLGA), lipid polymer, chitin, hyaluronic acid, fatty acid, a polymer, a low molecular weight compound, a nucleotide, and a combination thereof.

【Claim 30】

The isolated conjugate of claim 27,

wherein the biocompatible material is an FcRn-binding material, and

the isolated peptide is linked to a biocompatible material by a peptide linker or a non-peptide linker selected from the group consisting of polyethylene glycol, polypropylene glycol, an ethylene glycol-propylene glycol copolymer, polyoxyethylated polyol, polyvinyl alcohol, a polysaccharide, dextran, polyvinyl ethyl ether, a biodegradable polymer including polylactic acid (PLA) or polylactic-glycolic acid (PLGA), lipid polymer, chitin, hyaluronic acid, and a combination thereof.

【Claim 31】

The isolated conjugate of claim 30, wherein the FcRn-binding material is a polypeptide comprising an immunoglobulin Fc region.

【Claim 32】

A composition comprising the isolated peptide of claim 22 or the isolated conjugate of claim 32.

【Claim 33】

The composition of claim 32, which is a pharmaceutical composition for treating or

preventing hypoglycemia or metabolic syndrome.