Claims

[Claim 1]

A protein conjugate, characterized in that the protein conjugate comprises:

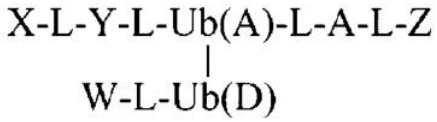
polyubiquitin,

a carrier linked directly or by a linker to the polyubiquitin, and

a biomolecule linked directly or by a linker to the polyubiquitin or the carrier,

wherein the polyubiquitin is composed of (i) an acceptor ubiquitin containing one or more lysines optionally substituted with arginine or alanine, and (ii) a donor ubiquitin in which all lysines of the ubiquitin are substituted with arginine or alanine,

wherein the protein conjugate is represented by the following formula:



wherein X is a glucagon (GCG) analogue composed of the amino acid sequence of SEQ ID NO: 2, Y is a glucagon-like peptide 1 (GLP-1) analogue composed of the amino acid sequence of SEQ ID NO: 12, Z is a fibroblast growth factor (FGF21) analogue composed of the amino acid sequence of SEQ ID NO: 20, and W is a glucose-dependent insulinotropic polypeptide (GIP) analogue composed of the amino acid sequence of SEQ ID NO: 24 or interleukin-1 receptor antagonist (IL-1RA) composed of the amino acid sequence of SEQ ID NO: 27;

Ub(A) is an acceptor ubiquitin;

Ub(D) is a donor ubiquitin;

L is each independently absent or a linker;

A is a carrier; and

Ub(A) and Ub(D) are linked by a covalent bond.

[Claim 2]

The protein conjugate according to claim 1, characterized in that the polyubiquitin is composed of an acceptor ubiquitin in which lysine residues at the 6th, 11th, 27th, 29th, 33rd, and 48th positions from the N-terminus of the ubiquitin are substituted with arginine and a donor ubiquitin in which all lysines of the ubiquitin are substituted with arginine.

[Claim 3]

The protein conjugate according to claim 1, characterized in that the polyubiquitin is composed of an acceptor ubiquitin composed of the amino acid sequence of SEQ ID NO: 30 and a donor ubiquitin composed of the amino acid sequence of SEQ ID NO: 31.

[Claim 4]

The protein conjugate according to claim 1, characterized in that the linker is a polypeptide composed of an amino acid sequence in which 1 to 30 repeats of GGGGS, EAAAK or VPPPPP are combined.

[Claim 5]

The protein conjugate according to claim 4, characterized in that the linker is a polypeptide composed of the amino acid sequence of SEQ ID NO: 29.

[Claim 6]

The protein conjugate according to claim 1, characterized in that the carrier is selected from the group consisting of albumin, antigen-binding fragment of an antibody, scFc (single chain Fc), scFc dimer (single chain Fc-dimer), transferrin, XTEN (genetic fusion of non-exact repeat peptide sequence), CTP (carboxy-terminal peptide), PAS (proline-alanine-serine polymer), ELP (elastin-like peptide), HAP (homo-amino acid polymer), GLK (gelatin-like protein), PEG (polyethylene glycol), and fatty acid.

[Claim 7]

The protein conjugate according to claim 6, characterized in that the carrier is albumin.

[Claim 8]

A pharmaceutical composition for preventing or treating non-alcoholic steatohepatitis, fatty liver, liver fibrosis, cirrhosis, liver cancer, obesity, or diabetes, comprising the protein conjugate according to any one of claims 1 to 7.