Claims

1. An isolated polypeptide having a length of less than 200 amino acids comprising or consisting of an amino acid sequence selected from the group consisting of:
    a. the amino acid sequence according to SEQ ID NO: 4 and/or SEQ ID NO: 19;
    b. a variant of SEQ ID NO: 4 and/or SEQ ID NO: 19, wherein said variant has at least 60%, such as at least 70%, such as at least 75%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 95% sequence identity to SEQ ID NO: 4 and/or SEQ ID NO: 19, but less than 99% sequence identity to SEQ ID NO: 4 and/or SEQ ID NO: 19;
    c. a variant of SEQ ID NO: 4 and/or SEQ ID NO: 19, wherein said variant has between 1 and 40 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19, such as 5, 10, 15, 20, 25, 30, or 35 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19;
    d. a fragment of SEQ ID NO: 4 and/or SEQ ID NO: 19 having a length of at least 10 amino acids, or a variant of said fragment having between 1 and 5 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19, respectively, such as 1, 2 or 3 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19, wherein said polypeptide has a length of less than 50 amino acids;
    e. an amino acid sequence differing from SEQ ID NO: 4 and/or SEQ ID NO: 19 by truncation at the N-terminus by at least one amino acid, such as between 1-67 amino acids, such as between 1-60 amino acids, for example between 1-50 amino acids, such as between 1-40 amino acids, for example between 1-30 amino acids, such as between 1-20 amino acids, for example between 1-10 amino acids, such as between 1-5 amino acids, or a variant thereof having between 1 and 10 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19, such as 1, 2, 3, 4, 5, 6, 7, 8 or 9 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19;
    f. an amino acid sequence differing from SEQ ID NO: 4 and/or SEQ ID NO: 19 by truncation at the C-terminus by at least one amino acid, such as between 1-21 amino acids, such as between 1-20 amino acids, for example between 1-15 amino acids, such as between 1-10 amino acids,

for example between 1-5 amino acids, or a variant thereof having between 1 and 30 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19, such as 1, 5, 10, 15, 20 or 25 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19;

g. an amino acid sequence differing from SEQ ID NO: 4 and/or SEQ ID NO: 19 by truncation at the N-terminus by at least one amino acid, 1-67 amino acids, such as between 1-60 amino acids, for example between 1-50 amino acids, such as between 1-40 amino acids, for example between 1-30 amino acids, such as between 1-20 amino acids, for example between 1-10 amino acids, such as between 1-5 amino acids, and at the C-terminus by at least one amino acid, such as between 1-21 amino acids, such as between 1-20 amino acids, for example between 1-15 amino acids, such as between 1-10 amino acids, for example between 1-5 amino acids, wherein said polypeptide has a length of at least 10 amino acids, or a variant thereof having between 1 and 5 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19, such as 1, 2 or 3 amino acid substitutions relative to SEQ ID NO: 4 and/or SEQ ID NO: 19;

h. the amino acid sequence according to SEQ ID NO: 5 and/or SEQ ID NO: 20;

i. a variant of SEQ ID NO: 5 and/or SEQ ID NO: 20, wherein said variant has at least 70%, such as at least 75%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 95% sequence identity to SEQ ID NO: 5 and/or SEQ ID NO: 20, but less than 99% sequence identity to SEQ ID NO: 5 and/or SEQ ID NO: 20;

j. a variant of SEQ ID NO: 5 and/or SEQ ID NO: 20, wherein said variant has between 1 and 10 amino acid substitutions relative to SEQ ID NO: 5 and/or SEQ ID NO: 20, such as 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions relative to SEQ ID NO: 5 and/or SEQ ID NO: 20, wherein said polypeptide has a length of less than 50 amino acids;

k. a fragment of SEQ ID NO: 5 and/or SEQ ID NO: 20 comprising at least 10 consecutive amino acids of SEQ ID NO: 5 and/or SEQ ID NO: 20, or a variant thereof having between 1 and 5 amino acid substitutions relative to SEQ ID NO: 5 and/or SEQ ID NO: 20, such as 1, 2, 3, or 4 amino acid substitutions relative to SEQ ID NO: 5 and/or SEQ ID NO: 20, wherein said polypeptide has a length of less than 50 amino acids;

l. a fragment of SEQ ID NO: 19, wherein said fragment is selected from the group consisting of SEQ ID NOs: 27, 33, 34, 35, 36, 37 and 95, and respective variants thereof having between 1 and 3 amino acid substitutions relative to SEQ ID NO: 19, such as 1, 2 or 3 amino acid substitutions relative to SEQ ID NO: 19, wherein said polypeptide has a length of less than 50 amino acids;

m. a fragment of SEQ ID NO: 4, wherein said fragment is selected from the group consisting of SEQ ID NOs: 107, 108, 109, 110, 111, 165 and 168, and respective variants thereof having between 1 and 3 amino acid substitutions relative to SEQ ID NO: 4, such as 1, 2 or 3 amino acid substitutions relative to SEQ ID NO: 4, wherein said polypeptide has a length of less than 50 amino acids;

n. a fragment of a variant of SEQ ID NO: 19, wherein said fragment is selected from the group consisting of SEQ ID NOs: 173, 176, 181 and 188, and respective variants thereof having between 1 and 3 amino acid substitutions relative to SEQ ID NO: 19, such as 1, 2 or 3 amino acid substitutions relative to SEQ ID NO: 19, wherein said polypeptide has a length of less than 50 amino acids;

o. a fragment of a variant of SEQ ID NO: 4, wherein said fragment is selected from the group consisting of SEQ ID NOs: 193, 196, 201 and 208, and respective variants thereof having between 1 and 3 amino acid substitutions relative to SEQ ID NO: 4, such as 1, 2 or 3 amino acid substitutions relative to SEQ ID NO: 4, wherein said polypeptide has a length of less than 50 amino acids;

p. a fragment of SEQ ID NO: 19, wherein said fragment is selected from the group consisting of SEQ ID NOs: 210, 211, 212, 213, 229, 232, 233, 234 and 235, and respective variants thereof having between 1 and 3 amino acid substitutions relative to SEQ ID NO: 19, such as 1, 2 or 3 amino acid substitutions relative to SEQ ID NO: 19, wherein said polypeptide has a length of less than 50 amino acids; and

q. a fragment of SEQ ID NO: 4, wherein said fragment is selected from the group consisting of SEQ ID NOs: 243, 244, 245, 246, 262, 265, 266, 267 and 268, and respective variants thereof having between 1 and 3 amino acid substitutions relative to SEQ ID NO: 4, such as 1, 2 or 3 amino acid

substitutions relative to SEQ ID NO: 4, wherein said polypeptide has a length of less than 50 amino acids.

2. The polypeptide according to claim 1, wherein the polypeptide has a length of at least 10 amino acids, such as at least 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 100 amino acids.

3. The polypeptide according to any one of the preceding claims, wherein the polypeptide has a length of 10-200 amino acids, such as 10-100, such as 10-50, such as 15-30, such as 15-25, such as 50-150, such as 50-100, such as 70-100, such as 80-90 amino acids.

4. The polypeptide according to any one of the preceding claims, wherein the variant has at least 90% sequence identity to SEQ ID NO: 4 and/or SEQ ID NO: 19, such as at least 95% sequence identity to SEQ ID NO: 4 and/or SEQ ID NO: 19, for example at least 97% sequence identity to SEQ ID NO: 4 and/or SEQ ID NO: 19.

5. The polypeptide according to any one of the preceding claims, wherein the variant has at least 90% sequence identity to SEQ ID NO: 5 and/or SEQ ID NO: 20, such as at least 95% sequence identity to SEQ ID NO: 5 and/or SEQ ID NO: 20, for example at least 97% sequence identity to SEQ ID NO: 5 and/or SEQ ID NO: 20.

6. The polypeptide according to any one of the preceding claims, wherein said fragment comprises or consists of an amino acid sequence according to positions 7 to 16 of SEQ ID NO: 4, corresponding to SEQ ID NO: 6, or a variant thereof having between 1 and 5 amino acid substitutions as compared to SEQ ID NO: 4.

7. The polypeptide according to any one of the preceding claims, wherein said fragment comprises or consists of an amino acid sequence according to positions 27 to 39 of SEQ ID NO: 4, corresponding to SEQ ID NO: 7, or a variant thereof having between 1 and 6 amino acid substitutions as compared to SEQ ID NO: 4.

8. The polypeptide according to any one of the preceding claims, wherein said fragment comprises or consists of an amino acid sequence according to positions

43 to 56 of SEQ ID NO: 4, corresponding to SEQ ID NO: 8, or a variant thereof having between 1 and 6 amino acid substitutions as compared to SEQ ID NO: 4.

9. A conjugate comprising the polypeptide according to any one of the preceding claims, wherein said polypeptide comprises one or more moieties conjugated to said polypeptide, optionally wherein the polypeptide and the one or more moieties are conjugated to each other by a linker.

10. The conjugate according to claim 9, wherein the one or more moieties are selected from the group consisting of alkyls, aryls, heteroaryls, olefins, fatty acids, polyethylene glycol (PEG), saccharides, and polysaccharides.

11. The polypeptide or conjugate according to any one of the preceding claims, wherein the polypeptide is capable of:
    a) binding to the αV/β5 integrin receptor;
    b) inducing thermogenesis in white adipocytes, such as for example by inducing expression of genes involved in thermogenesis;
    c) reducing the lipid content of adipocytes, such as for example by reducing expression of genes involved in lipogenesis;
    d) stimulating bone formation, such as for example by stimulating sclerostin expression in osteocytes;
    e) inducing cardiomyogenesis;
    f) inducing myotube formation and myogenesis in myoblasts;
    g) enhancing the intestinal barrier junction;
    h) stimulating secretion of glucagon like peptide-1 (GLP-1) and glucagon like peptide-2 (GLP-2);
    i) stimulating secretion of insulin;
    j) stimulating secretion of peptide-YY (PYY);
    k) stimulating secretion of somatostatin;
    l) inducing weight loss, such as for example by reducing fat mass and increasing the lean mass of a subject;
    m) improving glucose tolerance; and/or
    n) increasing the cortical thickness of the tibia bone.

12. An isolated polynucleotide encoding the polypeptide or conjugate according to any one of the preceding claims.

13. A vector comprising the polynucleotide according to claim 12.

14. A host cell comprising the polynucleotide according to claim 12, and/or the vector according to claim 13, such as wherein said polynucleotide and/or vector are heterologous to said host cell.

15. A pharmaceutical composition comprising:

a) the polypeptide or conjugate according to any one of claims 1 to 11;
b) a RUMTOR_00181 polypeptide comprising or consisting of
    i. the polypeptide according to SEQ ID NO: 21; or
    ii. a variant of SEQ ID NO: 21 with at least 85%, such as at least 90%, such as at least 95%, such as at least 98% sequence identity thereto;
c) the polynucleotide according to claim 12;
d) a polynucleotide encoding said RUMTOR_00181 polypeptide;
e) the vector according to claim 13,
f) a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide; and/or
g) the host cell according to claim 14; and/or
h) a host cell comprising
    i. a polynucleotide encoding said RUMTOR_00181 polypeptide; and/or
    ii. a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide.

16. A dietary composition comprising:

a) the polypeptide or conjugate according to any one of claims 1 to 11;
b) a RUMTOR_00181 polypeptide comprising or consisting of
    i. the polypeptide according to SEQ ID NO: 21; or
    ii. a variant of SEQ ID NO: 21 with at least 85%, such as at least 90%, such as at least 95%, such as at least 98% sequence identity thereto;
c) the polynucleotide according to claim 12;
d) a polynucleotide encoding said RUMTOR_00181 polypeptide;
e) the vector according to claim 13,

f) a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide; and/or

g) the host cell according to claim 14; and/or

h) a host cell comprising

i. a polynucleotide encoding said RUMTOR_00181 polypeptide; and/or

ii. a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide,

wherein the dietary composition comprises one or more of prebiotics, probiotics, Live Biopharmaceutical Products (LBPs), synbiotics, proteins, lipids, carbohydrates, vitamins, fibers, and/or nutrients, such as dietary minerals.

17. Use of a host cell comprising:

a) a polypeptide or conjugate according to any one of claims 1 to 11, and/or a RUMTOR_00181 polypeptide comprising or consisting of

i. the polypeptide according to SEQ ID NO: 21; or

ii. a variant of SEQ ID NO: 21 with at least 85%, such as at least 90%, such as at least 95%, such as at least 98% sequence identity thereto;

b) the polynucleotide according to claim 12, and/or a polynucleotide encoding said RUMTOR_00181 polypeptide; and/or

c) the vector according to claim 13, and/or a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide;

as a probiotic or as a Live Biopharmaceutical Product (LBP).

18. Use of the polypeptide or conjugate according to any of claims 1 to 11, or a RUMTOR_00181 polypeptide comprising or consisting of:

a) the polypeptide according to SEQ ID NO: 21, or a variant of SEQ ID NO: 21 with at least 85%, such as at least 90%, such as at least 95%, such as at least 98% sequence identity thereto;

b) the polynucleotide according to claim 12, or a polynucleotide encoding said RUMTOR_00181 polypeptide;

c) the vector according to claim 13, or a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide;

d) the host cell according to claim 14, or a host cell comprising

i. a polynucleotide encoding said RUMTOR_00181 polypeptide; or

ii. a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide;

and/or

e) the dietary composition according to claim 16,

as a food ingredient or as a food or beverage additive.

19. Use of the polypeptide or conjugate according to any of claims 1 to 11, or a RUMTOR_00181 polypeptide comprising or consisting of:

a) the polypeptide according to SEQ ID NO: 21, or a variant of SEQ ID NO: 21 with at least 85%, such as at least 90%, such as at least 95%, such as at least 98% sequence identity thereto;

b) the polynucleotide according to claim 12, or a polynucleotide encoding said RUMTOR_00181 polypeptide;

c) the vector according to claim 13, or a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide;

d) the host cell according to claim 14, or a host cell comprising

i. a polynucleotide encoding said RUMTOR_00181 polypeptide; or

ii. a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide; and/or

e) the pharmaceutical composition according to claim 15;

in the manufacture of a medicament for treatment of metabolic disorders, muscle disorders and injuries, and/or bone disorders.

20. Use of the polypeptide or conjugate according to any of claims 1 to 11, or a RUMTOR_00181 polypeptide comprising or consisting of:

a) the polypeptide according to SEQ ID NO: 21, or a variant of SEQ ID NO: 21 with at least 85%, such as at least 90%, such as at least 95%, such as at least 98% sequence identity thereto;

b) the polynucleotide according to claim 12, or a polynucleotide encoding said RUMTOR_00181 polypeptide;

c) the vector according to claim 13, or a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide;

d) the host cell according to claim 14, or a host cell comprising

iii. a polynucleotide encoding said RUMTOR_00181 polypeptide; or

iv. a vector comprising the polynucleotide encoding said RUMTOR_00181 polypeptide; and/or

e) the pharmaceutical composition according to claim 15;

in the manufacture of a medicament for treatment of metabolic syndrome, obesity, prediabetes, T2D, FLD, cardiovascular disease, muscular dystrophy, Duchenne muscular dystrophy, ALS, Lambert-Eaton syndrome, myasthenia gravis, polymyositis, peripheral neuropathy, osteoporosis, osteogenesis imperfect, and/or osteopetrosis.