

Claims

1. A glucose-dependent insulintropic peptide (GIP) analogue consisting of amino acid sequence of :

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3 - 4 - 5 - 6 7 8 9 10 11 12 13 14 15 16 17
E - G - T - F - I - S - E - Y - S - I - Aib - M - E - K - I

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18 19 20 21 22 23 24 25 26 27 28 29 30
K - Q - Q - D - F - V - E - W - L - L - A - Q - K - Z,

or a functional variant thereof, wherein said variant has 1 to 4 individual amino acid substitutions at any amino acid of said amino acid sequence,

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wherein said peptide is modified by attaching at least one fatty acid molecule at one or more amino acid residues at positions 3 to 29 of said sequence, or said functional variant thereof,

wherein Z is a peptide comprising one or more amino acid residues of GIP(31-42) (GKKNDWKHNITQ; SEQ ID NO: Z) or one or more amino acid residues of Exendin-4 (HGEGTFTSDLSKQMEEEEAVRLFIEWLKNGGPSSGAPPPS; SEQ ID NO: E).

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2. The GIP peptide analogue according to any one of the preceding claims, wherein said GIP peptide analogue is an antagonist of GIPR.

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3. The GIP peptide analogue according to any one of the preceding claims, wherein said GIP peptide analogue inhibits GIPR activity of at least 80%, such as of at least 85%, such as of at least 90%, such as of at least 95%, such as of about 100%, optionally wherein inhibition of GIPR activity is determined as a decrease in intracellular cAMP.

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4. The GIP peptide analogue according to any one of the preceding claims, wherein said GIP peptide analogue has a GIPR antagonistic potency corresponding to an IC₅₀ value of 50 nM or less than 50 nM.

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5. The GIP peptide analogue according to any one of the preceding claims, wherein:
the amino acid at position 5 is T or omitted;
the amino acid at position 11 is selected from S, K and A;

the amino acid at position 12 is selected from I, K and 2-Aminoisobutyric acid (Aib);

the amino acid at position 14 is selected from M, K, E, S, L and Nle;

the amino acid at position 16 is selected from K and R;

the amino acid at position 17 is selected from I and K;

5 the amino acid at position 20 is selected from Q and K;

the amino acid at position 21 is selected from D and E;

the amino acid at position 28 is selected from A and E;

the amino acid at position 29 is selected from Q and G; and/or

the amino acid at position 30 is selected from K, R, G and A.

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6. The GIP peptide analogue according to any one of the preceding claims, wherein said functional variant has 1 individual amino acid substitution, such as 2 individual amino acid substitutions, for example 3 individual amino acid substitutions, such as 4 individual amino acid substitutions at any amino acid residue of said amino acid sequence optionally wherein said substitutions are conservative amino acid substitutions.

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7. The GIP peptide analogue according to any one of the preceding claims, wherein the S at position 11 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with an amino acid residue selected from the group consisting of A, K and Orn and/or

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wherein the I at position 12 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with an amino acid residue selected from the group consisting of K, Orn and 2-Aminoisobutyric acid (Aib) and/or

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wherein the M at position 14 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with an amino acid residue selected from the group consisting of L, Norleucine (Nle), E, S, K and Orn and/or

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wherein the M at position 14 of said amino acid sequence, or a functional variant thereof, is substituted with an amino acid residue selected from the group consisting of L, Norleucine (Nle) and K and/or

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wherein the K at position 16 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid

substitution, such as substituted with R and/or

wherein the I at position 17 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with an amino acid residue selected from the group consisting of K or Orn and/or

wherein the Q at position 20 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with an amino acid residue selected from the group consisting of K and Orn and/or

wherein the D at position 21 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with E and/or

wherein the A at position 28 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with E and/or

wherein the Q at position 29 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with G and/or

wherein the K at position 30 of said amino acid sequence, or a functional variant thereof, is substituted with any amino acid, such as a conservative amino acid substitution, such as substituted with an amino acid residue selected from the group consisting of R, A and G and/or

wherein said GIP peptide analogue comprises at least one substitution to K and one substitution to E or Aib at any one of amino acid residues 3 to 30 of said amino acid sequence.

8. The GIP peptide analogue according to any one of the preceding claims, wherein Z consists of one or more consecutive amino acid residues of GIP(31-42) (SEQ ID NO: Z) and/or

wherein Z consists of one or more consecutive amino acid residues of Exendin-4 (SEQ ID NO: E) and/or

wherein Z consists of one or more amino consecutive acid residues of the C-terminus of Exendin-4(30-39) (PSSGAPPPS; SEQ ID NO: CE31-39) and/or wherein Z consists of one or more amino consecutive acid residues of the C-terminus of Exendin-4(29-39) (GPSSGAPPPS; SEQ ID NO: CE30-39).

9. The GIP peptide analogue according to any one of the preceding claims, wherein Z comprises at least one G or one P and/or wherein Z comprises at least two P.
- 5 10. The GIP peptide analogue according to any one of the preceding claims, wherein Z is a peptide selected from the group consisting of
- a glycine or a proline,
 - GP, GPS, GPSS, GPSSG, GPSSGA, GPSSGAP, GPSSGAPP, GPSSGAPPP and GPSSGAPPPS,
 - 10 - PS, PSS, PSSG, PSSGA, PSSGAP, PSSGAPP, PSSGAPPP and PSSGAPPPS,
 - GK, GKK, GKKN, GKKND, GKKNDW, GRKNDW, GKRNDW, GRRNDW, GKKNDWK, GKKNDWKH, GKKNDWKHN, GKKNDWKHNI, GKKNDWKHNIT and GKKNDWKHNITQ,
 - 15 - GPSSGA, GPSSGAP, GPSSGAPP, GPSSGAPPP, GPSSGAPPPS, GKKNDW, GKKKDW, GKKNDK GRKNDW, GKRNDW, GRRNDW, GKKNDWK, GKKNDWKH, GKKNDWKHN, GKKNDWKHNI, GKKNDWKHNIT and GKKNDWKHNITQ, or a variant thereof comprising 1 or 2 individual amino acid substitutions at any one of the amino acid
 - 20 residues, or
 - PSSG, PSSGA, PSSGAP, PSSGAPP, PSSGAPPP and PSSGAPPPS, or a variant thereof comprising 1 or 2 individual amino acid substitutions at any one of the amino acid residues.
- 25 11. The GIP peptide analogue according to any of the preceding claims, wherein one or more fatty acid molecule(s) is attached to the side chain of an amino acid residue at position 6, position 7, position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, position 16, position 17, position 18, position 19, position 20, position 21, position 22, position 23, position 24, position 25, position 26, position 27,

position 28 or position 29 of said GIP peptide analogue, such as of said amino acid sequence, or a functional variant thereof and/or

wherein a fatty acid molecule is attached to the epsilon-amino group of a K or Orn residue of said GIP peptide analogue, such as of said amino acid sequence, or a functional variant thereof comprising at least one K or Orn residue.

12. The GIP peptide analogue of any one of the preceding claims, wherein said GIP peptide analogue has an amino acid sequence selected from the group consisting of:
- EGTFISDYSIAMDKIKQQDFVNWLLAQK - Z; SEQ ID NO: 38; GIP(3-30) [H18K],
- 10 EGTFISEYSIAMEKIKQQEFVQWLLAQK - Z; SEQ ID NO: 50; GIP(3-30) [D9E;D15E;H18K;D21E;N24Q],
- EGTFISEYSIAMEKIKQQDFVQWLLAQK - Z; SEQ ID NO: 51; GIP(3-30) [D9E;D15E;H18K;N24Q],
- EGTFISEYSAibANleEKIKQQDFVEWLLAQK - Z; SEQ ID NO: 52; GIP(3-30)
- 15 [D9E;I12Aib;M14Nle;D15E;H18K;N24E],
- EGTFISEYSIAibMEKIKQQDFVEWLLAQK - Z; SEQ ID NO: 53; GIP(3-30) [D9E;A13Aib;D15E;H18K;N24E],
- EGTFISDYSIAMDKIKQQDFVEWLLAQK - Z; SEQ ID NO: 54; GIP(3-30) [H18K;N24E],
- EGTFISDYSIAMDKIKQQDFVEWLLAQA - Z; SEQ ID NO: 60; GIP(3-30)
- 20 [H18K;N24E;K30A],
- EGTFISDYSIAibMDKIKQQDFVEWLLAQK - Z; SEQ ID NO: 73; GIP(3-30) [A13Aib;H18K;N24E],
- EGTFISDYSIAibLDKIKQQDFVEWLLAQK - Z; SEQ ID NO: 74; GIP(3-30) [A13Aib;M14L;H18K;N24E],
- 25 EGTFISDYSIAibNleDKIKQQDFVEWLLAQK - Z; SEQ ID NO: 75; GIP(3-30) [A13Aib;M14Nle;H18K;N24E],
- EGTFISDYSIALDKIKQQDFVEWLLAQK - Z; SEQ ID NO: 76; GIP(3-30) [M14L;H18K;N24E],
- EGTFISDYSIANleDKIKQQDFVEWLLAQK - Z; SEQ ID NO: 77; GIP(3-30)
- 30 [M14Nle;H18K;N24E],
- EGTFISDYSIAKDKIKQQDFVEWLLAQK - Z; SEQ ID NO: 78; GIP(3-30) [M14K;H18K;N24E],
- EGTFISEYSIAibLEKIKQQEFVEWLLAQK - Z; SEQ ID NO: 81; GIP(3-30) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],
- 35 EGTFISEYSIAibNleEKIKQQEFVEWLLAQK - Z; SEQ ID NO: 82; GIP(3-30)

[D9E;A13Aib;M14Nle;D15E;H18K;D21E;N24E],

EGTFISEYSIALEKIKQQEFVEWLLAQK – Z; SEQ ID NO: 87; GIP(3-30)

[D9E;M14L;D15E;H18K;D21E;N24E], and

EGTFISEYSIANleEKIKQQEFVEWLLAQK – Z; SEQ ID NO: 88; GIP(3-30)

5 [D9E;M14Nle;D15E;H18K;D21E;N24E].

13. The GIP peptide analogue of any one of the preceding claims, wherein said GIP peptide analogue has an amino acid sequence of:

EGTFISEYSIAibLEKIKQQEFVEWLLAQK – Z; SEQ ID NO: 81; GIP(3-30)

10 [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E].

14. The GIP peptide analogue of any one of the preceding claims, wherein said fatty acid molecule is a straight-chain fatty acid and/or

wherein said fatty acid molecule is a branched fatty acid and/or

15 wherein said fatty acid molecule is a monoacyl fatty acid molecule, comprising one fatty acid and/or

wherein said fatty acid molecule is a diacyl fatty acid molecule and/or

wherein said fatty acid molecule comprises an acyl group of the formula $\text{CH}_3(\text{CH}_2)_n\text{CO}-$, wherein n is an integer from 4 to 24.

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15. The GIP peptide analogue according to any of the preceding claims, wherein said fatty acid molecule comprises an acyl group selected from the group consisting of $\text{COOH}(\text{CH}_2)_{14}\text{CO}-$, $\text{COOH}(\text{CH}_2)_{16}\text{CO}-$, $\text{COOH}(\text{CH}_2)_{18}\text{CO}-$ and $\text{COOH}(\text{CH}_2)_{20}\text{CO}-$.

25 16. The GIP peptide analogue according to any of the preceding claims, wherein said fatty acid molecule is attached to the epsilon amino group of the side chain of an amino acid residue of said GIP peptide analogue directly or wherein said fatty acid molecule is attached to an amino acid residue via a linker.

30 17. The GIP peptide analogue of any one of the preceding claims selected from the group consisting of:

EGTFISDYSIAMDKIKQQDFVNWLLAQKGKKNDW-2xAEEAc+y-glu-C16-diacid/K18; SEQ ID NO:106; GIP(3-36) [H18K],

EGTFISDYSIAMDKIKQQDFVNWLLAQKGKKNDW-3xAEEAc+y-glu-C16-diacid/K18; SEQ ID NO: GIP106; (3-36) [H18K],

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- EGTFISDYSIAMDKIKQQDFVNWLLAQKGKKNW-3xAEAAc+y-glu-C18-diacid/K18; SEQ ID NO: 106; GIP(3-36) [H18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-C16-diacid/K18; SEQ ID NO: 107; GIP(3-30)+Cex(31-39) [H18K],
- 5 EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS(NH₂)-2xAEAAc+yGlu-C18-diacid/K18; SEQ ID NO: 108; GIP(3-30)+Cex(31-39) [CexH18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-2xAEAAc+yGlu-C18-diacid/K18; SEQ ID NO: 107; GIP(3-30)+Cex(31-39) [CexH18K],
- 10 EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS(NH₂)-2xAEAAc+yGlu-C18-diacid/K18; SEQ ID NO: 108; GIP(3-30)+Cex(31-39) [CexH18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-C16-diacid/K18; SEQ ID NO: 107; GIP(3-30)+Cex(31-39) [CexH18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-C18-diacid/K18; SEQ ID NO: 107; GIP(3-30)+Cex(31-39) [CexH18K],
- 15 EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-C18/K18; SEQ ID NO: 107; GIP(3-30)+Cex(31-39) [CexH18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-2xAEAAc+yGlu-C16-diacid/K18; SEQ ID NO: 107; GIP(3-30)+Cex(31-39) [CexH18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-yGlu-C16-diacid/K18; SEQ ID NO: 107; GIP(3-30)+Cex(31-39) [CexH18K],
- 20 EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-C16-diacid/K18; SEQ ID NO: 109; GIP(3-30)+Cex [H18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-2xAEAAc+y-glu-C16-diacid/K18: 109; SEQ ID NO: GIP(3-30)+Cex [CexH18K],
- 25 EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-3xAEAAc+y-glu-C16-diacid/K18: SEQ ID NO: 109; GIP(3-30)+Cex [CexH18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-2xAEAAc+y-glu-C18-diacid/K18: SEQ ID NO: 109; GIP(3-30)+Cex [CexH18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-3xAEAAc+y-glu-C18-diacid/K18: SEQ ID NO: 109; GIP(3-30)+Cex [CexH18K],
- 30 EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS(NH₂)-2xAEAAc+yGlu-C18-diacid/K18; SEQ ID NO: 110; GIP(3-30)+Cex(31-39) [CexH18K],
- EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPPS-2xAEAAc+yGlu-C18-diacid/K18; SEQ ID NO: 109; GIP(3-30)+Cex(31-39) [CexH18K],
- 35 EGTFISDYSIAMDKIKQQDFVNWLLAQKPSSGAPPP- C16-diacid/K18: SEQ

ID NO: 111; GIP(3-30)+Cex(9) [CexH18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G P S S G A P P - C 16 - d i a c i d / K 18 : S E Q I D
 NO: 112; GIP(3-30)+Cex(Cex8) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G P S S G A P - C 16 - d i a c i d / K 18 : S E Q I D
 5 NO: 113; GIP(3-30)+Cex(Cex7) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G P S S G A - C 16 - d i a c i d / K 18 : S E Q I D
 NO: 114; GIP(3-30)+Cex(Cex6) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G P S S G - C 16 - d i a c i d / K 18 : S E Q I D NO:
 115; GIP(3-30)+Cex(Cex5) [H18K],
 10 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G P S S - C 16 - d i a c i d / K 18 : S E Q I D NO:
 116; GIP(3-30)+Cex(Cex4) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G P S - C 16 - d i a c i d / K 18 : S E Q I D NO:
 117; GIP(3-30)+Cex(Cex3) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G P - C 16 - d i a c i d / K 18 : S E Q I D NO: 118;
 15 GIP(3-30)+Cex(Cex2) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G - C 16 - d i a c i d / K 18 : S E Q I D NO: 119;
 GIP(3-31) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K - C 16 - d i a c i d / K 18 : S E Q I D NO: 120;
 GIP(3-32) [H18K],
 20 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K K - C 16 - d i a c i d / K 18 : S E Q I D NO:
 121; GIP(3-33) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K K N - C 16 - d i a c i d / K 18 : S E Q I D NO:
 122; GIP(3-34) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K K N D - C 16 - d i a c i d / K 18 : S E Q I D NO:
 25 123; GIP(3-35) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K K N D W - C 16 - d i a c i d / K 18 : S E Q I D
 NO: 106; GIP(3-36) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K K N D W K - C 16 - d i a c i d / K 18 : S E Q I D
 NO: 124; GIP(3-37) [H18K],
 30 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K K N D W K H - C 16 - d i a c i d / K 18 : S E Q I D
 NO: 125; GIP(3-38) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K K N D W K H N - C 16 - d i a c i d / K 18 : S E Q
 ID NO: 126; GIP(3-39) [H18K],
 EGT F I S D Y S I A M D K I K Q Q D F V N W L L A Q K G K K N D W K H N I - C 16 - d i a c i d / K 18 : S E Q
 35 ID NO: 127; GIP(3-40) [H18K],

- EGTFISDYSIAMDKIKQQDFVNWLLAQKGKKNDWKHNIT-C16-diacid/K18:
SEQ ID NO: 128; GIP(3-41) [H18K],
EGTFISDYSIAMDKIKQQDFVNWLLAQKGKKNDWKHNITQ-C16-diacid/K18:
SEQ ID NO: 129; GIP(3-42) [H18K],
- 5 EGTFISEYSIAMEKIKQQEFVQWLLAQKPSSGAPPPS- C16-diacid; SEQ ID
NO: 141; GIP(3-30)+Cex(31-39) [CexD9E;D15E;H18K;D21E;N24Q],
EGTFISEYSIAMEKIKQQDFVEWLLAQKPSSGAPPPS- C16-diacid; SEQ ID
NO: 142; GIP(3-30)+Cex(31-39) [D9E;D15E;H18K;N24E],
- 10 EGTFISEYSAibANleEKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K;
SEQ ID NO: 143; GIP(3-30)+Cex(31-39)
[D9E;I12Aib;M14Nle;D15E;H18K;N24E],
EGTFISEYSIAibMEKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ
ID NO: 144; GIP(3-30)+Cex(31-39) [D9E;A13Aib;D15E;H18K;N24E],
EGTFISDYSIAMDKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ
- 15 ID NO: 145; GIP(3-30)+Cex(31-39) [H18K;N24E],
EGTFISDYSIAMDKIKQQDFVEWLLAQAPSSGAPPPS-C16-diacid/18K; SEQ
ID NO: 151; GIP(3-30)+Cex(31-39) [H18K;N24E;K30A],
EGTFISDYSIAibMDKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ
ID NO: 166; GIP(3-30)+Cex(31-39) [A13Aib;H18K;N24E],
- 20 EGTFISDYSIAibLDKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ
ID NO: 167; GIP(3-30)+Cex(31-39) [A13Aib;M14L;H18K;N24E],
EGTFISDYSIAibLDKIKQQDFVEWLLAQKPSSGAPPPS-2xAEEAc+yGlu-C18-
diacid/18K; SEQ ID NO: 167; GIP(3-30)+Cex(31-39)
[A13Aib;M14L;H18K;N24E],
- 25 EGTFISDYSIAibNleDKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K;
SEQ ID NO: 167; GIP(3-30)+Cex(31-39) [A13Aib;M14Nle;H18K;N24E],
EGTFISDYSIAibNleDKIKQQDFVEWLLAQKPSSGAPPPS-2xAEEAc+yGlu-
C18-diacid/18K; SEQ ID NO: 167; GIP(3-30)+Cex(31-39)
[A13Aib;M14Nle;H18K;N24E],
- 30 EGTFISDYSIALDKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ ID
NO: 169; GIP(3-30)+Cex(31-39) [M14L;H18K;N24E],
EGTFISDYSIALDKIKQQDFVEWLLAQKPSSGAPPPS-2xAEEAc+yGlu-C18-
diacid/18K; SEQ ID NO: 169; GIP(3-30)+Cex(31-39) [M14L;H18K;N24E],
EGTFISDYSIANleDKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ
- 35 ID NO: 170; GIP(3-30)+Cex(31-39) [M14Nle;H18K;N24E],

EGTFISDYSIA**Nle**DKIKQQDFVEWLLAQKPSSGAPPPS-2xAEAAc+yGlu-C18-diacid/18K; SEQ ID NO: 170; GIP(3-30)+Cex(31-39) [M14Nle;H18K;N24E],
 EGTfISDYSIAKDKIKQQDFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ ID NO: 171; GIP(3-30)+Cex(31-39) [M14K;H18K;N24E],
 5 EGTfISEYSIA**Aib**LEKIKQQEFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ ID NO: 174; GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],
 EGTfISEYSIA**Aib**LEKIKQQEFVEWLLAQKPSSGAPPPS-2xAEAAc+yGlu-C18-diacid/18K; SEQ ID NO: 174; GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E],
 10 EGTfISEYSIA**Aib**NleEKIKQQEFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ ID NO: 175; GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14Nle;D15E;H18K;D21E;N24E],
 EGTfISEYSIA**Aib**NleEKIKQQEFVEWLLAQKPSSGAPPPS-2xAEAAc+yGlu-C18-diacid/18K; SEQ ID NO: 175; GIP(3-30)+Cex(31-39) [D9E;A13Aib;M14Nle;D15E;H18K;D21E;N24E],
 15 EGTfISEYSIA**LE**KIKQQEFVEWLLAQKPSSGAPPPS-2xAEAAc+yGlu-C18-diacid/18K; SEQ ID NO: 180; GIP(3-30)+Cex(31-39) [D9E;M14L;D15E;H18K;D21E;N24E],
 EGTfISEYSIA**Nle**EKIKQQEFVEWLLAQKPSSGAPPPS-2xAEAAc+yGlu-C18-diacid/18K; SEQ ID NO: 181; GIP(3-30)+Cex(31-39) [D9E;M14Nle;D15E;H18K;D21E;N24E], and
 20 EGTfISDYSIAMDKIKQQDFVNWLLAQK(NH₂)PSSGAPPPS C16-diacid/18K; SEQ ID NO: 165; GIP(3-30+CEX31-39 [H18K].

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18. The GIP peptide analogue of any one of the preceding claims, wherein said GIP peptide analogue is

EGTfISEYSIA**Aib**LEKIKQQEFVEWLLAQKPSSGAPPPS-C16-diacid/18K; SEQ ID NO: 174; GIP(3-30)+Cex(31-39)
 30 [D9E;A13Aib;M14L;D15E;H18K;D21E;N24E]

19. The GIP peptide analogue according to any of the preceding claims for use in a method of inhibiting or reducing one or more of i) GIP-induced glucagon secretion, ii) GIP-induced insulin secretion, iii) GIP-induced somatostatin secretion, iv) GIP-induced glucose uptake, v) GIP-induced fatty acid synthesis and/or fatty acid incorporation, vi)

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high or increased expression or activity of a GIPR, vii) post-prandial GIP release, viii) serum levels of free fatty acids and/or triglycerides, ix) GIP-induced appetite increases, x) GIP-induced reduction in energy expenditure, xi) GIP-induced increase in absorption of nutrients from the gut, xii) GIP-induced decrease in GLP-1's appetite suppressive effect, xiii) GIP-induced leptin resistance.

20. Use of a GIP peptide analogue according to any of the preceding claims for the manufacture of a medicament for the treatment of a condition selected from the group consisting of metabolic syndrome, obesity, pre-diabetes, type I diabetes, type 2 diabetes, insulin resistance, elevated fasting glucose, hyperglycemia, elevated fasting serum triglyceride levels, low levels of very low-density lipoprotein (VLDL) , low high-density lipoprotein (HDL) levels, dyslipidemia, increased/decreased low-density lipoprotein (LDL), high cholesterol levels, abnormal deposition of lipids, a cardiovascular disease, elevated blood pressure and atherosclerosis.