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TITULO: NUEVOS COMPUESTOS Y SUS EFECTOS SOBRE EL CONDUCTISMO DE LA ALIMENTACIÓN

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BOGOTÁ 17 de Junio de 2009

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(2) **SOLICITANTE (71)**

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- [x] Comprobante de pago de la tasa de presentación de la solicitud.
- [ ] Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.
- [ ] Poderes, si fuere el caso. Adjunto copia simple ver expediente No.
- [ ] Documento de cesión del inventor al solicitante o a su causante.
- [ ] Declaraciones
- [x] Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos).
- [x] Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos).
- [ ] Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen Preliminar (IPEA).
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- [ ] De ser el caso, certificado de depósito del material biológico.
- [ ] Arte final 12 x 12.
- [ ] De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.
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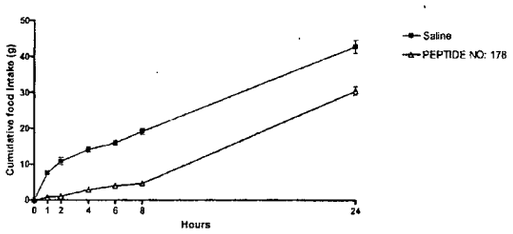
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[Continued on next page]

(54) Title: NOVEL COMPOUNDS AND THEIR EFFECTS ON FEEDING BEHAVIOUR



(57) Abstract: The invention provides a peptide comprising the amino acid sequence given below, together with use of the peptide and methods associated therewith. The peptide finds particular use as an appetite suppressant and in the treatment of obesity. Xaa1 Xaa2 Xaa3 Gly4 Thr5 Phe6 Thr7 Ser8 Asp9 Tyr1O Ser1 1 Lys12 Tyr13 Leu14 Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Trp25 Leu26 Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 Lys33 Asn34 Asn35 Ue36 Ala37; wherein: Xaa1 is His1 or D-His1, Xaa2 is Ser2 or Ala2, Xaa3 is Gln3 or Asp3; Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is: Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24, Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24, Glu15 Glu16 Glu17 Leul18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24, Glu15 Glu16 Glu17 Leul18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24, Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24, Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24, Glu15 Glu16 Glu17 Ilel18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24, Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24, Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24, Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24, Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24, Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ue23 Gln24, Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24, Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24, Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24, Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24, or Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24; Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is: Met27 Asn28 Thr29 Lys30 Arg31 Asn32, Lys27 Asn28 Ala29 Gly30 Pro31 Ser32, or Lys27 Asn28 Gly29 Gly30 Pro31 Scr32 or a peptide as set out above in which residue Asn34 is replaced with Asp34; or a peptide as set out above in which Xaa3 is Glu3; with the proviso that if Xaal5 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24, - - then Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is not Met27 Asn28 Thr29 Lys30 Arg31 Asn32.

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NOVEL COMPOUNDS AND THEIR EFFECTS ON FEEDING BEHAVIOUR

1. FIELD OF THE INVENTION

This application relates to the use of agents to control appetite, feeding, food intake, energy expenditure and calorie intake, treat excess weight, obesity and to prevent and treat the co-morbidities of obesity.

2. BACKGROUND OF THE INVENTION

According to the World Health Organisation (WHO), obesity represents a global epidemic in which more than one billion adults are overweight, of which at least 300 million are clinically obese. Furthermore, WHO estimate that 250,000 deaths per year in Europe, and more than 2.5 million deaths worldwide are weight related (World Health Organisation, Global Strategy on Diet, Physical Activity and Health, 2004).

The cause of obesity is complex and multi-factorial. Increasing evidence suggests that obesity is not a simple problem of self-control but is a complex disorder involving appetite regulation and energy metabolism. In addition, obesity is associated with a variety of conditions associated with increased morbidity and mortality in a population. Although the etiology of obesity is not definitively established, genetic, metabolic, biochemical, cultural and psychosocial factors are believed to contribute. In general, obesity has been described as a condition in which excess body fat puts an individual at a health risk.

There is strong evidence that obesity is associated with increased morbidity and mortality. Disease risk, such as cardiovascular disease risk and type 2 diabetes disease risk, increases independently with increased body mass index (BMI). Indeed, this risk has been quantified as a five percent increase in the risk of cardiac disease for females, and a seven percent increase in the risk of cardiac disease for males, for each point of a BMI greater than 24.9 (see Kenchaiah et al., N. Engl. J. Med. 347:305, 2002; Massie, N. Engl. J. Med. 347:358, 2002). In addition, there is substantial evidence that weight loss in obese or overweight persons reduces important disease risk factors. A weight loss of 10% of the initial body weight in both overweight and obese adults has been associated with a decrease in risk factors such as hypertension, hyperlipidemia, and hyperglycemia.

Although diet and exercise provide a simple process to decrease weight gain and promote weight loss, overweight and obese individuals often cannot sufficiently control these factors to lose weight effectively. Pharmacotherapy is available; several weight loss drugs have been approved by the US Food and Drug Administration that can be used as part of a comprehensive weight loss program. However, many of these drugs have serious adverse side effects. An example of a widely used appetite suppressant is sibutramine (reviewed by McNeely, W et al., Drugs, 1998, 56(6), 1093-1124). Sibutramine's primary and secondary metabolites are pharmacologically active and they are thought to induce enhancement of satiety and thermogenesis by inhibiting serotonin and noradrenaline reuptake. When less invasive methods have failed, and the patient is at high risk for obesity related morbidity or mortality, weight loss surgery is an option in carefully selected patients with clinically severe obesity. However, these treatments are high-risk, and suitable for use in only a limited number of patients (Wolfe and Morton, JAMA, 2005, 294,1960-1963). It is not only obese subjects who wish to lose weight. People with weight within the recommended range, for example, in the upper part of the recommended range, may wish to reduce their weight, to bring it closer to the ideal weight.

Oxyntomodulin (hereafter oxm) is a 37 amino acid peptide member of the glucagon superfamily (Sherwood et al, Endocrine Reviews, 2000, 21(6): 619-670) comprising the entire 29 amino acid sequence of glucagon, with an eight amino acid carboxy terminal extension, resulting from the tissue-specific processing of the pre-pro-glucagon precursor in the brain and gut (Holst, Ann Rev Physiol, 1997, 59:257-271). Administration of oxm to rats via intracerebroventricular injection and injection into the paraventricular and arcuate nuclei of the hypothalamus inhibits refeeding after a fast (Dakin et al, Endocrinology, 2001, 142:4244-4250; Dakin et al, Endocrinology, 2004, 145:2687-2695). Chronic central administration resulted in reduced weight gain consistent with a reduction in food intake (Dakin et al, Am J Physiol Endocrinol Metab, 2002, 283:E1173-E1177). Twice daily peripheral injections also resulted in reduced body weight gain and adiposity (Dakin et al, Endocrinology, 2004, 145:2687-2695).

WO 03/022304 discloses the use of oxm in its native form and analogues thereof as a medicament for use in control of appetite, feeding, food intake, energy expenditure and calorie intake, particularly in the field of obesity. Studies in humans have shown that intravenously infused oxm is an effective appetite suppressant (Cohen et al, J. Clin. Endocrinol Metab, 2003, 88(10): 4696-4701). In a study of the effects of oxm on weight loss in humans it was found that subcutaneous injections of 1.8 mg (approximately 400 nmol) of

oxm to human volunteers three times daily (30 mins before meals) for 28 days resulted in a significant reduction of body weight (Wynne et al, Diabetes, 2005, 54: 2390-2395).

Peptides are widely used in medical practice, although when native peptides or analogues thereof are used in therapy it is generally found that they have a high clearance rate and/or are sensitive to degradation. In particular, a high clearance or rapid degradation of a therapeutic agent is inconvenient in cases where it is desired to maintain a high blood level over a prolonged period of time since repeat administrations will then be necessary, decreasing patient compliance and increasing the cost of the therapy.

A need remains for agents that can be used to effect weight loss in overweight and obese subjects, and/or to treat patients with other conditions involving excess weight, for example diabetes and eating disorders. There is especially a need for agents structurally similar to oxm that show greater potency and/or a protracted or more therapeutically useful profile of action and/or a lower clearance rate than native oxm.

3. SUMMARY OF THE INVENTION

Compounds of the invention are novel peptide analogues of oxm (hereafter "oxm analogues") in which one or more amino acids or parts of the oxm sequence have been replaced by one or more particular substituent amino acids or sequences. Accordingly, the invention provides a peptide comprising the amino acid sequence:

Xaa1 Xaa2 Xaa3 Gly4 Thr5 Phe6 Thr7 Ser8 Asp9 Tyr10 Ser11 Lys12 Tyr13 Leu14

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Trp25 Leu26

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 Lys33 Asn34 Asn35 Ile36 Ala37;

wherein:

Xaa1 is His1 or D-His1,
Xaa2 is Ser2 or Ala2,
Xaa3 is Gln3 or Asp3;

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

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Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
or Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24;

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is:

Met27 Asn28 Thr29 Lys30 Arg31 Asn32,
Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,
or Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

or a peptide as set out above in which residue Asn34 is replaced with Asp34;

or a peptide as set out above in which Xaa3 is Glu3;

with the proviso that if
Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is
Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24,

then Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is not
Met27 Asn28 Thr29 Lys30 Arg31 Asn32

(SEQ ID NO: 356).

In one embodiment, the invention provides a peptide comprising the amino acid sequence:

Xaa1 Xaa2 Xaa3 Gly4 Thr5 Phe6 Thr7 Ser8 Asp9 Tyr10 Ser11 Lys12 Tyr13 Leu14

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Trp25 Leu26

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 Lys33 Asn34 Asn35 Ile36 Ala37;

wherein:

Xaa1 is His1 or D-His1,
Xaa2 is Ser2 or Ala2,
Xaa3 is Gln3 or Asp3;

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

or Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24;

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is:

Met27 Asn28 Thr29 Lys30 Arg31 Asn32,
Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,

or Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

with the proviso that if
Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is
Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24,

then Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is not
Met27 Asn28 Thr29 Lys30 Arg31 Asn32.

The peptides of the invention are potent and long-lasting appetite suppressants.

4. BRIEF DESCRIPTION OF THE FIGURES

Figure 1 discloses 355 specific peptide sequences falling within the scope of the invention.

Figures 2 to 41 show the results of Examples 1 to 19.

Figure 2 relates to Example 1.

Figure 3 relates to Example 2.

Figure 4 relates to Example 3 (PEPTIDE NO: 94).

Figure 5 relates to Example 3 (PEPTIDE NO: 82).

Figure 6 relates to Example 3 (PEPTIDE NO: 58).

Figure 7 relates to Example 3 (PEPTIDE NO: 52).

Figure 8 relates to Example 4 (PEPTIDE NO: 164).

Figure 9 relates to Example 4 (PEPTIDE NO: 167).

Figure 10 relates to Example 5 (PEPTIDE NO: 100).

Figure 11 relates to Example 5 (PEPTIDE NO: 148).

Figure 12 relates to Example 6 (PEPTIDE NO: 60).

Figure 13 relates to Example 6 (PEPTIDE NO: 178).

Figure 14 relates to Example 7 (PEPTIDE NO: 155).

Figure 15 relates to Example 8 (PEPTIDE NO: 142).

Figure 16 relates to Example 8 (PEPTIDE NO: 172).

Figure 17 relates to Example 8 (PEPTIDE NO: 184).

Figure 18 relates to Example 9 (PEPTIDE NO: 4).

Figure 19 relates to Example 9 (PEPTIDE NO: 108).

Figure 20 relates to Example 9 (PEPTIDE NO: 195).

Figure 21 relates to Example 9 (PEPTIDE NO: 136).

Figure 22 relates to Example 10 (PEPTIDE NO: 142).

Figure 23 relates to Example 10 (PEPTIDE NO: 22).

Figure 24 relates to Example 10 (PEPTIDE NO: 153).

Figure 25 relates to Example 10 (PEPTIDE NO: 199).

Figure 26 relates to Example 11 (PEPTIDE NO: 210).

Figure 27 relates to Example 11 (PEPTIDE NO: 211).

Figure 28 relates to Example 11 (PEPTIDE NO: 213).

Figure 29 relates to Example 11 (PEPTIDE NO: 214).

Figure 30 relates to Example 12 (PEPTIDE NO: 201).

Figure 31 relates to Example 12 (PEPTIDE NO: 202).

Figure 32 relates to Example 13 (PEPTIDE NO: 203).

Figure 33 relates to Example 14 (PEPTIDE NO: 204).

Figure 34 relates to Example 14 (PEPTIDE NO: 205).

Figure 35 relates to Example 15 (PEPTIDE NO: 206).

Figure 36 relates to Example 15 (PEPTIDE NO: 207).

Figure 37 relates to Example 15 (PEPTIDE NO: 209).

Figure 38 relates to Example 16 (PEPTIDE NO: 215).

Figure 39 relates to Example 17 (PEPTIDE NO: 216).

Figure 40 relates to Example 18 (PEPTIDE NO: 355).

Figure 41 relates to Example 19 (PEPTIDE NO: 130).

5. DEFINITIONS

In order to facilitate review of the various embodiments of this disclosure, the following explanations of specific terms are provided:

Animal: Living multi-cellular vertebrate organisms, a category that includes, for example, mammals and birds. The term mammal includes both human and non-human mammals. Similarly, the term "subject" includes both human and non-human subjects, including veterinary subjects.

Appetite: A natural desire, or longing for food. In one embodiment, appetite is measured by a survey to assess the desire for food. Increased appetite generally leads to increased feeding behavior.

Appetite Suppressants: Compounds that decrease the desire for food.. Commercially available appetite suppressants include, but are not limited to, amfepramone (diethylpropion), phentermine, mazindol and phenylpropanolamine fenfluramine, dexfenfluramine, sibutramine, rimonabant and fluoxetine.

Body Mass Index (BMI): A mathematical formula for measuring body mass, also sometimes called Quetelet's Index. BMI is calculated by dividing weight (in kg) by height^2 (in meters^2). The recommended classifications for BMI in humans, adopted by the Expert Panel on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults, and endorsed by leading organizations of health professionals, are as follows: Underweight <18.5 kg/m^2; Normal weight 18.5–24.9 kg/m^2; Overweight 25–29.9 kg/m^2; Obesity (Class 1) 30–34.9 kg/m^2; Obesity (Class 2) 35–39.9 kg/m^2; Extreme obesity (Class 3) ≥40 kg/m^2 (Practical Guide to the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults, The North American Association for the Study of Obesity (NAASO) and the National Heart, Lung, and Blood Institute (NHLBI) 2000). In one embodiment, a BMI of greater than 25 kg/m^2 can be used to identify a subject in need of a treatment for excess weight or obesity. Ideal body weight will vary among species and individuals based on height, body build, bone structure, and sex.

Conservative substitutions: The replacement of an amino acid residue by another similar residue in a polypeptide. Typical but not limiting conservative substitutions are the replacements, for one another, among the aliphatic amino acids Ala, Val, Leu and Ile;

interchange of Ser and Thr containing hydroxy residues, interchange of the acidic residues Asp and Glu, interchange between the amide-containing residues Asn and Gln, interchange of the basic residues Lys and Arg, interchange of the aromatic residues Phe and Tyr, and interchange of the small-sized amino acids Ala, Ser, Thr, Met and Gly. Additional conservative substitutions include the replacement of an amino acid by another of similar spatial or steric configuration, for example the interchange of Asn for Asp, or Gln for Glu.

Table 1: Non-limiting examples of conservative amino acid substitutions

Original Residue	Conservative Substitutions
Ala	Gly, Val, Leu, Ile, Ser, Thr, Met
Arg	Lys
Asn	Asp, Gln, His
Asp	Glu, Asn
Cys	Ser
Gln	Asn, His, Lys, Glu
Glu	Asp, Gln
Gly	Ala, Ser, Thr, Met
His	Asn, Gln
Ile	Ala, Leu, Val, Met
Leu	Ala, Ile, Val, Met,
Lys	Arg
Met	Leu, Ile, Ala, Ser, Thr, Gly
Phe	Leu, Tyr, Trp
Ser	Thr, Cys, Ala, Met, Gly
Thr	Ser, Ala, Ser, Met, Gly
Trp	Tyr, Phe
Tyr	Trp; Phe
Val	Ala, Ile, Leu

Non-conservative substitutions: The replacement, in a polypeptide, of an amino acid residue by another residue which is not biologically similar. For example, the replacement of an amino acid residue with another residue that has a substantially different charge, a substantially different hydrophobicity or a substantially different spatial or steric configuration.

The phrase "alternative amino acid" encompasses alternative amino acids that are the result of both conservative and non-conservative substitutions. In addition to the twenty commonly occurring amino acids that are typically found in naturally occurring polypeptides, rare amino acids, for example, canavanine, ornithine and 5-hydroxytryptophane, and artificial amino acids, that is to say amino acids not normally found *in vivo*, for example t-butylglycine, may

be used as "alternative amino acids" in accordance with the invention. Any chiral form of an amino acid may be used.

Diabetes: A failure of cells to transport endogenous glucose across their membranes either because of an endogenous deficiency of insulin and/or a defect in insulin sensitivity. Diabetes is a chronic syndrome of impaired carbohydrate, protein, and fat metabolism owing to insufficient secretion of insulin or to target tissue insulin resistance. It occurs in two major forms: insulin-dependent diabetes mellitus (IDDM, type I) and non-insulin dependent diabetes mellitus (NIDDM, type II) which differ in etiology, pathology, genetics, age of onset, and treatment.

The two major forms of diabetes are both characterised by an inability to deliver insulin in an amount and with the precise timing that is needed for control of glucose homeostasis. Diabetes type I, or insulin dependent diabetes mellitus (IDDM) is caused by the destruction of pancreatic β cells, which results in insufficient levels of endogenous insulin. Diabetes type II, or non-insulin dependent diabetes, results from a defect in both the body's sensitivity to insulin, and a relative deficiency in insulin production.

Food intake: The amount of food consumed by an individual subject. Food intake can be measured by volume or by weight. For example, food intake may be the total amount of food consumed by an individual subject. Or, food intake may be the amount of proteins, fat, carbohydrates, cholesterol, vitamins, minerals, or any other food component, of the individual subject. "Protein intake" refers to the amount of protein consumed by an individual. Similarly, "fat intake," "carbohydrate intake," "cholesterol intake," "vitamin intake," and "mineral intake" refer to the amount of fat, carbohydrates, cholesterol, vitamins, or minerals consumed by an individual subject respectively.

Normal Daily Diet: The average food intake for an individual of a given species. A normal daily diet can be expressed in terms of caloric intake, protein intake, carbohydrate intake, and/or fat intake. A normal daily diet in humans generally comprises the following: about 2,000, about 2,400, or about 2,800 to significantly more calories. In addition, a normal daily diet in humans generally includes about 12 g to about 45 g of protein, about 120 g to about 610 g of carbohydrate, and about 11 g to about 90 g of fat. A low calorie diet would be no more than about 85%, and preferably no more than about 70%, of the normal caloric intake of a human individual.

In animals, the caloric and nutrient requirements vary depending on the species and size of the animal. For example, in cats, the total caloric intake per pound, as well as the percent distribution of protein, carbohydrate and fat varies with the age of the cat and the reproductive state. A general guideline for cats, however, is 40 cal/lb/day (18.2 cal/kg/day). About 30% to about 40% should be protein, about 7% to about 10% should be from carbohydrate, and about 50% to about 62.5% should be derived from fat intake. One of skill in the art can readily identify the normal daily diet of an individual of any species.

Obesity: A condition in which excess body fat may put a person at health risk (see Barlow and Dietz, *Pediatrics* 102:E29, 1998; National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI), *Obes. Res.* 6 (suppl. 2):51S-209S, 1998). Excess body fat is a result of an imbalance of energy intake and energy expenditure. For example, the Body Mass Index (BMI) may be used to assess obesity. In one commonly used convention, a BMI of 25.0 kg/m^2 to 29.9 kg/m^2 is overweight, while a BMI of 30 kg/m^2 or greater is obese.

In another convention, waist circumference is used to assess obesity. Excess abdominal fat is an important, independent assessment of the risks associated with obesity or being overweight. Waist circumference measurement is particularly useful in patients who are categorised as normal or overweight. It is not usually necessary to measure waist circumference in individuals with BMIs $\geq$ 35 kg/m^2 since it adds little to the predictive power of the disease risk classification of BMI. Men who have waist circumferences greater than 40 inches (102 cm), and women who have waist circumferences greater than 35 inches (90 cm), are at higher risk of diabetes, dyslipidemia, hypertension, and cardiovascular disease because of excess abdominal fat. Individuals with waist circumferences greater than these values should be considered one risk category above that defined by their BMI.

Strong evidence shows that obesity affects both the morbidity and mortality of individuals. For example, an overweight or obese individual is at increased risk for heart disease, non-insulin dependent (type 2) diabetes, hypertension, stroke, cancer (e.g. endometrial, breast, prostate, and colon cancer), dyslipidemia, gall bladder disease, sleep apnea, reduced fertility, and osteoarthritis, amongst others (see Lyznicki et al., *Am. Fam. Phys.* 63:2185, 2001).

Overweight: An individual who weighs more than their ideal body weight. An overweight individual can be obese, but is not necessarily obese. For example, an overweight individual is any individual who desires to decrease their weight. In one convention, an overweight individual is an individual with a BMI of 25.0 kg/m^2 to 29.9 kg/m^2.

Pegylation: the process of reacting a poly(alkylene glycol), preferably an activated poly(alkylene glycol) to form a covalent bond. A facilitator may be used, for example an amino acid, e.g. lysine. Although "pegylation" is often carried out using poly(ethylene glycol) or derivatives thereof, such as methoxy poly(ethylene glycol), the term is not limited herein to the use of methoxy poly(ethylene glycol) but also includes the use of any other useful poly(alkylene glycol), for example poly(propylene glycol). Pegylated shall be defined accordingly.

Peripheral Administration: Administration outside of the central nervous system. Peripheral administration does not include direct administration to the brain. Peripheral administration includes, but is not limited to intravascular, intramuscular, subcutaneous, inhalation, oral, rectal, transdermal, buccal, sub-lingual or intra-nasal administration

Polypeptide: A polymer in which the monomers are amino acid residues which are joined together through amide bonds. When the amino acids are alpha-amino acids, either the L-optical isomer or the D-optical isomer can be used, the L-isomers being preferred. Throughout this specification, an alpha-amino acid will be assumed to be the L-isomer if it not explicitly stated to be the D-isomer. The terms "polypeptide" or "protein" as used herein encompass any amino acid sequence and include modified sequences such as glycoproteins. The term "polypeptide" covers naturally occurring proteins, as well as those which are recombinantly or synthetically produced. The term "polypeptide fragment" refers to a portion of a polypeptide, for example such a fragment which exhibits at least one useful sequence in binding a receptor. The term "functional fragments of a polypeptide" refers to all fragments of a polypeptide that retain an activity of the polypeptide. Biologically functional peptides can also include fusion proteins, in which the peptide of interest is fused to another peptide(s).

Therapeutically effective amount: A dose sufficient to prevent advancement, or to cause regression of a disorder, or which is capable of relieving a sign or symptom of a disorder, or which is capable of achieving a desired result. In several embodiments, a therapeutically effective amount of a compound of the invention is an amount sufficient to inhibit or halt weight gain, or an amount sufficient to decrease appetite, or an amount sufficient to reduce caloric intake or food intake or increase energy expenditure, or an amount sufficient to reduce weight, or to reduce the risk of mortality or morbidity from conditions associated with the disorder.

6. DETAILED DESCRIPTION

The inventors have found that, surprisingly, oxm analogues of the invention are effective appetite suppressants and/or have a more sustained effect than native oxm on food intake, and/or have a more potent effect than native oxm on food intake.

The human oxm sequence (which is the same as the rat and hamster) is as follows:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn Arg Asn Asn Ile Ala (SEQ ID NO: 357)

The peptides of the invention also have a longer half-life or clearance time or improved resistance to degradation as compared with oxm. Increased duration of appetite suppression can be particularly important to avoid the effect known as "escape". A short duration appetite suppressant may reduce appetite for the time covered by one meal and, in that meal, the subject typically eats less food. If, however, the appetite suppressant has a short half-life or rapid clearance time or is then metabolized or otherwise removed from the circulation of the subject, then by the time of the next mealtime, the subject can regain its "normal" appetite. In view of the subject having eaten a small meal at the previous mealtime, the subject may in fact have an increased appetite by the time of the subsequent meal. If the subject satisfies that appetite, it is possible for the food intake over the two meals, in total, to be no lower than the food intake would have been without the appetite suppressant. That is to say that the subject may have "escaped" from the effects of the appetite suppressant. "Escape" can be reduced by using additional doses of appetite suppressant, or by using an appetite suppressant with a longer duration of action. If the subject has a reduced appetite for longer, then the degree to which it can make up the missed food from one meal in the next meal is reduced as there is a practical limit to the total capacity for food in a particular meal. Repeated or continuous administration of a compound over a period of time, for example over a period of days or weeks, will lead to extended appetite suppression and reduced potential for escape from the effects of the appetite suppression.

The improved activity and/or duration of action of the oxm analogues as compared with oxm offers various advantages. For example, effective suppression of appetite at lower dosages will be permitted (with the lower dosage and/or lower peak levels, offering the prospect of reduced side effects (including nausea) and reduction in the cost of treatment), or usage at relatively high dosages will be better tolerated by the patient enabling quicker and/or greater weight loss. Certain of the compounds of the invention used in the Examples herein exhibit a pattern of appetite suppression indicative of a 'flatter blood curve', that is to say they have improved pharmacokinetids, by virture of displaying either or both of (i) a more gradual onset

of the appetite suppressant activity than oxm and thereby potentially avoid an initial sharp peak (which may be associated with nausea); and (ii) a potentially longer duration of action.

Further advantages of many compounds of the invention include that the compounds have improved storage characteristics and are amenable to large scale synthesis, for example some compounds of the invention do not contain sequence motifs associated with the formation of aspartimide species, and/or are less prone to reduced stability.

In one embodiment, the invention provides a peptide wherein

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
or Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24.

(SEQ ID NO: 359).

In particular embodiments, a peptide of the invention is one wherein

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is:
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
or Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24.

In a further embodiment, a peptide of the invention is one wherein

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is:
Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24.

In a further embodiment, a peptide of the invention comprises Xaa1 Xaa2 Xaa3 selected from the group consisting of:

His1 Ser2 Gln3,

D-His1 Ser2 Gln3,
D-His1 Ala2 Gln3, and
D-His1 Ala2 Asp3.

(SEQ ID NO: 360).

In a further embodiment, a peptide of the invention is one wherein

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is:
Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,
Lys27 Asn28 Gly29 Gly30 Pro31 Ser32,
or Met27 Asn28 Thr29 Lys30 Arg31 Asn32.

In a further embodiment, a peptide of the invention is one wherein

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is:

Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,
or Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

(SEQ ID NO: 361).

In one embodiment, a peptide of the invention is one wherein

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is:
Lys27 Asn28 Ala29 Gly30 Pro31 Ser32.

In particular, the peptide of the invention may have an amino acid sequence selected from the group comprising:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 1)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 2)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 3)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 4)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 5)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 6)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 7)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 8)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 9)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 10)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 11)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 12)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 13)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 14)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 15)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 16)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 17)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 18)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 19)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 20)

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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 21)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 22)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 23)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 24)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 25)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 26)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 27)

HisSer Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 28)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 29)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 30)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 31)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 32)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 33)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 34)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 35)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 36)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 37)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 38)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 39)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 40)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 41)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 42)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 43)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 44)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 45)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 46)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 47)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 48)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 49)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 50)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 51)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 52)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 53)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 54)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 55)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 56)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 57)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 58)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 59)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 60)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 61)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 62)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 63)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 64)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 65)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 66)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 67)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 68)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 69)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 70)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 71)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 72)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 73)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 74)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 75)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 76)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 77)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 78)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 79)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 80)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 81)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 82)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 83)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 84)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 85)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 86)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 87)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 88)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 89)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 90)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 91)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 92)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 93)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 94)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 95)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 96)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 97)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 98)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 99)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 100)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 101)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 102)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 103)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 104)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 105)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 106)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 107)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 108)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 109)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 110)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 111)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 112)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 113)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 114)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 115)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 116)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 117)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 118)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 119)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 120)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 121)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 122)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 123)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 124)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 125)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 126)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 127)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 128)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 129)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 130)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 131)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 132)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 133)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 134)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 135)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 136)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 137)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 138)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 139)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 140)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 141)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 142)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 143)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 144)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 145)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 146)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 147)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 148)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 149)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 150)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 151)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 152)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 153)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 154)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 155)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 156)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 157)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 158)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 159)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 160)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 161)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 162)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 163)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 164)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 165)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 166)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 167)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 168)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 169)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 170)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 171)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 172)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 173)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 174)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 175)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 176)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 177)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 178)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 179)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 180)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 181)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 182)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 183)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 184)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 185)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 186)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 187)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 188)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 189)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 190)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 191)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 192)

For example, the peptide of the invention may have the amino acid sequence

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 193)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 194)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 195)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 196)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 197)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 198)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 199)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 200)

Optionally, the peptide of the invention has an extension moiety –A-B-C at the C-terminus. Accordingly, the peptide of the invention may have an additional extension moiety of sequence -A-B-C,

wherein:

A is absent or 1, 2, 3 or 4 Ala residues or 1, 2, 3 or 4 Glu residues
B is absent or 1, 2, 3 or 4 Ala residues or 1, 2, 3 or 4 Glu residues

provided that A and B do not both comprise Ala residues, and that A and B do not both comprise Glu residues; and

C is Lys, or Lys with an acid selected from capric acid, lauric acid, myristic acid, palmitic acid, stearic acid and arachidic acid, attached via its –COOH group to the $-NH_2$ group of the Lys side chain by means of a peptide bond.

In one embodiment, groups A or B or both A and B are absent. In an embodiment when A and B are both present, A is Glu and B is Ala. For example, in one embodiment A is one Glu residue, and B is one Ala residue.

In one embodiment, C is a Lys residue without substitution.

In one embodiment, C is a Lys residue with a fatty acid attached via its –COOH group to the -NH2 group of the Lys side chain by means of a peptide bond. For example, the fatty acid may be selected from

- capric acid
- lauric acid
- myristic acid,
- palmitic acid,
- stearic acid, and
- arachidic acid. (icosanoic acid)

In further emobodiments, the C-terminal extension moiety –A-B-C is:

Lys38,
Lys38-caproyl
Lys38-lauroyl,
Lys38-myristoyl,
Lys38-palmitoyl,
Lys38-stearoyl,
Lys38-arachidoyl,
Glu38 Ala39 Lys40,
Glu38 Ala39 Lys40-caproyl,
Glu38 Ala39 Lys40-lauroyl,
Glu38 Ala39 Lys40-myristoyl,
Glu38 Ala39 Lys40-palmitoyl,
Glu38 Ala39 Lys40-stearoyl,
or Glu38 Ala39 Lys40-arachidoyl.

The arachidoyl group is also known as the icosanoyl group.

Exemplary compounds comprising the C-termainal extension moiety –A-B-C may be selected from the group comprising:

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 201)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 202)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala Lys (SEQ ID NO: 203)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 204)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 205)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-myristoyl (SEQ ID NO: 206)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-palmitoyl (SEQ ID NO: 207)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-stearoyl (SEQ ID NO: 208)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-arachidoyl (SEQ ID NO: 209)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys (SEQ ID NO: 210)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-myristoyl (SEQ ID NO: 211)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-myristoyl (SEQ ID NO: 212)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-palmitoyl (SEQ ID NO: 213)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-arachidoyl (SEQ ID NO: 214)

As mentioned above, the native human oxm sequence (which is the same as the rat and hamster) is as follows:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn Arg Asn Asn Ile Ala (SEQ ID NO: 357)

The native bovine oxm sequence (which is the same as the porcine) is as follows:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 358)

That is to say that it is the same as the human sequence except that Arg33 in the human peptide is replaced by Lys33 in the bovine peptide. The present invention provides analogues of oxyntomodulin as set out above. The invention further provides peptides that are analogues in which the Lys33 residue of the peptide recited above is replaced with Arg33.

In an embodiment, the invention provides a peptide of the invention in which residue Asn34 is replaced with Asp34. Certain peptides with Asn34 replaced by Asp34 are shown as PEPTIDES No 215 to 292 in Figure 1. In a further embodiment, the invention provides a

peptide in which residue Gln3 or Asp3 is replaced with Glu3. Certain peptides with Glu3 are shown as PEPTIDES No 293 to 355 in Figure 1.

The invention further comprises embodiments incorporating the sequences disclosed in the attached examples and/or figures.

Derivatives

A compound of the invention may comprise a structure set forth above, modified by well known processes including amidation, glycosylation, carbamylation, alkylation, acylation, for example acetylation, sulfation, phosphorylation, cyclization, lipidization, protein (for example albumin) conjugation and pegylation. Analogues of the invention may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

A compound of the invention may be a fusion protein, whereby the analogue of oxyntomodulin is fused to another protein or polypeptide (the fusion partner) using recombinant methods known in the art. Alternatively, such a fusion protein may be synthetically synthesized by any known method. Such a fusion protein comprises the analogue of oxyntomodulin. Any suitable peptide or protein can be used as the fusion partner (e.g., serum albumin, carbonic anhydrase, glutathione-S-transferase, single chain antibodies, antibodies, antibody fragments or thioredoxin, etc.). For example, a compound of the invention could be fused to an immunoglobulin light chain variable domain that has binding specificity for serum albumin, as described in WO 05/118642. Preferred fusion partners will not have an adverse biological activity in vivo.

Such fusion proteins, including hybrid polypeptides, may be made by linking the carboxy-terminus of the fusion partner to the amino-terminus of the analogue of oxyntomodulin or vice versa, directly, or via a linker that preferably does not involve the loss of activity of components. Where present, the linker may be chemically stable, or labile, for example a cleavable linker may be used to link the analogue of oxyntomodulin to one or more fusion partners. A resulting cleavable fusion protein may be cleaved in vivo such that an active form of a compound of the invention is released. Examples of such cleavable linkers include, but are not limited to, the linkers D-D-D-D-Y, G-P-R, A-G-G and H-P-F-H-L, which can be cleaved by enterokinase, thrombin, ubiquitin cleaving enzyme and renin, respectively. See, e.g., U.S. Patent No. 6,410,707.

Alternatively a compound of the invention may be a fusion protein, whereby the structure of the compound of the invention is attached to a fusion partner via disulphide bond(s) resulting in a covalent linkage between at least one Cys residue of the compound of the invention, and at least one Cys residue of the fusion partner.

When a protein is used as a fusion partner, it is preferably chosen so as not to exhibit undesirable antigenicity. Undesirable antigenicity may be avoided by chosing a protein which is allogenic to the animal to which the compound is to be administered.

A compound of the invention may be a physiologically functional derivative of a compound of the invention. The term "physiologically functional derivative" is used herein to denote a chemical derivative of a compound of the invention having the same physiological function as the corresponding unmodified compound of the invention. For example, a physiologically functional derivative may be convertible in the body to a compound of the invention. According to the present invention, examples of physiologically functional derivatives include esters, amides, and carbamates; preferably esters and amides.

Pharmaceutically acceptable esters and amides of the compounds of the invention may comprise a C_{1-6} alkyl-, C_{5-10} aryl-, C_{5-10} ar-C_{1-6} alkyl-, or amino acid-ester or -amide attached at an appropriate site, for example at an acid group.

Acyl side chains may be advantageous, for example, by their lipophilic nature causing the moiety to bind with albumin, thus causing a greatly reduced rate of clearance from a subject and so increasing half life and duration of effect. Whilst the acyl side chains may be lower acyl, for example C_1- C_9 acyl, especially C_{1-6} acyl, they are preferred to be C_{4-40}, in particular C_{8-25} acyl, especially C_{16} or C_{18} acyl. Palmitoyl is especially preferred as an acyl side chain as is lauroyl. Acyl side chains may be added at any position on the peptide back bone. An acyl substituent may be attached to an amino acid residue in such a way that a carboxyl group of the acyl substituent forms an amide bond with an amino group of the amino acid residue. Alternatively, an acyl substituent may be attached to an amino acid residue in such a way that an amino group of the acyl substituent forms an amide bond with a carboxyl group of the amino acid residue. In a further preferred embodiment, the present invention relates to an oxm derivative wherein an acyl substituent is attached to the parent peptide by means of a spacer. For example, the acyl substituent may be attached to the oxm moiety by means of a spacer in such a way that a carboxyl group of the spacer forms an amide bond with an amino group of the oxm moiety. It is especially preferred to add an acyl side chain (optionally via a

spacer) at a position in the peptide back bone where a lysine residue is found. This is because lysine, having a four carbon atom side chain terminating at an epsilon-amino group, is particularly suitable for easily adding an acyl side chain. It may be necessary to introduce lysine residue into the sequence solely for the purpose of providing a convenient site at which to add an acyl side chain. Alternatively the acyl side chain may be added to the lysine residue in advance of the synthesis of the peptide, whereupon its incorporation at the relevant synthetic step will result directly in acylation. This methodology is advantageous if the peptide sequence contains more than one lysine residue as it avoids the necessity of using selective conditions that acylate only the particular lysine of interest. Preferably, the peptide derivatives have three, more preferably two, and most preferably one acyl side chain substituent. Examples of acyl (and other lipophilic substituents), approaches and specific synthetic methods of attaching such to peptides (with and without the use of spacers) are described in U.S. Patent No. 6,268,343; and U.S. Patent Number 6,458,924. Further examples of saturated fatty acids suitable for acyl derivatisation of compounds of the invention are butyric (butanoic acid): $CH_3(CH_2)_2COOH$; caproic (hexanoic acid): $CH_3(CH_2)_4COOH$; caprylic (octanoic acid): $CH_3(CH_2)_6COOH$; capric (decanoic acid): $CH_3(CH_2)_8COOH$; lauric (dodecanoic acid): $CH_3(CH_2)_{10}COOH$; myristic (tetradecanoic acid): $CH_3(CH_2)_{12}COOH$; palmitic (hexadecanoic acid): $CH_3(CH_2)_{14}COOH$; stearic (octadecanoic acid): $CH_3(CH_2)_{16}COOH$; arachidic (eicosanoic acid): $CH_3(CH_2)_{18}COOH$; behenic (docosanoic acid): $CH_3(CH_2)_{20}COOH$.

According to certain preferred embodiments, acyl side chains may be added at position 30 and/or position 33 and/or positions 38 to 46 of the peptide back bone.

Pharmaceutically acceptable amides and carbonates of the compounds of Formula (I) may comprise a C_{1-6} alkyl-, C_{5-10} aryl-, C_{5-10} ar-C_{1-6} alkyl-, or amino acid-ester or -amide, or -carbamate attached at an appropriate site, for example at an amino group.

Methods for lipidization of sulfhydryl-containing compounds with fatty acid derivatives are disclosed in U.S. Patent No. 5,936,092; U.S. Patent No. 6,093,692; and U.S. Patent No. 6,225,445. Fatty acid derivatives of a compound of the invention comprising a compound of the invention linked to fatty acid via a disulfide linkage may be used for delivery of a compound of the invention to neuronal cells and tissues. Lipidisation markedly increases the absorption of the compounds relative to the rate of absorption of the corresponding unlipidised compounds, as well as prolonging blood and tissue retention of the compounds.

Moreover, the disulfide linkage in lipidised derivative is relatively labile in the cells and thus facilitates intracellular release of the molecule from the fatty acid moieties. Suitable lipid-containing moieties are hydrophobic substituents with 4 to 26 carbon atoms, preferably 5 to 19 carbon atoms. Suitable lipid groups include, but are not limited to, the following: palmitoyl ($C_{15}H_{31}$,), oleoyl ($C_{15}H_{29}$), stearoyl ($C_{17}H_{35}$), cholate; and deoxycholate.

It will be appreciated by the skilled artisan that particular amino acid residues may be introduced to the oxm sequence in order to facilitate one or more of the modifications described herein.

Cyclization methods include cyclization through the formation of a disulfide bridge and head-to-tail cyclization using a cyclization resin. Cyclized peptides may have enhanced stability, including increased resistance to enzymatic degradation, as a result of their conformational constraints. Cyclization may in particular be expedient where the uncyclized peptide includes an N-terminal cysteine group. Suitable cyclized peptides include monomeric and dimeric head-to-tail cyclized structures. Cyclized peptides may include one or more additional residues, especially an additional cysteine incorporated for the purpose of formation of a disulfide bond or a side chain incorporated for the purpose of resin-based cyclization.

A compound of the invention may be pegylated. Pegylated compounds of the invention may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent No. 4,179,337). WO 2006/082517 and US 2006/171920, which are incorporated herein by reference, provide examples and associated methods of pegylating peptides and analogues and derivatives thereof.

Chemical moieties for derivitization of a compound of the invention may also be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. A polymer moiety for derivatisation of a compound of the invention may be of any molecular weight, and may be branched or unbranched. For ease in handling and manufacturing, the preferred molecular weight of a polyethylene glycol for derivatisation of a compound of the invention is from about l kDa to about 100 kDa, the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight. Polymers of other molecular weights may be used, depending on the desired therapeutic profile, for example the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known

effects of the polyethylene glycol to a therapeutic protein or analog. For example, the polyethylene glycol may have an average molecular weight of about 200, 500, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11,000, 11,500, 12,000, 12,500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18,500, 19,000, 19,500, 20,000, 25,000, 30,000, 35,000, 40,000, 50,000, 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, 95,000, or 100,000 kDa.

Salts and solvates of compounds of the invention that are suitable for use in a medicament are those wherein a counterion or associated solvent is pharmaceutically acceptable. However, salts and solvates having non-pharmaceutically acceptable counterions or associated solvents are within the scope of the present invention, for example, for use as intermediates in the preparation of the compounds of the invention and their pharmaceutically acceptable salts or solvates.

Suitable salts according to the invention include those formed with organic or inorganic acids or bases. Pharmaceutically acceptable acid addition salts include those formed with hydrochloric, hydrobromic, sulphuric, nitric, citric, tartaric, acetic, phosphoric, lactic, pyruvic, acetic, trifluoroacetic, succinic, perchloric, fumaric, maleic, glycollic, lactic, salicylic, oxaloacetic, methanesulfonic, ethanesulfonic, p-toluenesulfonic, formic, benzoic, malonic, naphthalene-2-sulfonic, benzenesulfonic, and isethionic acids. Other acids such as oxalic, while not in themselves pharmaceutically acceptable, may be useful as intermediates in obtaining the compounds of the invention and their pharmaceutical acceptable salts. Pharmaceutically acceptable salts with bases include ammonium salts, alkali metal salts, for example potassium and sodium salts, alkaline earth metal salts, for example calcium and magnesium salts, and salts with organic bases, for example dicyclohexylamine and N-methyl-D-glucomine.

Those skilled in the art of organic chemistry will appreciate that many organic compounds can form complexes with solvents in which they are reacted or from which they are precipitated or crystallized. Such complexes are known as "solvates". For example, a complex with water is known as a "hydrate". The present invention provides solvates of compounds of the invention.

Peptides of the invention may be made by any suitable technique for making peptides, including but not limited to conventional methodology, for example, synthesis from

individual amino acids, especially step-wise synthesis using an automatic peptide synthesizer; modification of native peptides; or recombinant manufacturing techniques.

Conditions

The invention provides a pharmaceutical composition comprising a peptide according to the invention and one or more pharmaceutically acceptable carriers. The invention also provides a pharmaceutical composition for use in the control of appetite, feeding, food intake, energy expenditure and calorie intake, the composition comprising an effective amount of a compound according to the invention. More particularly, the invention provides a pharmaceutical composition for use in the treatment of obesity, for use in the treatment of eating disorders, or for use in the treatment of diabetes or a symptom of diabetes, or for use in the treatment or prevention of comorbidities associated with obesity or excess weight.

Moreover, the invention provides a method of reducing excess weight, for example cosmetic excess weight, comprising administering to a patient desiring to reduce weight an effective amount of a compound or a pharmaceutical composition according to the invention.

Furthermore, the invention provides a method of of treating or preventing obesity or diabetes or another co-morbitity of obesity in a subject in need thereof comprising administering to the subject an effective amount of a compound or a pharmaceutical composition according to the invention.

The invention also provides a method of reducing appetite in a subject, reducing food intake in a subject or reducing calorie intake in a subject, reducing body weight in a subject, reducing body weight gain in a subject or increasing energy expenditure in a subject in need thereof comprising administering to the subject a peptide or a pharmaceutical composition according to the invention.

The invention also provides a method of causing weight loss or preventing weight gain for cosmetic purposes comprising administering to the subject a peptide or a pharmaceutical composition according to the invention.

The invention also provides a peptide of the invention for use as a medicament. It may for use as a medicament for the treatment of obesity or diabetes or of a co-morbidity of obesity. It may be for use as a medicament for reducing appetite in a subject, reducing food intake in a subject or reducing calorie intake in a subject, reducing body weight in a subject, reducing body weight gain in a subject or increasing energy expenditure in a subject.

The invention also provides use of a compound according to the invention in the manufacture of a medicament for use in the treatment of a condition selected from obesity, eating disorders, diabetes, heart disease, hypertension, lipid disease, and disorders of intestinal and gastric motor activity and other aspects of gut and intestinal function, for example, water absorption and fluid handling, or pancreatic function including the endocrine pancreas, or disorders of hepato-biliary function, or prevention of cancer. In particular, the invention provides the use of a peptide of the invention for the manufacture of a medicament for the treatment of obesity or diabetes or of a co-morbidity of obesity. Further, the invention provides use of a compound according to the invention in the manufacture of a medicament for use in the control of any one or more of appetite, feeding, food intake, energy expenditure and calorie intake. In particular, the invention provides the use of a peptide of the invention for the manufacture of a medicament for reducing appetite in a subject, reducing food intake in a subject or reducing calorie intake in a subject, reducing body weight in a subject, reducing body weight gain in a subject or increasing energy expenditure in a subject.

The subject to whom the compound is administered may be overweight, for example, obese. Alternatively, or in addition, the subject may be diabetic, for example having insulin resistance or glucose intolerance, or both. The subject may have diabetes mellitus, for example, the subject may have Type II diabetes. The subject may be overweight, for example, obese and have diabetes mellitus, for example, Type II diabetes.

In addition, or alternatively, the subject may have, or may be at risk of having, a disorder in which obesity or being overweight is a risk factor. Such disorders include, but are not limited to, cardiovascular disease, for example hypertension, atherosclerosis, congestive heart failure, and dyslipidemia; stroke; gallbladder disease; osteoarthritis; sleep apnea; reproductive disorders for example, polycystic ovarian syndrome; cancers, for example breast, prostate, colon, endometrial, kidney, and esophagus cancer; varicose veins; acanthosis nigricans; eczema; exercise intolerance; insulin resistance; hypertension; hypercholesterolemia; cholithiasis; osteoarthritis; orthopedic injury; insulin resistance, for example, type 2 diabetes and syndrome X; metabolic syndrome; and thromboembolic disease (see Kopelman (2000), Nature 404:635-43; Rissanen et al., British Med. J. 301, 835, 1990).

Other disorders associated with obesity include depression, anxiety, panic attacks, migraine headaches, PMS, chronic pain states, fibromyalgia, insomnia, impulsivity, obsessive-compulsive disorder, irritable bowel syndrome (IBS), and myoclonus. Furthermore, obesity

is a recognized risk factor for increased incidence of complications of general anesthesia. (See e.g., Kopelman, Nature 404:635-43, 2000). In general, obesity reduces life span and carries a serious risk of co-morbidities such as those listed above.

Other diseases or disorders associated with obesity are birth defects, maternal obesity being associated with increased incidence of neural tube defects, carpal tunnel syndrome (CTS); chronic venous insufficiency (CVI); daytime sleepiness; deep vein thrombosis (DVT); end stage renal disease (ESRD); gout; heat disorders; impaired immune response; impaired respiratory function; infertility; liver disease; lower back pain; obstetric and gynecologic complications; pancreatititis; as well as abdominal hernias; acanthosis nigricans; endocrine abnormalities; chronic hypoxia and hypercapnia; dermatological effects; elephantitis; gastroesophageal reflux; heel spurs; lower extremity edema; mammegaly which causes considerable problems such as bra strap pain, skin damage, cervical pain, chronic odors and infections in the skin folds under the breasts, etc.; large anterior abdominal wall masses, for example abdominal panniculitis with frequent panniculitis, impeding walking, causing frequent infections, odors, clothing difficulties, lower back pain; musculoskeletal disease; pseudo tumor cerebri (or benign intracranial hypertension), and sliding hiatil hernia.

Wynne et al (Intenational Journal of Obesity 12: 1729-1736, 2006) described how administering 400 nmoles of pre-prandial oxyntomodulin, three times daily for four days, increased activity-related energy expenditure by 143+/-109 kcal/day or 26.2+/-9.9% (P=0.0221); total energy expenditure by 9.4+/-4.8% (P=0.0454) and physical activity level by 9.5+/-4.6% (P=0.0495). Accordingly, the present invention further provides a method for increasing energy expenditure in a subject. The method includes, for example, peripherally administering a therapeutically effective amount of a compound of the invention to the subject, thereby altering energy expenditure. Energy is burned in all physiological processes. The body can alter the rate of energy expenditure directly, by modulating the efficiency of those processes, or changing the number and nature of processes that are occurring. For example, during digestion the body expends energy moving food through the bowel, and digesting food, and within cells, the efficiency of cellular metabolism can be altered to produce more or less heat.

In one aspect the method of the invention involves manipulation of the arcuate circuitry that alter food intake coordinately, and reciprocally alter energy expenditure. Energy expenditure is a result of cellular metabolism, protein synthesis, metabolic rate, and calorie utilization. Thus, in this aspect of the invention, administration of a compound of the invention may result in increased energy expenditure, and decreased efficiency of calorie utilization.

The invention also provides a method for improving a lipid profile in a subject. The invention also provides a method for alleviating a condition or disorder that can be alleviated by reducing nutrient availability.

Appetite can be measured by any means known to one of skill in the art. For example, decreased appetite can be assessed by a psychological assessment. For example, administration of a compound of the invention results in a change in perceived hunger, satiety, and/or fullness. Hunger can be assessed by any means known to one of skill in the art. For example, hunger is assessed using psychological assays, such as by an assessment of hunger feelings and sensory perception using a questionnaire, such as, but not limited to, a Visual Analog Score (VAS) questionnaire. In one specific, non-limiting example, hunger is assessed by answering questions relating to desire for food, drink, prospective food consumption, nausea, and perceptions relating to smell or taste.

A compound of the invention may be used for weight control and treatment, for example reduction or prevention of obesity, in particular any one or more of the following: preventing and reducing weight gain; inducing and promoting weight loss; and reducing obesity as measured by the Body Mass Index. A compound of the invention may be used in the control of any one or more of appetite, satiety and hunger, in particular any one or more of the following: reducing, suppressing and inhibiting appetite; inducing, increasing, enhancing and promoting satiety and sensations of satiety; and reducing, inhibiting and suppressing hunger and sensations of hunger. A compound of the invention may be used in maintaining any one or more of a desired body weight, a desired Body Mass Index, a desired appearance and good health.

A subject may be a subject who desires weight loss, for example female and male subjects who desire a change in their appearance. A subject may desire decreased feelings of hunger, for example the subject may be a person involved in a lengthy task that requires a high level of concentration, for example soldiers on active duty, air traffic controllers, or truck drivers on long distance routes, etc.

The present invention may also be used in treating, prevention, ameliorating or alleviating conditions or disorders caused by, complicated by, or aggravated by a relatively high nutrient availability. The term "condition or disorder which can be alleviated by reducing caloric (or nutrient) availability" is used herein to denote any condition or disorder in a subject that is either caused by, complicated by, or aggravated by a relatively high nutrient availability, or

that can be alleviated by reducing nutrient availability, for example by decreasing food intake. Subjects who are insulin resistant, glucose intolerant, or have any form of diabetes mellitus, for example, type 1, 2 or gestational diabetes, can also benefit from methods in accordance with the present invention.

Conditions or disorders associated with increased caloric intake include, but are not limited to, insulin resistance, glucose intolerance, obesity, diabetes, including type 2 diabetes; eating disorders, insulin-resistance syndromes, and Alzheimer's disease.

According to the present invention, a compound of the invention is preferably used in the treatment of a human. However, while the compounds of the invention will typically be used to treat human subjects they may also be used to treat similar or identical conditions in other vertebrates for example other primates; farm animals for example swine, cattle and poultry; sport animals for example horses; companion animals for example dogs and cats.

In summary, the invention also provides a peptide of the invention for use as a medicament for the prevention or treatment of obesity. There is also provided a peptide of the invention for use as a medicament for the prevention or treatment of diabetes or of a co-morbidity of obesity. Further, there is provided a peptide of the invention for use as a medicament for reducing appetite in a subject, reducing food intake in a subject or reducing calorie intake in a subject, reducing body weight in a subject, reducing body weight gain in a subject or increasing energy expenditure in a subject.

The invention also provides a method of treating or preventing obesity in a subject in need thereof comprising administering to the subject a peptide according to the invention. There is also provided a method of treating or preventing diabetes or of a co-morbidity of obesity in a subject in need thereof comprising administering to the subject a peptide according to the invention. Further, there is provided a method of reducing appetite in a subject, reducing food intake in a subject or reducing calorie intake in a subject, reducing body weight in a subject, reducing body weight gain in a subject or increasing energy expenditure in a subject in need thereof comprising administering to the subject a peptide according to the invention or a pharmaceutical composition according to the invention.

Compositions

While it is possible for the active ingredient to be administered alone, it is preferable for it to be present in a pharmaceutical formulation or composition. Accordingly, the invention provides a pharmaceutical formulation comprising a compound of the invention, or a variant

or derivative thereof, or a salt or solvate thereof, as defined above, and a pharmaceutically acceptable excipient. Pharmaceutical compositions of the invention may take the form of a pharmaceutical formulation as described below.

The pharmaceutical formulations according to the invention include those suitable for oral, parenteral (including subcutaneous, intradermal, intramuscular, intravenous, and intraarticular), inhalation (including fine particle dusts or mists which may be generated by means of various types of metered doses, pressurized aerosols, nebulizers or insufflators, and including intranasally or via the lungs), rectal and topical (including dermal, transdermal, transmucosal, buccal, sublingual, and intraocular) administration, although the most suitable route may depend upon, for example, the condition and disorder of the recipient.

The formulations may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. All methods include the step of bringing the active ingredient into association with a pharmaceutical carrier which constitutes one or more accessory ingredients. In general the formulations are prepared by uniformly and intimately bringing into association the active ingredient with liquid carriers or finely divided solid carriers or both and then, if necessary, shaping the product into the desired formulation.

Formulations of the present invention suitable for oral administration may be presented as discrete units such as capsules, cachets or tablets, each containing a predetermined amount of the active ingredient; as a powder or granules; as a solution or a suspension in an aqueous liquid or a non-aqueous liquid; or as an oil-in-water liquid emulsion or a water-in-oil liquid emulsion. The active ingredient may also be presented as a bolus, electuary or paste. Various pharmaceutically acceptable carriers and their formulation are described in standard formulation treatises, e.g., Remington's Pharmaceutical Sciences by E. W. Martin. See also Wang, Y. J. and Hanson, M. A., Journal of Parenteral Science and Technology, Technical Report No. 10, Supp. 42:2S, 1988.

A tablet may be made by compression or moulding, optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing in a suitable machine the active ingredient in a free-flowing form such as a powder or granules, optionally mixed with a binder, lubricant, inert diluent, lubricating, surface active or dispersing agent. Moulded tablets may be made by moulding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent. The tablets may optionally be coated or scored and may be formulated so as to provide slow or controlled release of the active ingredient therein. The present compounds can, for example, be administered in a form suitable for immediate

release or extended release. Immediate release or extended release can be achieved by the use of suitable pharmaceutical compositions comprising the present compounds, or, particularly in the case of extended release, by the use of devices such as subcutaneous implants or osmotic pumps. The compounds can be formulated, for administration orally, with delivery agents or carriers that facilitate the transport of therapeutic macromolecules and highly charged compounds across cell membranes, especially in the small intestine. Such delivery agents or carriers may in addition inhibit enzymatic degradation of peptides during passage through the gastrointestinal (GI) tract and/or the formulation may include additional agents that protect against such degradation. The present compounds can also be administered liposomally.

Exemplary compositions for oral administration include suspensions which can contain, for example, microcrystalline cellulose for imparting bulk, alginic acid or sodium alginate as a suspending agent, methylcellulose as a viscosity enhancer, and sweeteners or flavoring agents such as those known in the art; and immediate release tablets which can contain, for example, microcrystalline cellulose, dicalcium phosphate, starch, magnesium stearate and/or lactose and/or other excipients, binders, extenders, disintegrants, diluents and lubricants such as those known in the art. The compounds of the invention can also be delivered through the oral cavity by sublingual and/or buccal administration. Moulded tablets, compressed tablets or freeze-dried tablets are exemplary forms which may be used. Exemplary compositions include those formulating the present compound(s) with fast dissolving diluents such as mannitol, lactose, sucrose and/or cyclodextrins. Also included in such formulations may be high molecular weight excipients such as celluloses (avicel) or polyethylene glycols (PEG). Such formulations can also include an excipient to aid mucosal adhesion such as hydroxy propyl cellulose (HPC), hydroxy propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (SCMC), maleic anhydride copolymer (e.g., Gantrez), and agents to control release such as polyacrylic copolymer (e.g. Carbopol 934). Lubricants, glidants, flavors, coloring agents and stabilizers may also be added for ease of fabrication and use.

Formulations for parenteral administration include aqueous and non-aqueous sterile injection solutions which may contain anti-oxidants, buffers, bacteriostats and solutes which render the formulation isotonic with the blood of the intended recipient; and aqueous and non-aqueous sterile suspensions which may include suspending agents and thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example sealed ampoules and vials, and may be stored in a freeze-dried (lyophilised) condition requiring only the addition of the sterile liquid carrier, for example saline or water-for-injection, immediately prior to use. Extemporaneous injection solutions and suspensions may be prepared from

sterile powders, granules and tablets of the kind previously described. Exemplary compositions for parenteral administration include injectable solutions or suspensions which can contain, for example, suitable non-toxic, parenterally acceptable diluents or solvents, such as mannitol, 1,3-butanediol, water, Ringer's solution, an isotonic sodium chloride solution, or other suitable dispersing or wetting and suspending agents, including synthetic mono- or diglycerides, and fatty acids, including oleic acid, or Cremaphor. An aqueous carrier may be, for example, an isotonic buffer solution at a pH of from about 3.0 to about 8.0, preferably at a pH of from about 3.5 to about 7.4, for example from 3.5 to 6.0, for example from 3.5 to about 5.0. Useful buffers include sodium citrate-citric acid and sodium phosphate-phosphoric acid, and sodium acetate/acetic acid buffers. The composition preferably does not include oxidizing agents and other compounds that are known to be deleterious to oxm and oxm agonists.

Excipients that can be included are, for instance, other proteins, such as human serum albumin or plasma preparations. If desired, the pharmaceutical composition may also contain minor amounts of non-toxic auxiliary substances, such as wetting or emulsifying agents, preservatives, and pH buffering agents and the like, for example sodium acetate or sorbitan monolaurate.

Exemplary compositions for nasal aerosol or inhalation administration include solutions in saline, which can contain, for example, benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, and/or other solubilizing or dispersing agents such as those known in the art. Conveniently in compositions for nasal aerosol or inhalation administration the compound of the invention is delivered in the form of an aerosol spray presentation from a pressurized pack or a nebulizer, with the use of a suitable propellant, e.g., dichlorodifluoro-methane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit can be determined by providing a valve to deliver a metered amount. Capsules and cartridges of e.g., gelatin for use in an inhaler or insufflator can be formulated to contain a powder mix of the compound and a suitable powder base, for example lactose or starch. In one specific, non-limiting example, a compound of the invention is administered as an aerosol from a metered dose valve, through an aerosol adapter also known as an actuator. Optionally, a stabilizer is also included, and/or porous particles for deep lung delivery are included (e.g., see U.S. Patent No. 6,447,743). Intranasal formulations may include delivery agents for reversibly opening the nasal tight junction, thereby increasing drug permeability (e.g., see US Patent Application 10/322,266).

Formulations for rectal administration may be presented as a retention enema or a suppository with the usual carriers such as cocoa butter, synthetic glyceride esters or polyethylene glycol. Such carriers are typically solid at ordinary temperatures, but liquefy and/or dissolve in the rectal cavity to release the drug.

Formulations for topical administration in the mouth, for example buccally or sublingually, include lozenges comprising the active ingredient in a flavoured basis such as sucrose and acacia or tragacanth, and pastilles comprising the active ingredient in a basis such as gelatin and glycerine or sucrose and acacia. Exemplary compositions for topical administration include a topical carrier such as Plastibase (mineral oil gelled with polyethylene).

Preferred unit dosage formulations are those containing an effective dose, as hereinbefore recited, or an appropriate fraction thereof, of the active ingredient.

It should be understood that in addition to the ingredients particularly mentioned above, the formulations of this invention may include other agents conventional in the art having regard to the type of formulation in question, for example those suitable for oral administration may include flavouring agents.

The compounds of the invention are also suitably administered as sustained-release systems. Suitable examples of sustained-release systems of the invention include suitable polymeric materials, for example semi-permeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules; suitable hydrophobic materials, for example as an emulsion in an acceptable oil; or ion exchange resins; and sparingly soluble derivatives of the compound of the invention, for example, a sparingly soluble salt. Sustained-release systems may be administered orally; rectally; parenterally; intracistemally; intravaginally; intraperitoneally; topically, for example as a powder, ointment, gel, drop or transdermal patch; bucally; or as an oral or nasal spray.

Preparations for administration can be suitably formulated to give controlled release of compounds of the invention. For example, the pharmaceutical compositions may be in the form of particles comprising one or more of biodegradable polymers, polysaccharide jellifying and/or bioadhesive polymers, amphiphilic polymers, agents capable of modifying the interface properties of the particles of the compound of the invention. These compositions exhibit certain biocompatibility features which allow a controlled release of the active substance. See U.S. Patent No. 5,700,486.

A compound of the invention may be delivered by way of a pump (see Langer, Science 249:1527-1533, 1990; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201, 1987; Buchwald et al., Surgery 88:507, 1980; Saudek et al., N. Engl. J. Med. 321:574, 1989) or by a continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The key factor in selecting an appropriate dose is the result obtained, as measured by decreases in total body weight or ratio of fat to lean mass, or by other criteria for measuring control or prevention of obesity or prevention of obesity-related conditions, as are deemed appropriate by the practitioner. Other controlled release systems are discussed in the review by Langer, supra. In another aspect of the disclosure, compounds of the invention are delivered by way of an implanted pump, described, for example, in U.S. Patent No. 6,436,091; U.S. Patent No. 5,939,380; U.S. Patent No. 5,993,414.

Implantable drug infusion devices are used to provide patients with a constant and long term dosage or infusion of a drug or any other therapeutic agent. Essentially such device may be categorized as either active or passive. A compound of the present invention may be formulated as a depot preparation. Such a long acting depot formulation can be administered by implantation, for example subcutaneously or intramuscularly; or by intramuscular injection. Thus, for example, the compounds can be formulated with suitable polymeric or hydrophobic materials, for example as an emulsion in an acceptable oil; or ion exchange resins; or as a sparingly soluble derivatives, for example, as a sparingly soluble salt.

A therapeutically effective amount of a compound of the invention may be administered as a single pulse dose, as a bolus dose, or as pulse doses administered over time. Thus, in pulse doses, a bolus administration of a compound of the invention is provided, followed by a time period wherein a compound of the invention is administered to the subject, followed by a second bolus administration. In specific, non-limiting examples, pulse doses of a compound of the invention are administered during the course of a day, during the course of a week, or during the course of a month.

In one embodiment, a therapeutically effective amount of a compound of the invention is administered with a therapeutically effective amount of another agent, for example an additional appetite suppressant, a food-intake-reducing, dipetidyl peptidase-IV (DPP-IV) inhibiting, plasma glucose-lowering or plasma lipid-altering agent. Specific, non-limiting examples of an additional appetite suppressant include amfepramone (diethylpropion), phentermine, mazindol and phenylpropanolamine, fenfluramine, dexfenfluramine, sibutramine, rimonabant, and fluoxetine. Specific, non-limiting examples of DPP-IV inhibitors include Januvia (sitagliptin phosphate), and Galvus (vildagliptin). The compound

of the invention can be administered simultaneously with the additional agent, or it may be administered sequentially. Thus, in one embodiment, the compound of the invention is formulated and administered with an additional agent as a single dose.

In another embodiment, a therapeutically effective amount of a compound of the invention is administered in combination with a therapeutically effective amount of another agent, for the treatment of diseases other than obesity, for example diabetes, in which specific non limiting examples of an additional therapeutic agent are GLP-1 or an analogue thereof, exenatide, and pramlintide.

A compound of the invention may be administered whenever the effect, e.g., appetite suppression, decreased food intake, or decreased caloric intake, is desired, or slightly before to whenever the effect is desired, such as, but not limited to about 10 minutes, about 15 minutes, about 30 minutes, about 60 minutes, about 90 minutes, about 120 minutes, about 4 hours, about 8 hours, or about 12 hours, before the time the effect is desired.

A compound of the invention may be administered in combination with whenever the effect, e.g., appetite suppression, decreased food intake, or decreased caloric intake, is desired, or slightly before to whenever the effect is desired, such as, but not limited to about 10 minutes, about 15 minutes, about 30 minutes, about 60 minutes, about 90 minutes, about 120 minutes, about 4 hours, about 8 hours, or about 12 hours, before the time the effect is desired.

Dosages

The therapeutically effective amount of a compound of the invention will be dependent on the molecule utilized, the subject being treated, the severity and type of the affliction, and the manner and route of administration. For example, a therapeutically effective amount of a compound of the invention may vary from about 0.01 μg per kilogram (kg) body weight to about 1 g per kg body weight, for example about .0.1 μg to about 5 mg per kg body weight, or about 1 μg to about 1 mg per kg body weight per day. A compound of the invention may be administered to a subject at 0.5 to 200 picomole (pmol) per kg body weight, or about 20 pmol per kg body weight. For especially active compounds or compounds administered by an especially efficient route, in one specific, non-limiting example, a compound of the invention is administered in a dose of about 1 nmol or more, 2 nmol or more, 5 nmol or more, or 10 nmol or more and the dose of the compound of the invention is generally not more than 100 nmol, for example, the dose is 90 nmols or less, 80 nmols or less, 70 nmols or less, 60 nmols or less, 50 nmols or less, 40 nmols or less, 30 nmols or less, 20 nmols or less, or 10 nmols or less. For a less active compound or a compound administered by a less efficient route, in

another specific, non-limiting example, a compound of the invention is administered in a dose of about 100 nmol or more, 200 nmol or more, 300 nmol or more, 400 nmol or more, 500 nmol or more, 600 nmol or more, 700 nmol or more, 800 nmol or more, 900 nmol or more, or 1 μmol or more and the dose of the compound of the invention is generally not more than 10 μmols, for example, the dose is 9 μmols or less, 8 μmols or less, 7 μmols or less, 6 μmols or less, 5 μmols or less, 4 μmols or less, 3 μmols or less, 2 μmols or less, 1 μmol or less. For example, a dosage range may comprise any combination of any of the specified lower dose limits with any of the specified upper dose limits. Thus, examples of non-limiting dose ranges of compounds of the invention are within the range of from 1 nmol to 1 μmol, from 1 to 900 nmols, or from 1 to 800 nmols. For especially active compounds or compounds administered by an especially efficient route, the dose may be from 1 nmol to 100 nmol, from 2 to 80 nmols, or from 5 to 60 nmols. For a less active compound or a compound administered by a less efficient route, the dose may be from 100 nmol to 10 μmol, from 200 nmol to 5 μmols, or from 500 nmols to 2 μmols.

In one specific, non-limiting example, from about 0.5 to about 50 nmol of a compound of the invention is administered, for example about 1 to about 20 nmol, for example, about 2 nmol is administered as a subcutaneous injection. The exact dose is readily determined by one of skill in the art based on the potency of the specific compound utilized, the age, weight, sex and physiological condition of the subject.

In another specific non-limiting example, a compound of the invention is administered to a subject in a dose of about 1 μg to about 2 mg per dose, about once, about twice, about three times, or about four times per day., A therapeutically effective amount of a compound of the invention may vary from about 0.01 μg per kilogram (kg) body weight to about 1 g per kg body weight, for example about 0.1 μg to about 5 mg per kg body weight, or about 5 μg to about 1 mg per kg body weight per day. Bearing in mind that a typical oxyntomudilin analogue of the invention has a molecular weight of around 4500, a compound of the invention may be administered to a subject at 2.25 to 900 ng per kg body weight, or about 90 ng per kg body weight. For especially active compounds or compounds administered by an especially efficient route, in one specific, non-limiting example, a compound of the invention is administered in a dose of about 4.5 μg or more, 9 μg or more, 22.5 μg or more, or 45 μg or more and the dose of the compound of the invention is generally not more than 450 μg, for example, the dose is 405 μg or less, 360 μg or less, 315 μg or less, 270 μg or less, 225 μg or less, 180 μg or less, 135 μg or less, 90 μg or less, or 45 μg or less. For a less active compound or a compound administered by a less efficient route, in another specific, non-

limiting example, a compound of the invention is administered in a dose of about 450 μg or more, 900 μg or more, 1350 μg or more, 1800 μg or more, 2250 μg or more, 2700 μg or more, 3150 μg or more, 3600 μg or more, 4050 μg or more, or 4500 μg or more and the dose of the compound of the invention is generally not more than 45000 μg , for example, the dose is 40500 μg or less, 36000 μg or less, 31500 μg or less, 27000 μg or less, 22500 μg or less, 18000 μg or less, 13500 μg or less, 9000 μg or less, 45000 μg or less. For example, a dosage range may comprise any combination of any of the specified lower dose limits with any of the specified upper dose limits. Thus, examples of non-limiting dose ranges of compounds of the invention are within the range of from 4.5 μg to 4500 μg, from 4.5 to 4050 μg , or from 4.5 to 3600 μg. For especially active compounds or compounds administered by an especially efficient route, the dose may be from 4.5 μg to 450 μg, from 9 to 360 μg, or from 22.5 to 270 μg. For a less active compound or a compound administered by a less efficient route, the dose may be from 450 μg to 45000 μg, from 900 μg to 22500 μg, or from 2250 to 9000 μg.

Suitable doses of compounds of the invention also include those that result in a reduction in calorie intake, food intake, or appetite, or increase in energy expenditure that is equivalent to the reduction in calorie intake, food intake, or appetite, or to increase the energy expenditure, caused by levels of oxm that have been observed in man. Examples of doses include, but are not limited to doses that produce the effect demonstrated when the serum levels of oxm are from about 800 pM to about 1300 pM, or from about 900 pM to about 1000 pM, or about 950 pM.

Suitable doses of compounds of the invention also include those that are equivalent to levels of oxm seen in subjects experiencing conditions associated with reduced appetite, for example jejunoileal bypass (Sarson *et al., Int J Obes*, 1981, 5:471–480; Holst *et al., Scand J Gastroenterol*, 1979, 14:205–207).

In a study of the effects of oxyntomodulin on appetite suppression and food intake reduction in humans (Cohen *et al., J. Clin. Endocrinol. Metab.*, 2003, 88(10), 4696-4701) it was found that an infusion of oxyntomodulin to human volunteers at 3.0 pmol/kg.min for 90 minutes led to a significantly reduced *ad libitum* energy intake (19.3 +/- 5.6%; P<0.01). The total oxyntomodulin infused was 270 pmol/kg body weight. The observed oxyntomodulin-like immunoreactivity in the blood of the subjects rose to around 800 pmol/L during the infusion.

In a study of the effects of oxyntomodulin on weight loss in humans (Wynne *et al., Diabetes.*, 2005, 54(Aug), 2390-2395) it was found that subcutaneous injections of oxyntomodulin to humans volunteers resulted in a significant reduction of body weight. Over the study period of 28 days, body weight of the treatment group was reduced by 2.3 ± 0.4 kg in the treatment group compared with 0.5 ± 0.5 kg in the control group (P = 0.0106). 1.8 mg (approximately 400 nmol) of oxyntomodulin was administered three times daily 30 mins before meals. On average, the treatment group had an additional 0.45kg weight loss per week. Energy intake by the treatment group was significantly reduced by 170 ± 37 kcal (25 ± 5%) at the initial study meal within the 28 day study period (P = 0.0007) and by 250 ± 63 kcal (35 ± 9%) at the final study meal during the 28 day study period (P = 0.0023), with no change in subjective food palatability. Oxyntomodulin treatment resulted in weight loss and a change in the levels of adipose hormones consistent with a loss of adipose tissue. The anorectic effect was maintained over the 4-week period.

The compounds of the invention have been found to be more active and/or longer-lasting than native oxyntomodulin as used in human studies to date (Cohen *et al.* (2003) and Wynne *et al.* (2005) *Diabetes* 54(Aug), 2390-2395). The dosage required for a compound of the invention may be somewhat lower than that required for native oxyntomodulin. The dosages of peptides of the invention required to observe an effect in humans can be expected to be a lower, for example 2.5 times, 200 times, 400 times, and 1-4000 times lower than the dose of native oxyntomodulin. The magnitude of the potency of the peptides of the invention in comparison to the native oxyntomodulin peptide may also allow the frequency of administration a compound of the invention to be lower than that required for native oxyntomodulin.

The disclosure is illustrated by the following non-limiting Examples.

EXAMPLES

Materials and Methods

Animals: All animal procedures were approved by the British Home Office Animals (Scientific Procedures) Act 1986 (Project License number 70/5516). Male C57BL/6 mice and male Wistar rats were maintained in individual cages under controlled temperature (21-23 °C) with *ad libitum* access to standard chow (RM1 diet, SDS Ltd, Witham, Essex, UK) and to water. The light cycle was 12 hours light and 12 hours dark with 'dawn' at 07:00, lights full on at 07:30, 'dusk' at 19:00 with lights off at 19:30. These times were fixed in the animal facility. All animals were handled almost daily for on average nine days prior to the first

study. During the acclimatization period, mice received two saline injections at least two days apart in order to further acclimatize to the procedure on the study days. It was found in rats that minimising the number of injections provided an optimal response, and so acclimatization injections were not used.

Intra-peritoneal (IP) injections: IP injections were administered to mice via a 0.5 ml syringe with a 29-gauge needle (maximum injection volume 0.1 ml). The maximum volume administered IP was 0.1 ml.

Subcutaneous (SC) injections: SC injections were administered to rats via a 0.5 ml syringe with a 29-gauge needle (maximum injection volume 0.2 ml), in a volume of 0.1 ml if administered to the thigh skin, or 0.2 ml if administered to the neck scruff.

Study protocol: C57BL/6 mice (20-35 g) were injected with the peptide under investigation following a 20-hour fast. Wistar rats were injected following a 24-hour fast. Typically 6 to 10 rodents were used per experimental group. Injections were typically administered at 9:00. A pre-weighed quantity of chow was presented immediately after injection. The remaining food was measured at regular time intervals (e.g. 1, 2, 3,4, 6, 8, 24, 32 and 48 hours following injection) and food intake calculated.

Peptides Synthesis

Synthesis of peptides

Peptides were produced by solid phase step-wise synthesis (SPSS) using the Fmoc N-terminal protection strategy. Chain assembly was performed on Applied Biosystems 431, 433 or Pioneer automated synthesisers. Solid phase resins were used with factory pre-loaded C terminal amino acid or with an amide linker as appropriate. The following side-chain protecting groups were used: Asn(Trt), Gln(Trt), Cys(Trt), His(Trt), Asp(tBu), Glu(tBu), Ser(tBu), Thr(tBu), Tyr(tBu), Arg(Pbf), Lys(Boc), Trp(Boc). In some cases, where synthesis difficulty was anticipated, pre-formed oxazolidine dipeptides were used in place of respective monomers. All chemicals (from various suppliers including Applied Biosystems, Merck Biosciences and AGCT) were synthesis grade. Feedback monitoring to optimise syntheses was employed on all instruments.

Recovery of peptides

After synthesis, peptides were cleaved from the solid phase resin support and fully side chain deprotected. This was achieved by treatment for 2 hours with trifluoroacetic acid (TFA) containing 4% water and 2.5% tri-isopropylsilane to scavenge side-chain protecting groups. Peptide-TFA solutions were filtered from the resins and the peptides precipitated with methyl tertiary butyl ether (MTBE). Peptides were isolated by centrifugation, washed in MTBE and dried under vacuum.

Analysis and purification of peptides

Peptides were dissolved in de-ionized water, with addition of acetic acid where necessary. Peptide solutions were clarified by centrifugation or filtration (Whatman GD/X syringe filter) prior to analysis and purification.

All peptide products were analysed by reverse phase HPLC on an Applied Biosystems BioCad instrument using an analytical Brownlee Aquapore RP300 C8 or Phenomenex Synergi Hydro C18 column. Purification was performed by reverse phase HPLC using preparative columns of the above types. Acetonitrile-water gradients (with TFA as counter–ion) were used for elution of products. Capillary Zone Electrophoresis (CZE) was performed on crude and purified peptides using a Hewlett Packard 3DCE instrument. Molecular weight determination was performed on a Micromass MALDI –R mass spectrometer.

Purified peptides were freeze-dried in pharmaceutical grade glass vials (Adelphi Vials) and closed under vacuum.

Derivatised side chains

Peptides having side chains derivatised with an acyl or alkyl group were prepared by standard methods.

Solubility of derivatised peptides

Derivatised polypeptides should be fully dissolved before administration. In order to achieve solubility it may be necessary to dissolve the polypeptides in a small amount of dilute alkali (for example, 50 µl 0.01 NaOH) and then dilute the dissolved peptide in saline.

Inhibition of food intake experiments.

Example 1 (comparative example).

The feeding effect of native oxyntomodulin (human) was investigated by intraperitoneal injection of 1400 nmoles/kg to groups of fasted mice. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figure 2. Due to the relatively low activity of native oxyntomodulin, a high dose was given. Less significant results are observed with lower doses.

Example 2 (comparative example).

The feeding effect of native oxyntomodulin (human) was investigated by subcutaneous injection of 1400 nmoles/kg to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 6 hours is shown in comparison to saline in Figure 3. It can be seen that even at a high dose of 1400 nmol/kg, native oxyntomodulin is not capable of reducing food intake in fasted rats under these conditions. At lower doses, the same lack of effectiveness is observed.

Example 3.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 178 [SEQ.ID NO:178]; PEPTIDE NO: 82 [SEQ ID NO:82]; PEPTIDE NO: 58 [SEQ ID NO:58]; and PEPTIDE NO: 52 [SEQ ID NO:52]. The analogues were administered at a dose of 10 (PEPTIDE NO: 178 [SEQ ID NO:178]) and 10 (PEPTIDE NO: 82 [SEQ ID NO:82]; PEPTIDE NO: 58 [SEQ ID NO:58]; and PEPTIDE NO: 52 [SEQ ID NO:52]) nmoles/kg by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figures 4 to 7. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 4.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 164 [SEQ ID NO:164]; and PEPTIDE NO: 167 [SEQ ID NO:167]. The analogues were administered at a dose of 4 and 5 nmoles/kg respectively, by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 48 hours (PEPTIDE NO: 164 [SEQ ID NO:164]) and 32 hours (PEPTIDE NO:167 [SEQ ID NO:167]) is shown in comparison to saline in Figures 8 and 9. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the

whole 48 (PEPTIDE NO: 164 [SEQ ID NO:164]) and 32 (PEPTIDE NO: 167 [SEQ ID NO:167]) hour period; that is to say that the food intake over the first 24 hour period is lower than in the saline control and continues to remain below it in the following 24 hours (PEPTIDE NO: 164 [SEQ ID NO:164]) or 8 hours (PEPTIDE NO:167 [SEQ ID NO:167]). It is also lower than in the control group treated with native oxyntomodulin.

Example 5.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 100 [SEQ ID NO:100]; and PEPTIDE NO: 148 [SEQ ID NO:148]. The analogues were administered at a dose of 20 and 10 nmoles/kg respectively, by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figures 10 and 11. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 6.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 60 [SEQ ID NO:60]; and PEPTIDE NO: 94 [SEQ ID NO:94]. The analogues were administered at a dose of 100 and 5 nmoles/kg respectively, by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figures 12 and 13. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 7.

The feeding effects of the following analogue of oxyntomodulin was investigated: PEPTIDE NO: 155 [SEQ ID NO:155]. The analogue was administered at a dose of 4 nmoles/kg by subcutaneous injection to a group of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 32 hours is shown in comparison to saline in Figure 14. The analogue demonstrates a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 32 hour period; that is to say that the food intake over the first 24 hour period is lower

than in the saline control and continues to remain below it in the following 8 hours. It is also lower than in the control group treated with native oxyntomodulin.

Example 8.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 142 [SEQ ID NO:142]; PEPTIDE NO: 184 [SEQ ID NO:184]; and PEPTIDE NO: 172 [SEQ ID NO:172]. The analogues were administered at a dose of 3 nmoles/kg by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figures 15 to 17. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 9.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 4 [SEQ ID NO:4]; PEPTIDE NO: 195 [SEQ ID NO:195]; PEPTIDE NO: 136 [SEQ ID NO:136]; and PEPTIDE NO: 108 [SEQ ID NO:108]. The analogues were administered at doses of 5, 800, 5 and 100 nmoles/kg respectively, by intraperitoneal injection to groups of fasted mice. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figures 18 to 21. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 10.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 142 [SEQ ID NO:142]; PEPTIDE NO: 22 [SEQ ID NO:22]; PEPTIDE NO: 153 [SEQ ID NO:153]; and PEPTIDE NO: 199 [SEQ ID NO:199]. The analogues were administered at a dose of 3 nmoles/kg, 200 nmoles/kg (PEPTIDE NO: 153 [SEQ ID NO:153]), and 500 nmoles/kg (PEPTIDE NO: 199 [SEQ ID NO:199]) by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figures 22 to 25. The analogues demonstrate a potent and long acting suppression of food

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intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 11.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 210 [SEQ ID NO:210]; PEPTIDE NO: 211 [SEQ ID NO:211]; PEPTIDE NO: 213 [SEQ ID NO:213]; and PEPTIDE NO: 214 [SEQ ID NO:214]. The analogues were administered at a dose of 20, 200, 400 and 400 nmoles/kg respectively by intraperitoneal injection to groups of fasted mice. A further group was administered saline (control). Mean cumulative food intake over the course of 48 hours is shown in comparison to saline in Figures 26 to 29. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 48 hour period; that is to say that the food intake over the first 24 hour period is lower than in the saline control and continues to remain below it in the following 24 hours. It is also lower than in the control group treated with native oxyntomodulin.

Example 12.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 201 [SEQ ID NO:201]; and PEPTIDE NO: 202 [SEQ ID NO:202]. The analogues were administered at a dose of 5 nmoles/kg by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 48 hours is shown in comparison to saline in Figures 30 and 31. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 48 hour period; that is to say that the food intake over the first 24 hour period is lower than in the saline control and continues to remain below it in the following 24 hours. It is also lower than in the control group treated with native oxyntomodulin.

Example 13.

The feeding effect of the following analogue of oxyntomodulin was investigated: PEPTIDE NO: 203 [SEQ ID NO:203]. The analogue was administered at a dose of 100 nmoles/kg by subcutaneous injection to a group of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figure 32. The analogue demonstrates a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the

whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 14.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 204 [SEQ ID NO:204]; and PEPTIDE NO: 205 [SEQ ID NO:205]. The analogues were administered at a dose of 5 nmoles/kg by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 32 hours is shown in comparison to saline in Figures 33 and 34. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 32 hour period; that is to say that the food intake over the first 24 hour period is lower than in the saline control and continues to remain below it in the following 8 hours. It is also lower than in the control group treated with native oxyntomodulin.

Example 15.

The feeding effects of the following analogues of oxyntomodulin were investigated: PEPTIDE NO: 206 [SEQ ID NO:206]; PEPTIDE NO: 207 [SEQ ID NO:207]and PEPTIDE NO: 209 [SEQ ID NO:209]. The analogues were administered at a dose of 80 nmoles/kg by subcutaneous injection to groups of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 48 hours is shown in comparison to saline in Figures 35 to 37. The analogues demonstrate a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 48 hour period; that is to say that the food intake over the first 24 hour period is lower than in the saline control and continues to remain below it in the following 24 hours. It is also lower than in the control group treated with native oxyntomodulin.

Example 16.

The feeding effect of the following analogue of oxyntomodulin was investigated: PEPTIDE NO: 215 [SEQ ID NO:215]. The analogue was administered at a dose of 5 nmoles/kg by subcutaneous injection to a group of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figure 38. The analogue demonstrates a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than

in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 17.

The feeding effect of the following analogue of oxyntomodulin was investigated: PEPTIDE NO: 216 [SEQ ID NO:216]. The analogue was administered at a dose of 10 nmoles/kg by subcutaneous injection to a group of fasted rats. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figure 39. The analogue demonstrates a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 18.

The feeding effect of the following analogue of oxyntomodulin was investigated: PEPTIDE NO: 355 [SEQ ID NO:355]. The analogue was administered at a dose of 5 nmoles/kg by subcutaneous injection to a group of fasted mice. A further group was administered saline (control). Mean cumulative food intake over the course of 4 hours is shown in comparison to saline in Figure 40. The analogue demonstrates a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 4 hour period; that is to say that the food intake over the 4 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

Example 19.

The feeding effect of the following analogue of oxyntomodulin was investigated: PEPTIDE NO: 130 [SEQ ID NO:130]. The analogue was administered at a dose of 20 nmoles/kg by subcutaneous injection to a group of fasted mice. A further group was administered saline (control). Mean cumulative food intake over the course of 24 hours is shown in comparison to saline in Figure 41. The analogue demonstrates a potent and long acting suppression of food intake in comparison to the saline control. The food intake suppression continues for the whole 24 hour period; that is to say that the food intake over the 24 hour period is lower than in the saline control. It is also lower than in the control group treated with native oxyntomodulin.

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It will be appreciated that throughout the above examples, compounds of the invention are capable of inhibiting food intake at doses markedly lower than that of the native peptide used in the comparator experiments.

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Claims

1. A peptide comprising the amino acid sequence:

Xaa1 Xaa2 Xaa3 Gly4 Thr5 Phe6 Thr7 Ser8 Asp9 Tyr10 Ser11 Lys12 Tyr13 Leu14

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Trp25 Leu26

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 Lys33 Asn34 Asn35 Ile36 Ala37;

wherein:

Xaa1 is His1 or D-His1,
Xaa2 is Ser2 or Ala2,
Xaa3 is Gln3 or Asp3;

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
or Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24;

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is:

Met27 Asn28 Thr29 Lys30 Arg31 Asn32,
Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,
or Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

or a peptide as set out above in which residue Asn34 is replaced with Asp34;

or a peptide as set out above in which Xaa3 is Glu3;

with the proviso that if
Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is
Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24,

then Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is not
Met27 Asn28 Thr29 Lys30 Arg31 Asn32

(SEQ ID NO: 356).

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2. A peptide as claimed in claim 1, wherein

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 is:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
or Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24

(SEQ ID NO: 359).

3. A peptide as claimed in any of claims 1 to 2, wherein

Xaa1 Xaa2 Xaa3 is

His1 Ser2 Gln3, or.
D-His1 Ser2 Gln3, or
D-His1 Ala2 Gln3, or
D-His1 Ala2 Asp3

(SEQ ID NO: 360).

4. A peptide as claimed in any of claims 1 to 3, wherein

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is:

Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,
or Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

(SEQ ID NO: 361).

5. A peptide as claimed in claim 1 having an amino acid sequence selected from the group consisting of:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 1)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 2)

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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 3)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 4)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 5)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 6)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 7)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 8)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 9

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 10)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 11)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 12)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 13)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 14)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 15)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 16)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 17)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 18)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 19)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 20)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 21)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 22)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 23)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 24)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 25)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 26)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 27)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 28)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 29)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 30)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 31)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 32)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 33)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 34)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 35)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 36)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 37)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 38)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 39)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 40)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 41)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 42)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 43)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 44)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 45)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 46)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 47)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 48)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 49)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 50)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 51)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 52)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 53)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 54)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 55)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 56)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 57)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 58)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 59

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 60

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 61

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 62)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 63)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 64)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 65)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 66)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 67)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 68)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 69)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 70)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 71)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 72)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 73)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 74)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 75)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 76)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 77)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 78)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 79)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 80)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 81)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 82)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 83)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 84)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 85)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 86)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 87)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 88)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 89)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 90)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 91)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 92)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 93)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 94)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 95)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 96)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 97)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 98)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 99)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 100)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 101)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 102)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 103)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 104)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 105)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 106)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 107)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 108)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 109)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 110)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 111)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 112)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 113)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 114)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 115)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 116)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 117)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 118)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 119)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 120)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 121)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 122)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 123)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 124)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 125)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 126)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 127)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 128)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 129)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 130)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 131)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 132)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 133)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 134)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 135)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 136)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 137)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 138)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 139)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 140)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 141)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 142)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 143)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 144)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 145)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 146)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 147)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 148)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 149)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 150)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 151)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 152)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 153)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 154)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 155)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 156)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 157)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 158)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 159)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 160)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 161)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 162)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 163)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 164)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 165)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 166)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 167)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 168)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 169)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 170)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 171)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 172)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 173)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 174)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 175)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 176)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 177)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 178)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 179)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 180)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 181)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 182)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 183)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 184)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 185)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 186)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 187)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 188)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 189)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 190)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 191)

D-HisAla Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 192)

6. A peptide as claimed in any one of claims 1 to 5, wherein the peptide has an additional extension moiety of sequence -A-B-C, wherein:

A is absent or 1, 2, 3 or 4 Ala residues or 1, 2, 3 or 4 Glu residues
B is absent or 1, 2, 3 or 4 Ala residues or 1, 2, 3 or 4 Glu residues

provided that A and B do not both comprise Ala residues, and that A and B do not both comprise Glu residues; and

C is Lys, or Lys with an acid selected from capric acid, lauric acid, myristic acid, palmitic acid, stearic acid and arachidic acid, attached via its –COOH group to the $-NH_2$ group of the Lys side chain by means of a peptide bond.

7. A peptide as claimed in claim 6, wherein A or B or both A and B are absent.

8. A peptide as claimed in claim 6, wherein A is one Glu residue, and B is one Ala residue.

9. A peptide as claimed in any of claims 6 to 8, wherein C is a Lys residue.

10. A peptide as claimed in any of claims 6 to 8, wherein:
- C is a Lys residue with lauric acid attached via its –COOH group to the -NH2 group of the Lys side chain by means of a peptide bond.
- C is a Lys residue with myristic acid attached via its –COOH group to the -NH2 group of the Lys side chain by means of a peptide bond.
- C is a Lys residue with palmitic acid attached via its –COOH group to the -NH2 group of the Lys side chain by means of a peptide bond.
-C is a Lys residue with stearic acid attached via its –COOH group to the -NH2 group of the Lys side chain by means of a peptide bond.
- C is a Lys residue with arachidic acid attached via its –COOH group to the -NH2 group of the Lys side chain by means of a peptide bond.
- C is a Lys residue with capric acid attached via its –COOH group to the -NH2 group of the Lys side chain by means of a peptide bond.

11. A peptide according to claim 6 having a structure sequence selected from the group consisting of:

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 201)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 202)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala Lys (SEQ ID NO: 203)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 204)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 205)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-myristoyl (SEQ ID NO: 206)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-palmitoyl (SEQ ID NO: 207)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-stearoyl (SEQ ID NO: 208)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-arachidoyl (SEQ ID NO: 209)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys (SEQ ID NO: 210)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-myristoyl (SEQ ID NO: 211)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-myristoyl (SEQ ID NO: 212)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-palmitoyl (SEQ ID NO: 213)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-arachidoyl (SEQ ID NO: 214)

12. A peptide according to claim 1 having a structure sequence selected from the group consisting of:

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 215)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 216)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 217)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 218)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 219)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 220)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 221)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEQ ID NO: 222)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 223)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 224)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 225)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEQ ID NO: 226)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 227)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 228)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 229)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 230)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 231)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEQ ID NO: 232)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 233)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 234)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 235)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 236)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 237)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 238)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 239)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 240)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEQ ID NO: 241)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEQ ID NO: 242)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala Lys (SEQ ID NO: 243)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEQ ID NO: 244)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEQ ID NO: 245)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-myristoyl (SEQ ID NO: 246)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-palmitoyl (SEQ ID NO: 247)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-stearoyl (SEQ ID NO: 248)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-arachidoyl (SEQ ID NO: 249)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys (SEQ ID NO: 250)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-myristoyl (SEQ ID NO: 251)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-palmitoyl (SEQ ID NO: 252)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-arachidoyl (SEQ ID NO: 253)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 254)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 255)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 256)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 257)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 258)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 259)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 260)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEQ ID NO: 261)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 262)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 263)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 264)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEQ ID NO: 265)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 266)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 267)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 268)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 269)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 270)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEQ ID NO: 271)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 272)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 273)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 274)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 275)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 276)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 277)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 278)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEQ ID NO: 279)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEQ ID NO: 280)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEQ ID NO: 281)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala Lys (SEQ ID NO: 282)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEQ ID NO: 283)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEQ ID NO: 284)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-myristoyl (SEQ ID NO: 285)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-palmitoyl (SEQ ID NO: 286)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-stearoyl (SEQ ID NO: 287)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-arachidoyl (SEQ ID NO: 288)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys (SEQ ID NO: 289)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-myristoyl (SEQ ID NO: 290)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-palmitoyl (SEQ ID NO: 291)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-arachidoyl (SEQ ID NO: 292)

13. A peptide according to claim 1 having a structure sequence selected from the group comprising:

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 293)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 294)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 295)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 296)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 297)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 298)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 299)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 300)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 301)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 302)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 303)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 304)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 305)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 306)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 307)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 308)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 309)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 310)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 311)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 312)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala Lys (SEQ ID NO: 313)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 314)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 315)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-myristoyl (SEQ ID NO: 316)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-palmitoyl (SEQ ID NO: 317)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-stearoyl (SEQ ID NO: 318)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-arachidoyl (SEQ ID NO: 319)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys (SEQ ID NO: 320)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-myristoyl (SEQ ID NO: 321)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-palmitoyl (SEQ ID NO: 322)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-arachidoyl (SEQ ID NO: 323)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 324)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 325)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 326)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 327)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 328)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 329)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 330)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 331)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 332)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEQ ID NO: 333)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 334)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 335)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 336)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 337)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 338)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 339)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 340)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEQ ID NO: 341)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 342)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 343)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala Lys (SEQ ID NO: 344)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 345)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEQ ID NO: 346)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-myristoyl (SEQ ID NO: 347)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-palmitoyl (SEQ ID NO: 348)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-stearoyl (SEQ ID NO: 349)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-arachidoyl (SEQ ID NO: 350)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys (SEQ ID NO: 351)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-myristoyl (SEQ ID NO: 352)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-palmitoyl (SEQ ID NO: 353)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-arachidoyl (SEQ ID NO: 354)

14. A pharmaceutical composition comprising a peptide as claimed in any one of claims 1 to 13 and one or more pharmaceutically acceptable carriers.

15. A pharmaceutical composition as claimed in claim 14 which is for peripheral administration.

16. A pharmaceutical composition as claimed in claim 14 or 15 which is for administration subcutaneously, intravenously, intramuscularly, intranasally, transdermally, transmucosally, orally, bucally, sublingually or via the lungs.

17. Use of a peptide as claimed in any one of claims 1 to 13 for the manufacture of a medicament for the prevention or treatment of obesity.

18. Use of a peptide as claimed in any one of claims 1 to 13 for the manufacture of a medicament for the prevention or treatment of diabetes or of a co-morbidity of obesity.

19. Use of a peptide as claimed in any of claims 1 to 13 for the manufacture of a medicament for reducing appetite in a subject, reducing food intake in a subject or reducing calorie intake in a subject, reducing body weight in a subject, reducing body weight gain in a subject or increasing energy expenditure in a subject.

20. The use as claimed in claim any one of claims 17 to 19, wherein the peptide is administered peripherally.

21. The use as claimed in claim any one of claims 17 to 20, wherein the peptide is administered subcutaneously, intravenously, intramuscularly, intranasally, transdermally, transmucosally, orally, bucally, sublingually or via the lungs.

22. A peptide as claimed in any of claims 1 to 13 for use as a medicament.

23. A peptide as claimed in any of claims 1 to 13 for use as a medicament for the prevention or treatment of obesity.

24. A peptide as claimed in any of claims 1 to 13 for use as a medicament for the prevention or treatment of diabetes or of a co-morbidity of obesity.

25. A peptide as claimed in any of claims 1 to 13 for use as a medicament for reducing appetite in a subject, reducing food intake in a subject or reducing calorie intake in a subject, reducing body weight in a subject, reducing body weight gain in a subject or increasing energy expenditure in a subject.

26. A peptide as claimed in any one of claims 22 to 25, wherein the peptide composition is administered peripherally.

27. A peptide as claimed in any one of claims 22 to 26, wherein the peptide is administered subcutaneously, intravenously, intramuscularly, intranasally, transdermally, transmucosally, orally, bucally, sublingually or via the lungs.

28. A method of treating or preventing obesity in a subject in need thereof comprising administering to the subject a peptide according to any of claims 1 to 13 or a pharmaceutical composition according to any of claims 14 to 16.

29. A method of treating or preventing diabetes or of a co-morbidity of obesity in a subject in need thereof comprising administering to the subject a peptide according to any of claims 1 to 13 or a pharmaceutical composition according to any of claims 14 to 16.

30. A method of reducing appetite in a subject, reducing food intake in a subject or reducing calorie intake in a subject, reducing body weight in a subject, reducing body weight gain in a subject or increasing energy expenditure in a subject in need thereof comprising administering to the subject a peptide according to any of claims 1 to 13 or a pharmaceutical composition according to any of claims 14 to 16.

31. A method of causing weight loss or preventing weight gain for cosmetic purposes comprising administering to the subject a peptide according to any of claims 1 to 13 or a pharmaceutical composition according to claim 14 to 16.

32. A method as claimed in any of claims 28 to 31, wherein the subject is overweight.

33. A method as claimed in any of claims 28 to 32, wherein the subject is obese.

34. A method as claimed in any of claims 28 to 33, wherein the subject is diabetic.

35. The method of any of claims 28 to 34, wherein the peptide or pharmaceutical composition is administered peripherally.

36. The method of any of claims 28 to 35, wherein the peptide or pharmaceutical composition is administered subcutaneously, intravenously, intramuscularly, intranasally, transdermally, transmucosally, orally, bucally, sublingually or via the lungs.

SUBSTITUTE SHEET (RULE 26)

Figure 1

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
PEPTIDE NO: 1	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 2	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 3	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 4	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 5	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 6	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 7	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 8	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 9	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 10	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 11	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 12	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 13	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 14	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 15	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 16	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 17	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 18	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 19	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 20	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 21	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 22	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 23	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 24	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 25	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 26	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 27	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 28	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 29	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 30	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 31	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 32	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 33	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 34	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 35	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 36	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 37	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 38	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 39	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 40	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 41	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 42	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 43	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 44	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 45	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 46	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 47	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 48	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 49	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 50	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
PEPTIDE NO: 51	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 52	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 53	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 54	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 55	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 56	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 57	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 58	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 59	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 60	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 61	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 62	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 63	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 64	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 65	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 66	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 67	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 68	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 69	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 70	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 71	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 72	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 73	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 74	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 75	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 76	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 77	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 78	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 79	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 80	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 81	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 82	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 83	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 84	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 85	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 86	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 87	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 88	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 89	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 90	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 91	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 92	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 93	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 94	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 95	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 96	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 97	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 98	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 99	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 100	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Asn	Lys	Asn	Asn	Ile	Ala

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
PEPTIDE NO: 101	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 102	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 103	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 104	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 105	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 106	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 107	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 108	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 109	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 110	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 111	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 112	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 113	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 114	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 115	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 116	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 117	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 118	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 119	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 120	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 121	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 122	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 123	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 124	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 125	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 126	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 127	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 128	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 129	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 130	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 131	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 132	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 133	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 134	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 135	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 136	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 137	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 138	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 139	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 140	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 141	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 142	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 143	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 144	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 145	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 146	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 147	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 148	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 149	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala
PEPTIDE NO: 150	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Ile	Ile	Ala

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PEPTIDE NO: 151	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 152	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 153	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 154	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 155	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 156	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 157	D-His	Ala	Asp	Gly	Tyr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 158	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 159	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 160	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 161	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 162	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 163	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 164	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 165	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 166	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 167	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 168	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 169	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 170	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 171	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 172	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 173	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 174	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 175	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 176	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 177	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 178	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 179	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 180	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 181	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 182	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 183	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 184	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 185	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 186	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 187	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 188	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 189	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 190	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 191	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 192	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Gln	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Ser	Asn	Asn	Ile	Ala
PEPTIDE NO: 193	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 194	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 195	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 196	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 197	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 198	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 199	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 200	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
PEPTIDE NO: 201	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-myristoyl
PEPTIDE NO: 202	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-palmitoyl
PEPTIDE NO: 203	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Thr	Gly	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala	Lys	Lys-stearoyl
PEPTIDE NO: 204	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-arachidoyl
PEPTIDE NO: 205	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys
PEPTIDE NO: 206	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-myristoyl
PEPTIDE NO: 207	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-myristoyl
PEPTIDE NO: 208	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-palmitoyl
PEPTIDE NO: 209	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-arachidoyl
PEPTIDE NO: 210	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys
PEPTIDE NO: 211	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-myristoyl
PEPTIDE NO: 212	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-myristoyl
PEPTIDE NO: 213	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-palmitoyl
PEPTIDE NO: 214	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Lys-arachidoyl
PEPTIDE NO: 215	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 216	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 217	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 218	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 219	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 220	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 221	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 222	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 223	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 224	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 225	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 226	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 227	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 228	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 229	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 230	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 231	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 232	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 233	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 234	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 235	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 236	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 237	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 238	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 239	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 240	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 241	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 242	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 243	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 244	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 245	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 246	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 247	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 248	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 249	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	
PEPTIDE NO: 250	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	

PEPTIDE NO: 251	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-myristoyl
PEPTIDE NO: 252	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-palmitoyl
PEPTIDE NO: 253	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-arachidoyl
PEPTIDE NO: 254	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 255	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 256	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 257	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 258	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 259	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 260	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 261	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 262	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 263	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 264	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 265	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 266	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 267	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 268	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 269	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 270	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 271	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 272	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 273	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 274	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
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PEPTIDE NO: 276	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
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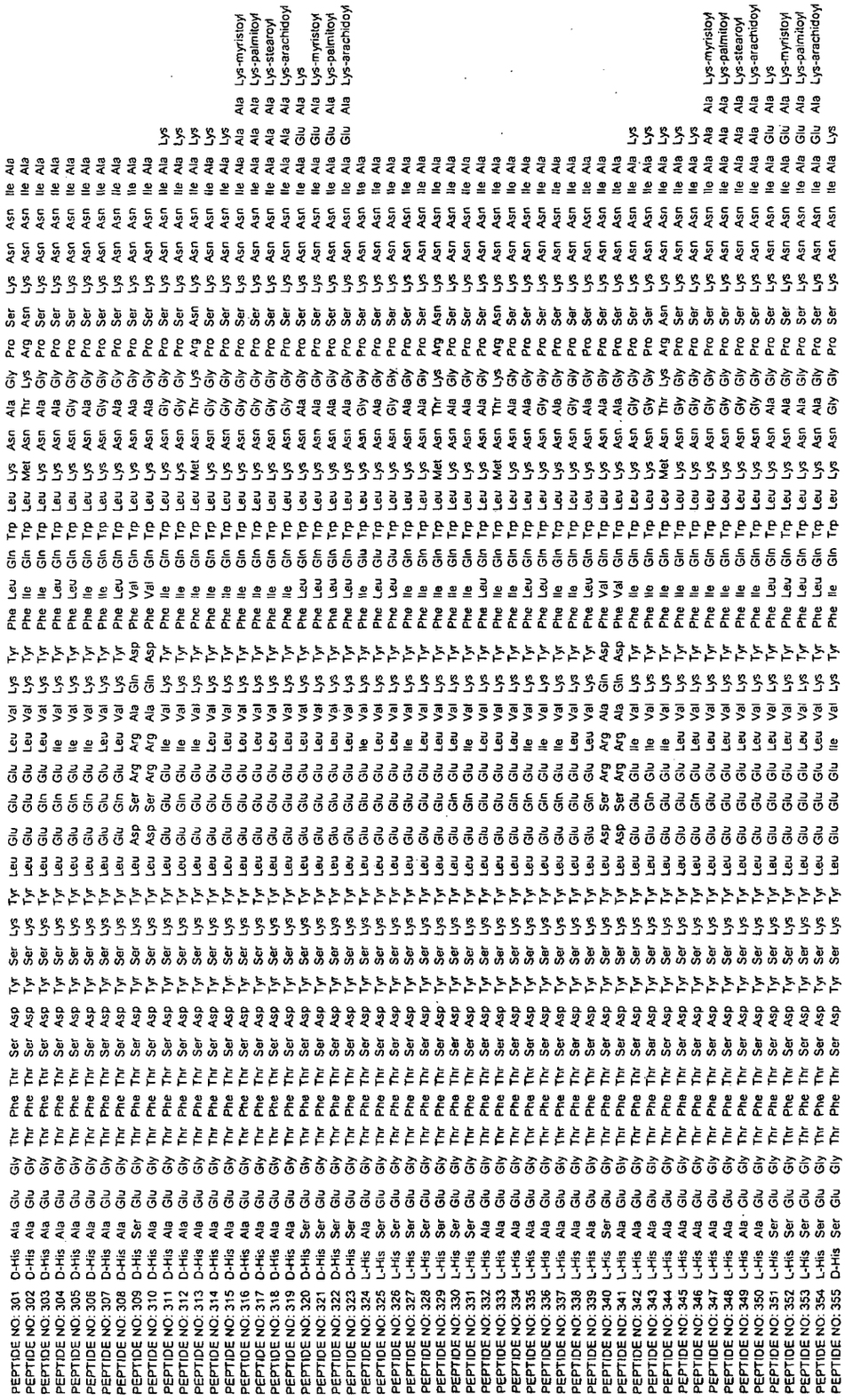


Figure 2

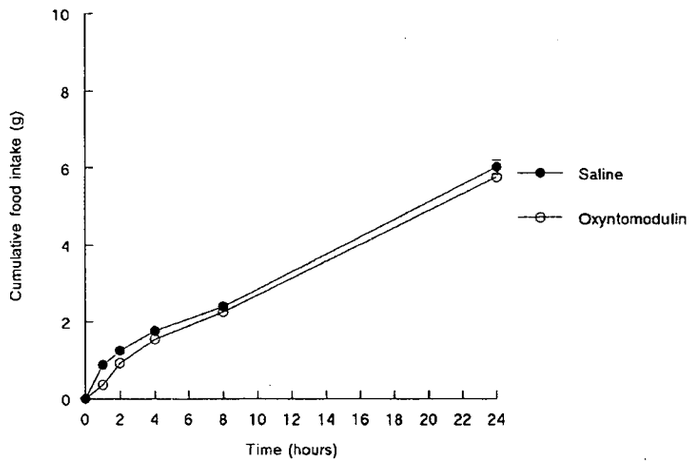


Figure 3.

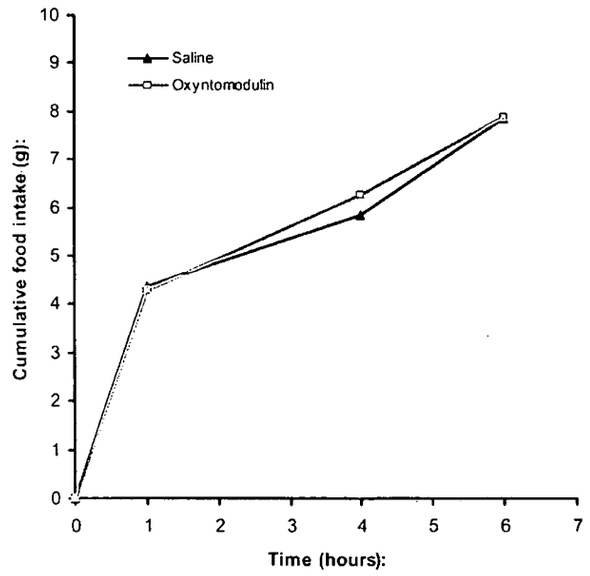


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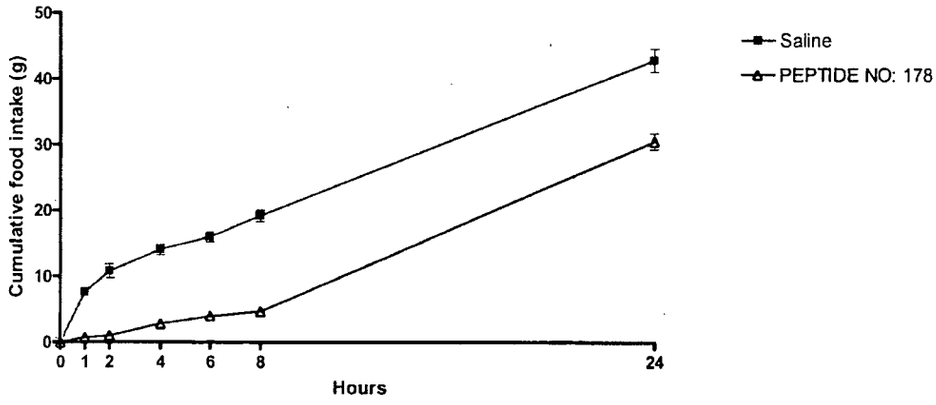


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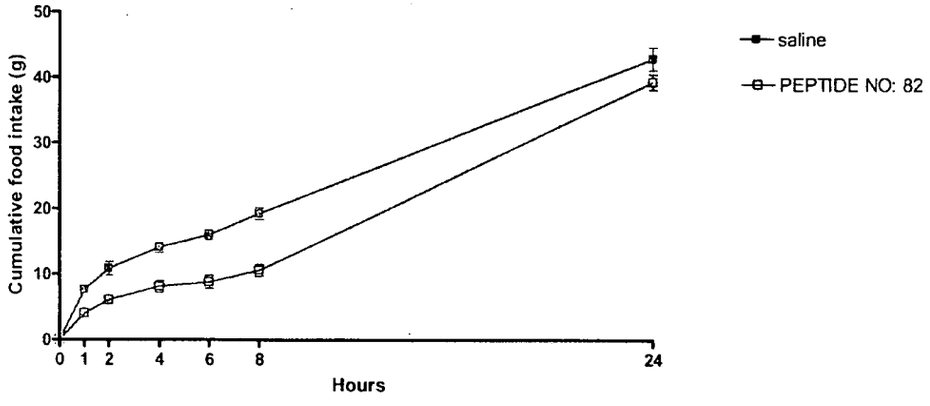


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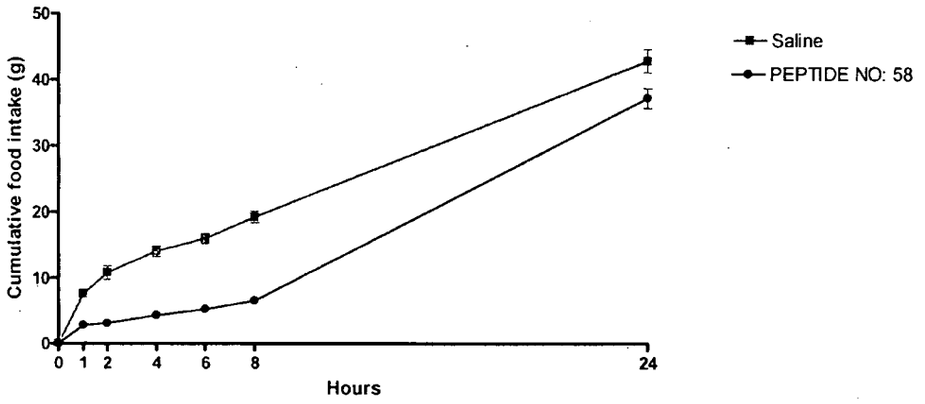


Figure 7

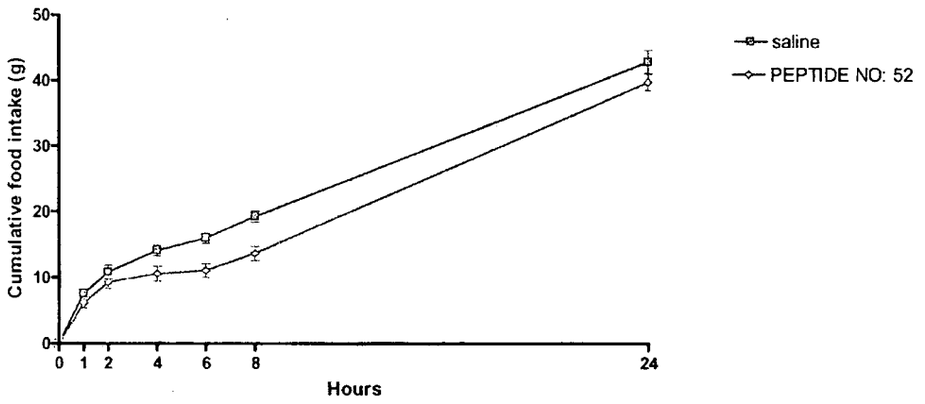


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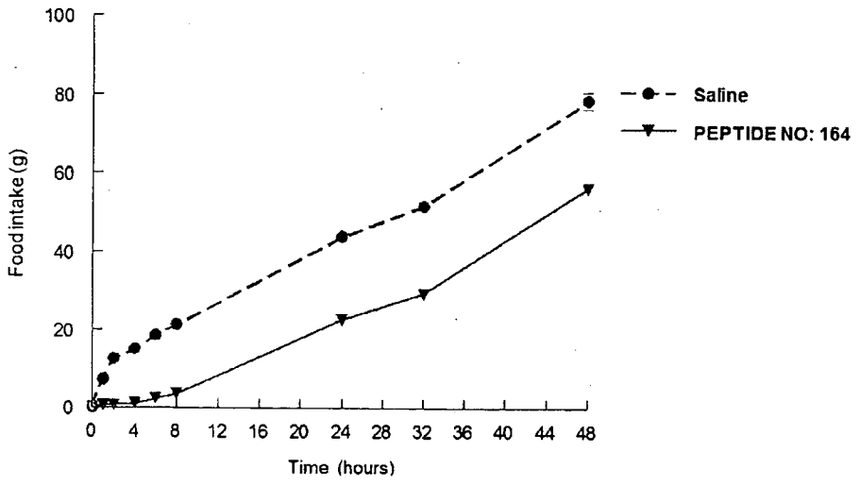


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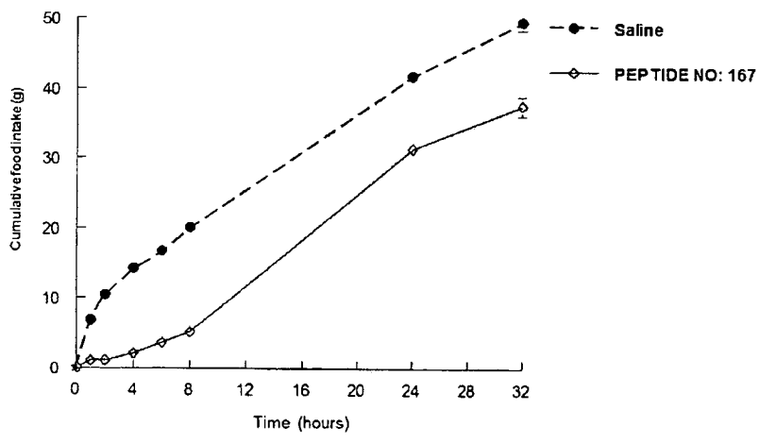


Figure 10

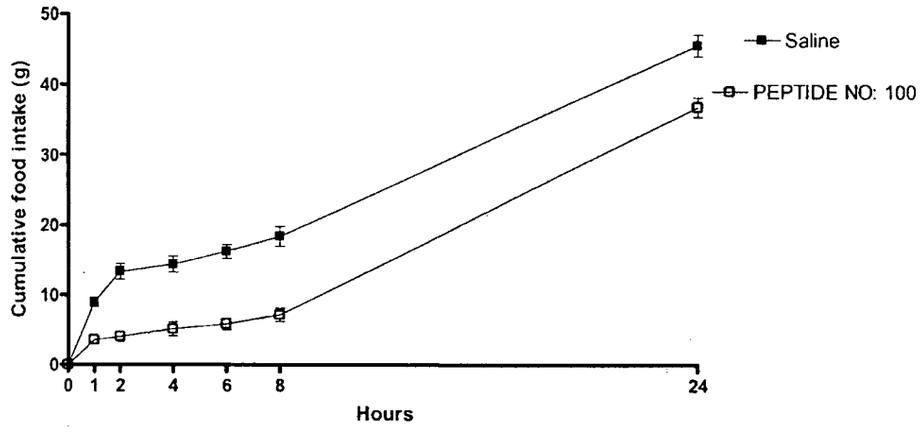


Figure 11

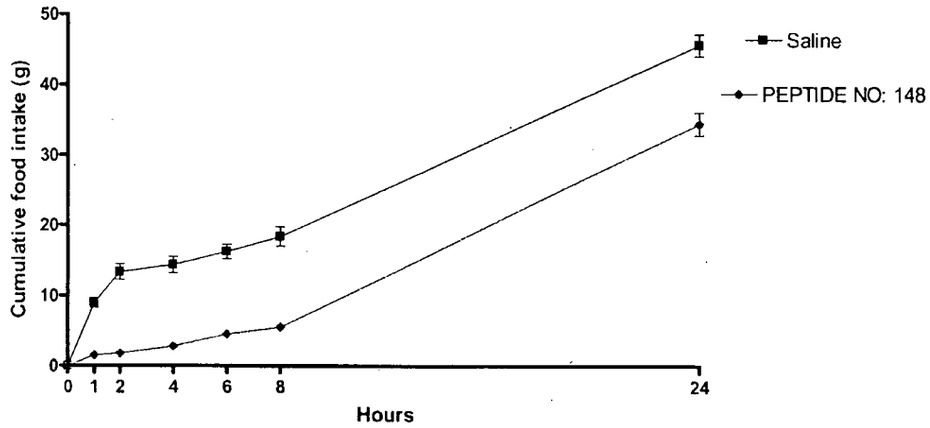


Figure 12

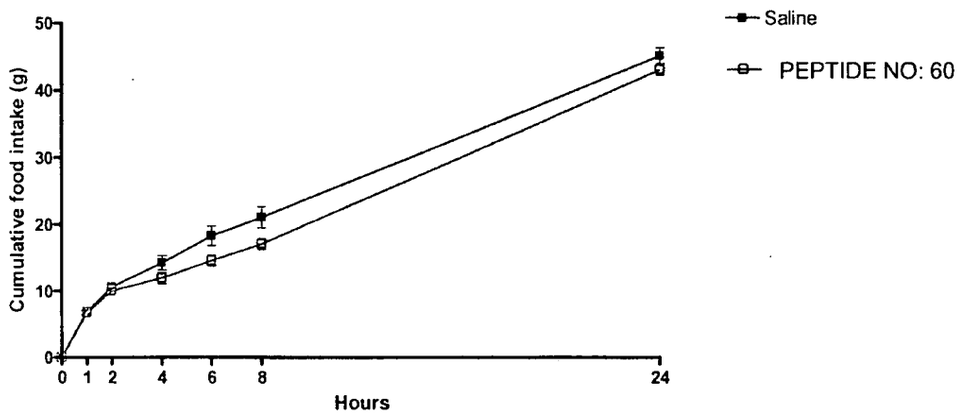


Figure 13

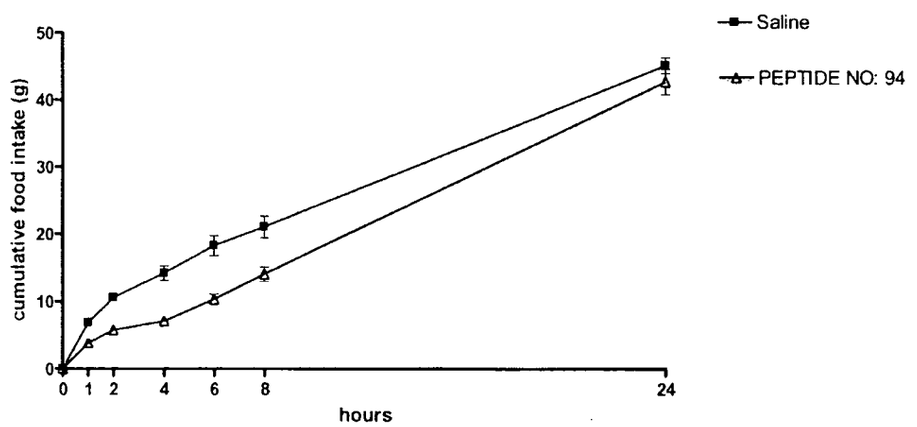


Figure 14

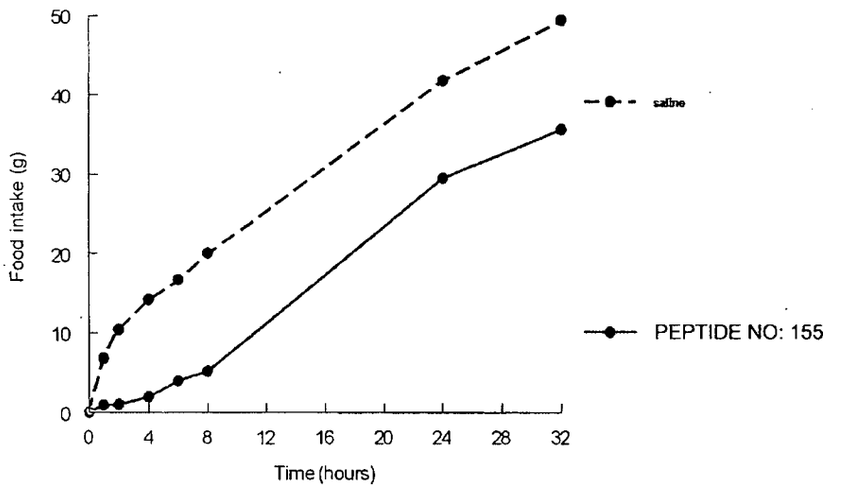


Figure 15

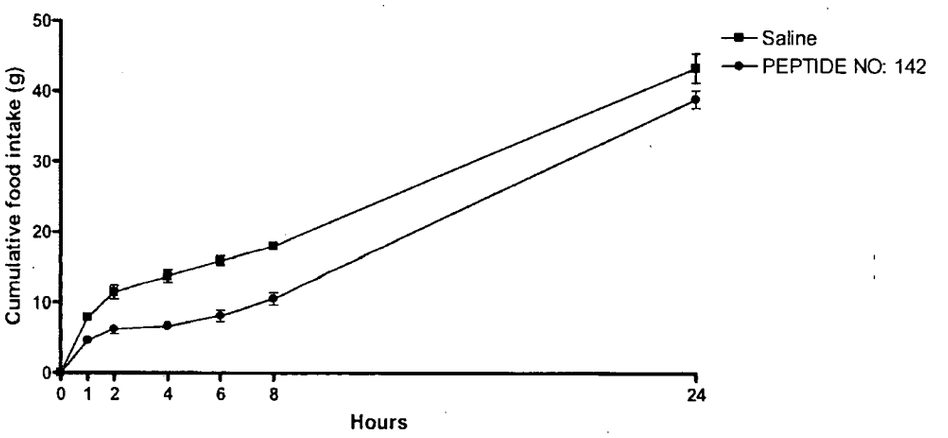


Figure 16

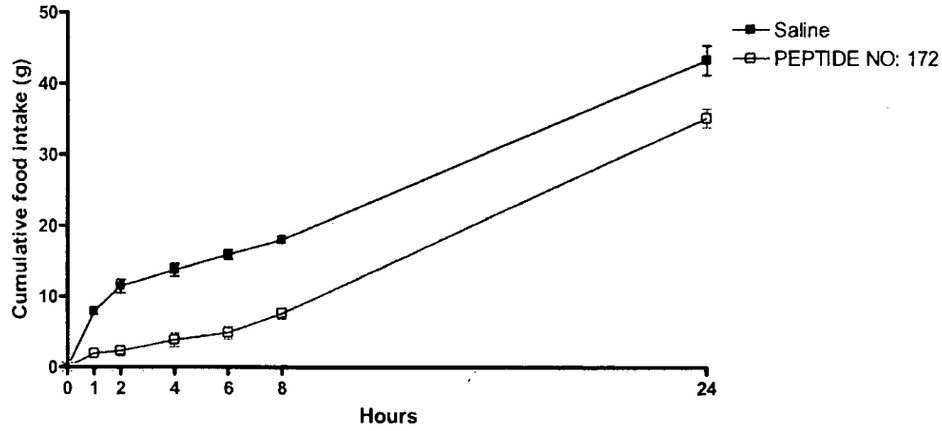


Figure 17

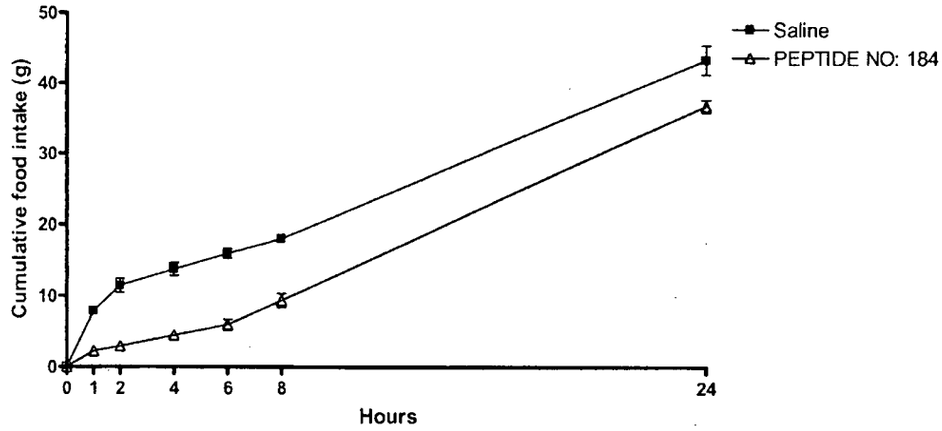


Figure 18

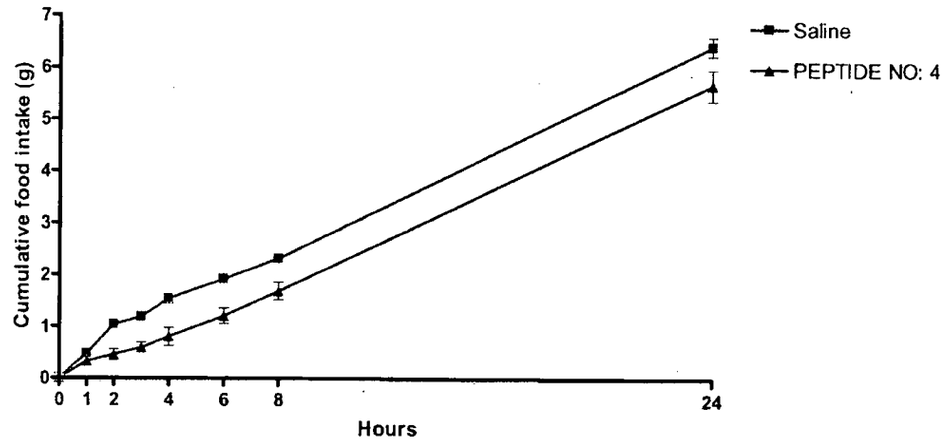


Figure 19

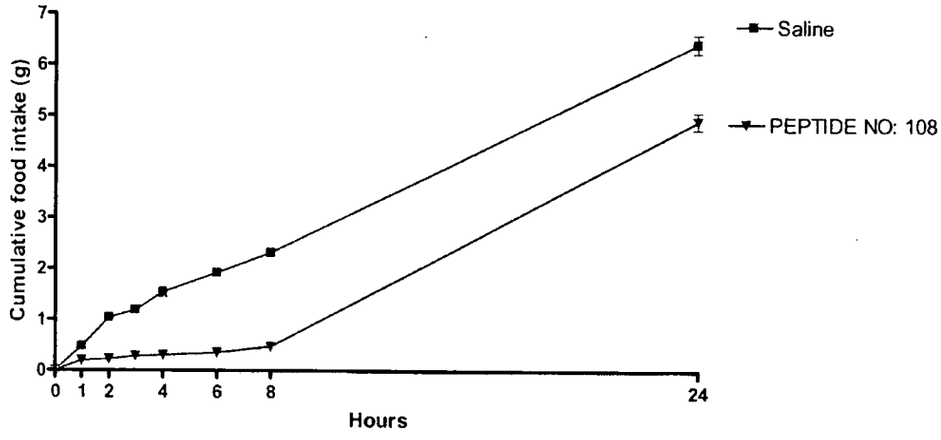


Figure 20

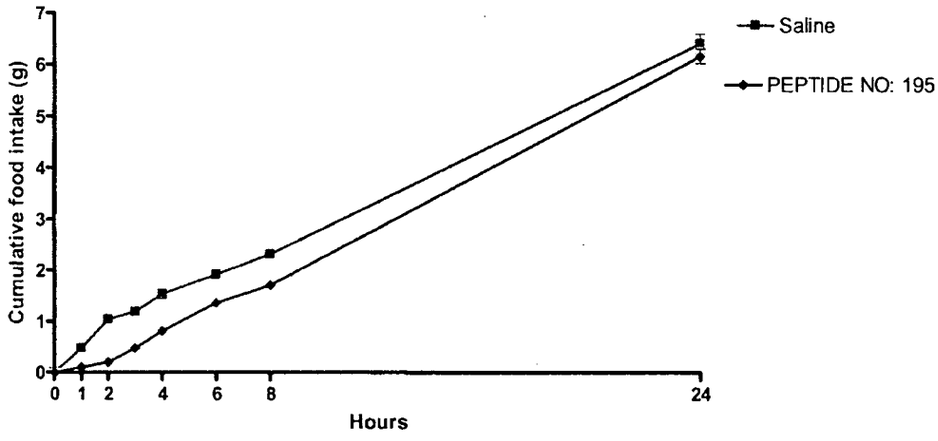


Figure 21

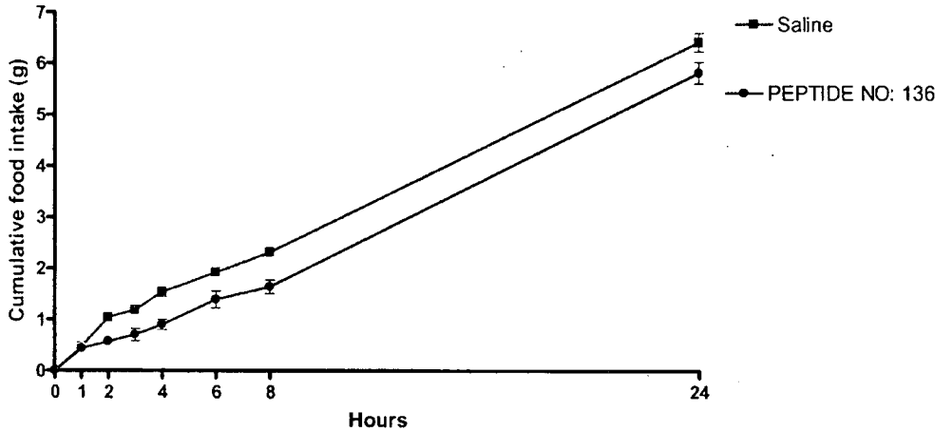


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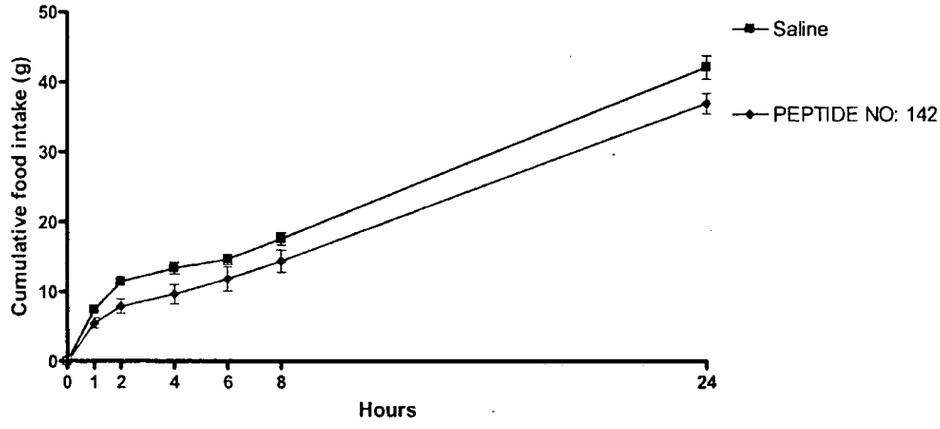


Figure 23

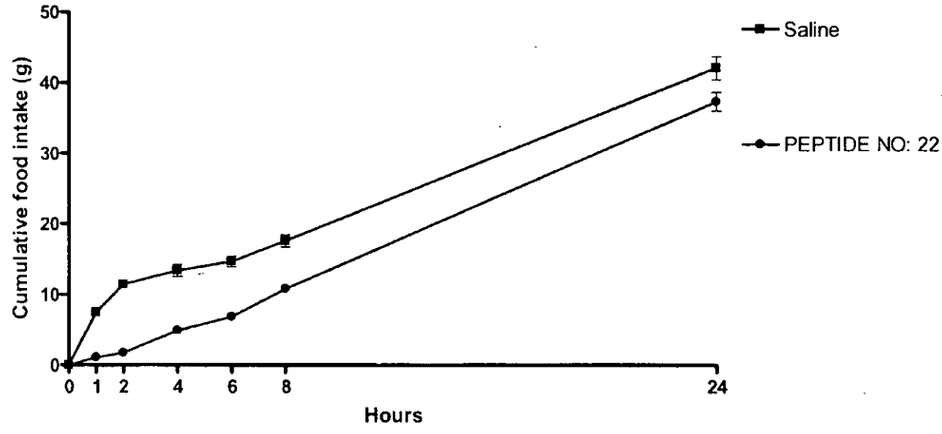


Figure 24

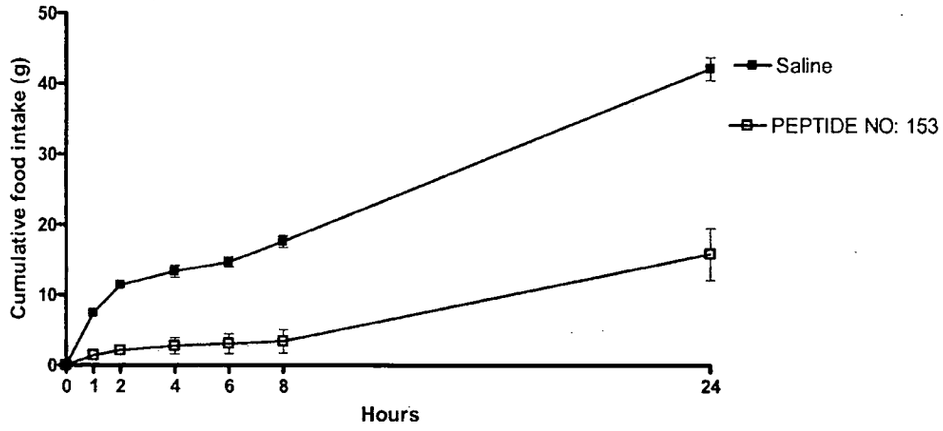


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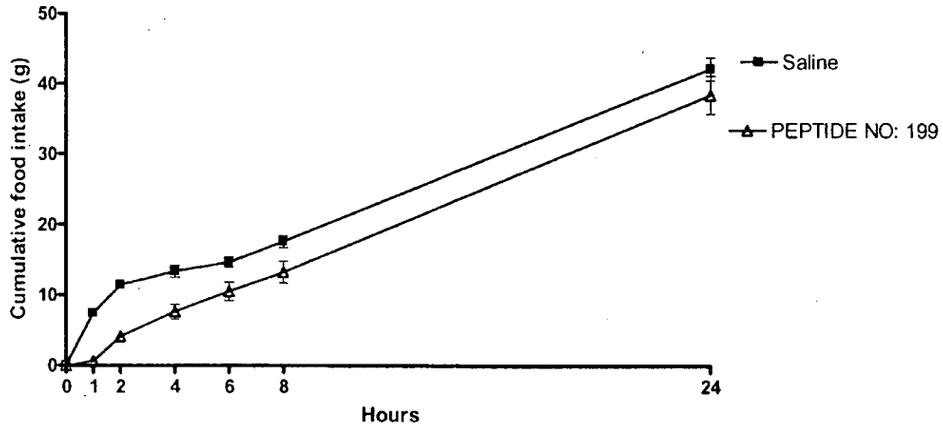


Figure 26

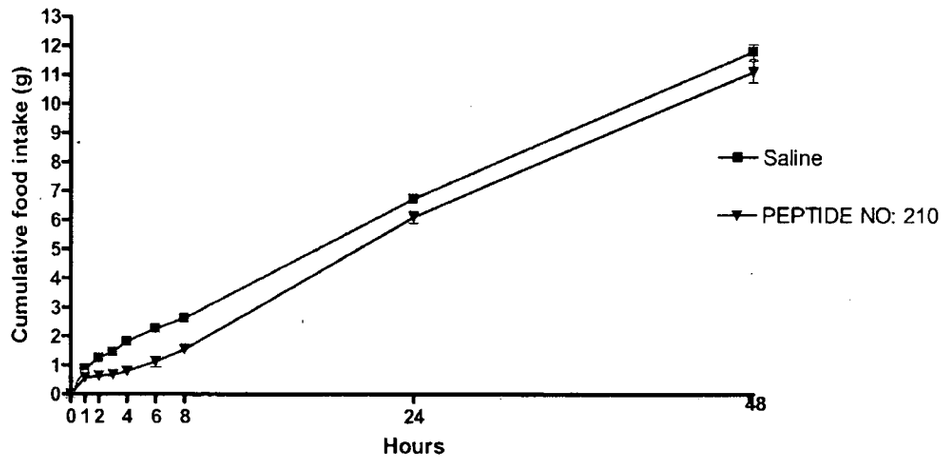


Figure 27

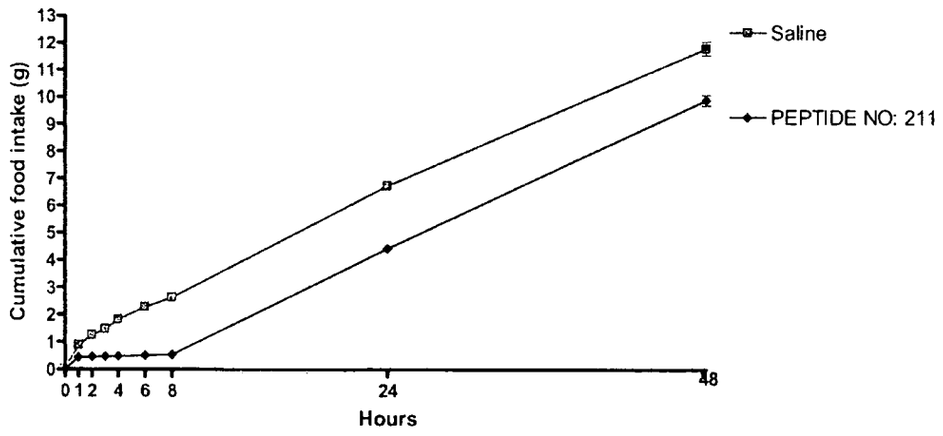


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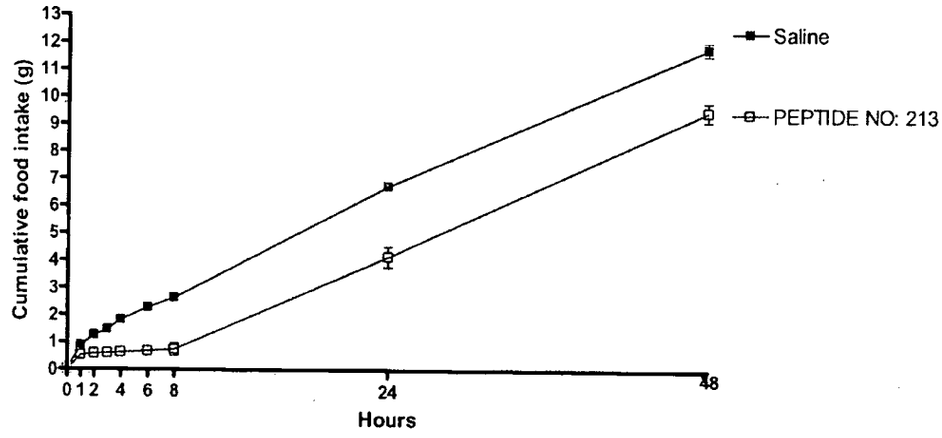


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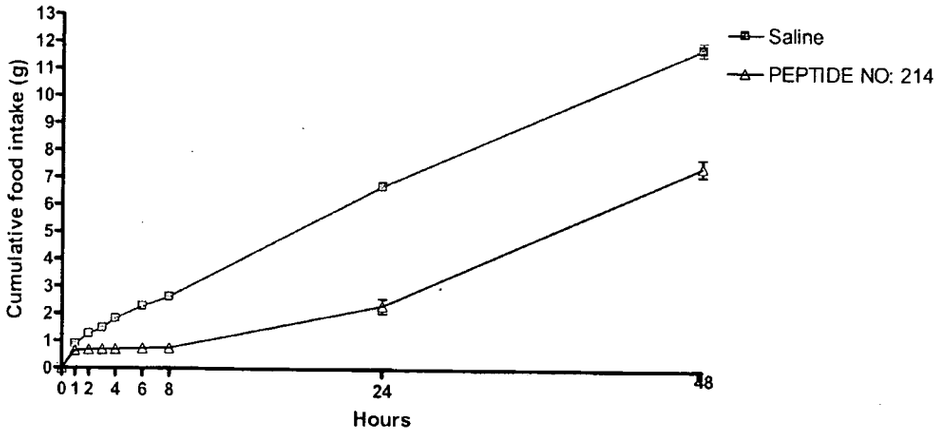


Figure 30

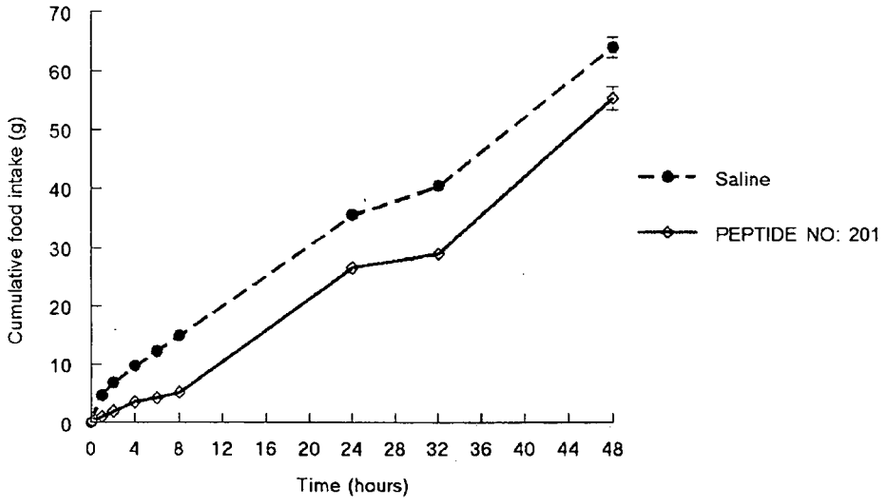


Figure 31

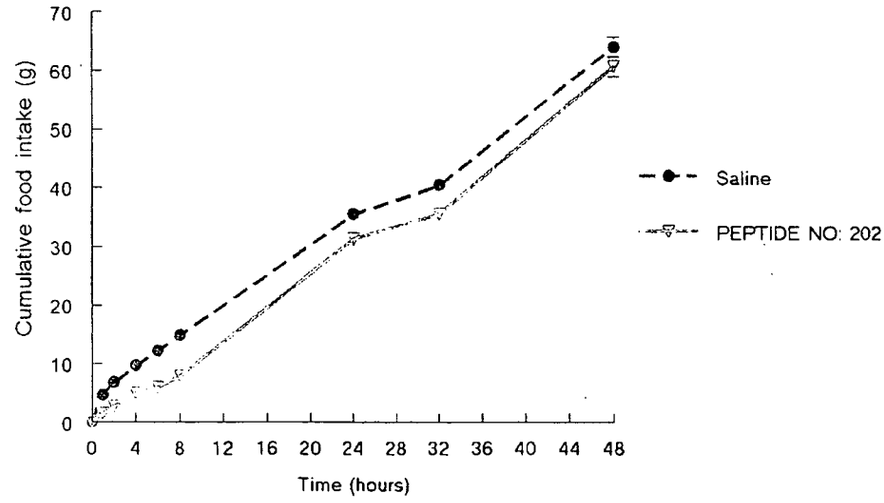


Figure 32

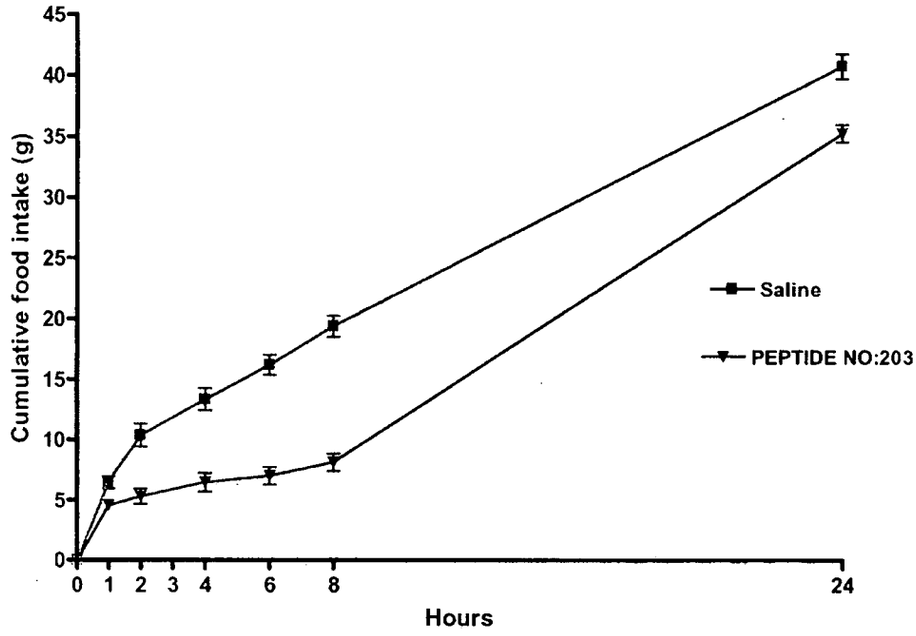


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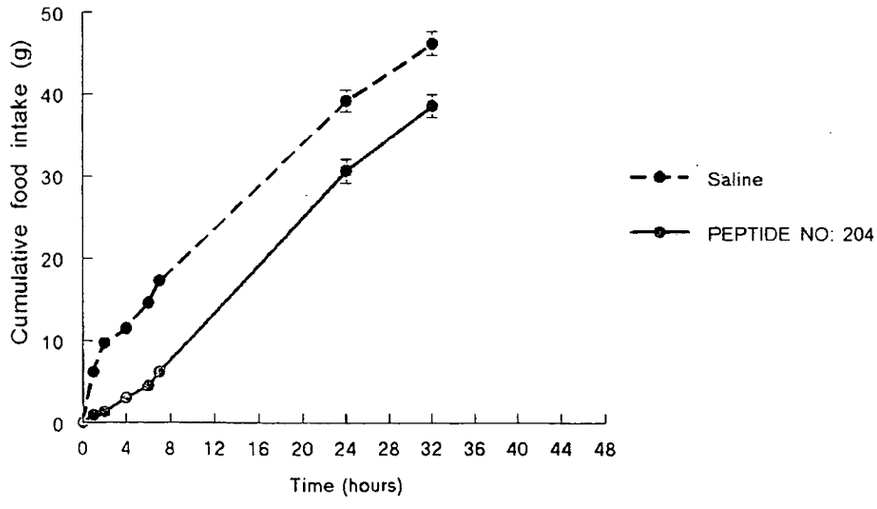


Figure 34

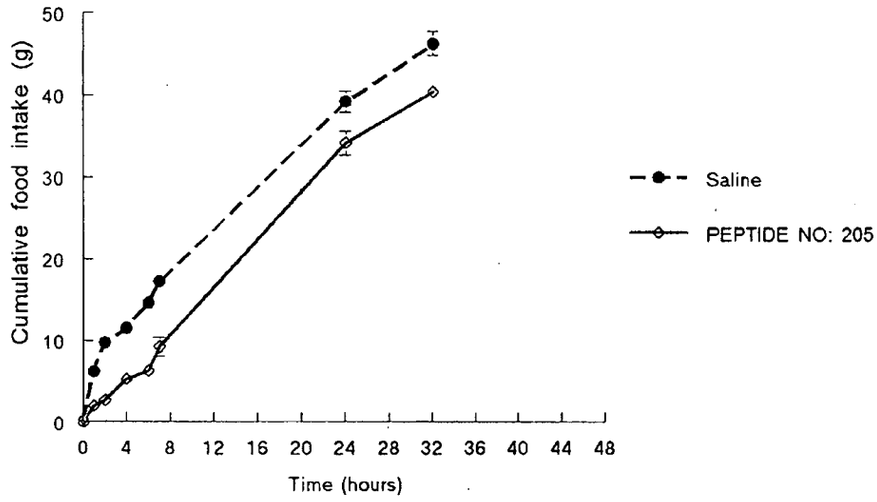


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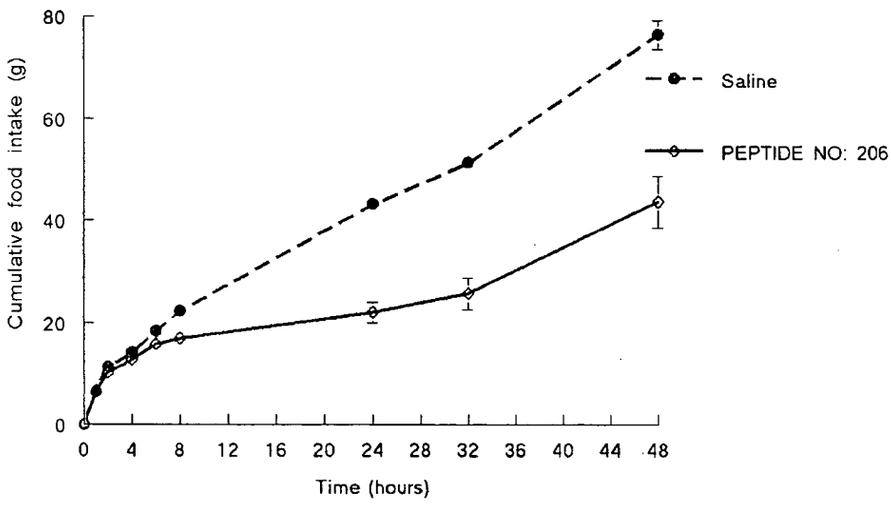


Figure 36

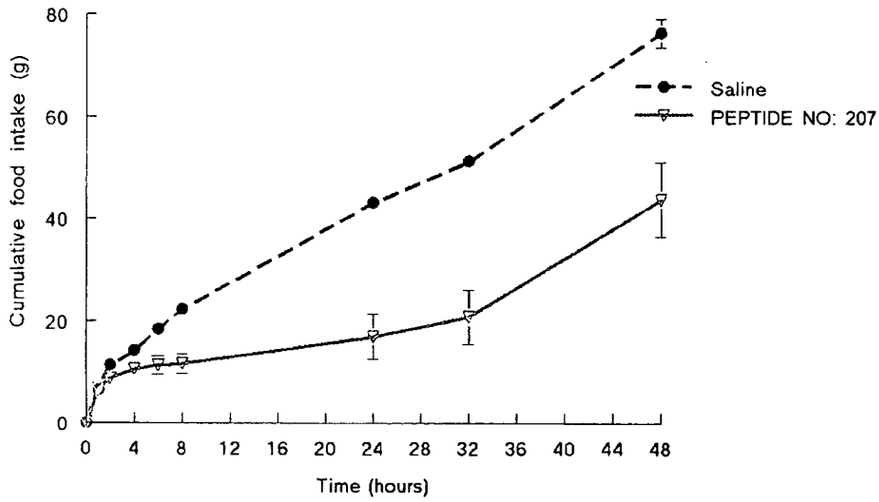


Figure 37

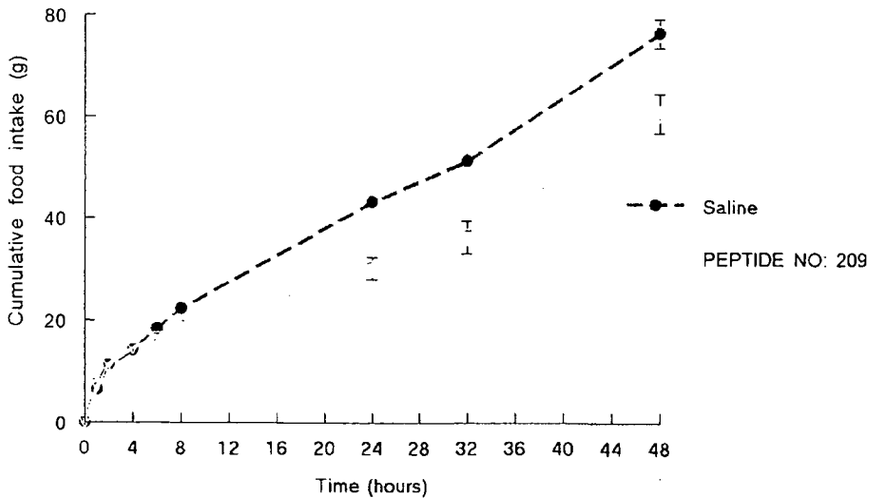


Figure 38

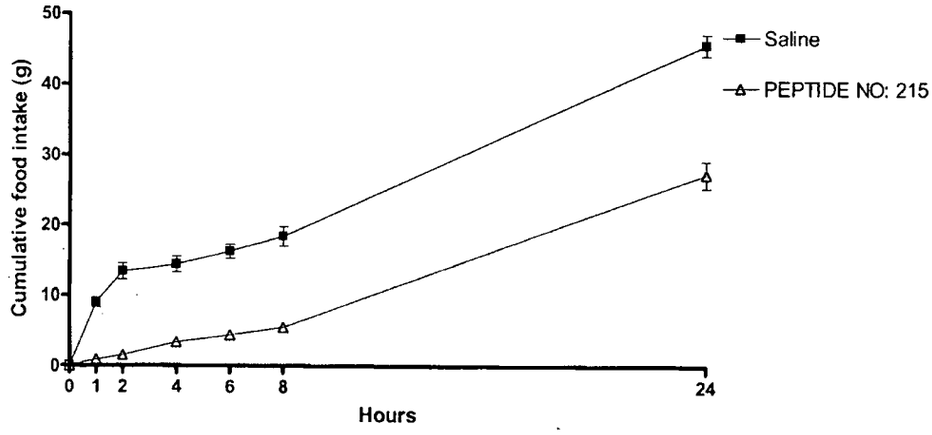


Figure 39

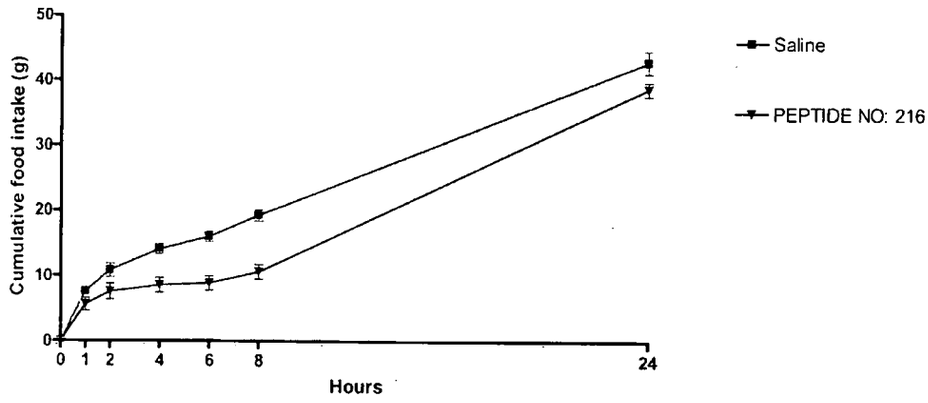


Figure 40

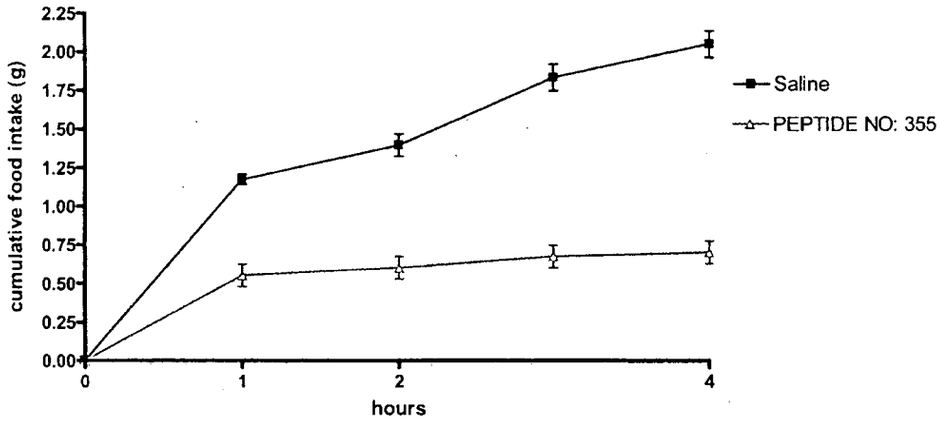
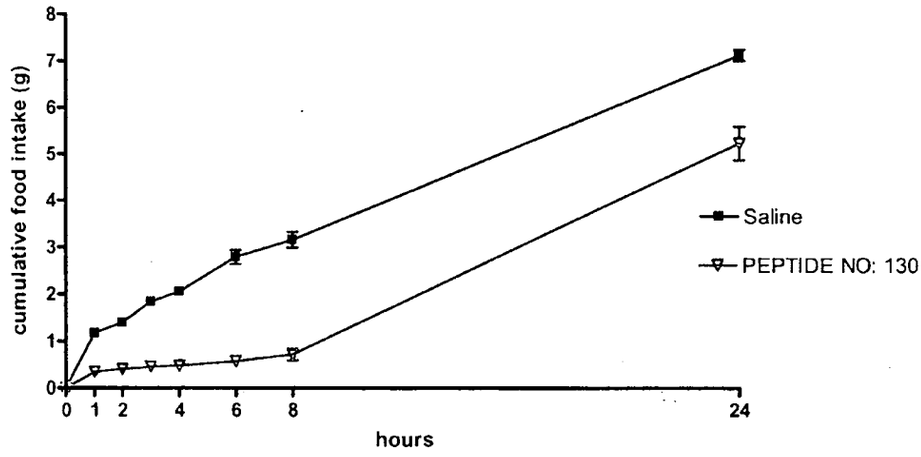


Figure 41



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NUEVOS COMPUESTOS Y SUS EFECTOS SOBRE EL CONDUCTISMO DE LA ALIMENTACIÓN

1. CAMPO DE LA INVENCIÓN

Esta solicitud se refiere al uso de agentes para controlar el apetito, la alimentación, la ingestión de comida, el gasto de energía y la ingestión de calorías, para tratar el peso excesivo, la obesidad y para prevenir y tratar las co-morbilidades de la obesidad.

2. ANTECEDENTES DE LA INVENCIÓN

De acuerdo con la Organización Mundial de la Salud (WHO) la obesidad representa una epidemia global en la cual más de un billón de adultos sufren de sobrepeso, de los cuales por lo menos 300 millones son clínicamente obesos. Además, la WHO estima que 250.000 muertes por añó en Europa y más de 2,5 millones de muertes en el mundo entero están relacionadas con el peso (Organización Mundial de la Salud, Estrategia Global sobre las Dietas, Actividad Física y Salud, 2004).

La causa de la obesidad es compleja y multifactorial. Evidencia creciente sugiere que la obesidad no es un simple problema de autocontrol, sino que es un trastorno complejo que involucra el metabolismo de la regulación del apetito y la energía. Además, la obesidad está asociada con una variedad de trastornos relacionados con un aumento de la morbilidad y la mortalidad en una población. Aunque la etiología de la obesidad no está definitivamente establecida, se cree que contribuyen los factores genéticos, metabólicos, químicos, culturales y psicosociales. En general, la obesidad ha sido descrita como un trastorno en el cual el exceso de grasa corporal pone a un individuo frente a un riesgo de salud.

Existe fuerte evidencia de que la obesidad está asociada con un aumento de la morbilidad y la mortalidad. El riesgo de enfermedad, tal como un riesgo de

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enfermedad cardiovascular y el riesgo de enfermedad de diabetes de tipo II, aumenta independientemente con un aumento del índice de masa corporal (BMI). En realidad este riesgo ha sido cuantificado como un aumento del 5% en el riesgo de enfermedades cardíacas para mujeres, y un aumento del 7% en el riesgo de enfermedades cardíacas para hombres, para cada punto de un BMI superior a 24,9 (ver Kenchaiah et al., N. Engl. J. Med. 347:305, 2002; Massie, N. Engl. J. Med. 347:358, 2002). Además, existe una evidencia sustancial de que la pérdida de peso en personas obesas o con sobrepeso reduce importantes factores de riesgo de la salud. Una pérdida de peso del 10% del peso corporal inicial tanto en adultos obesos como con sobrepeso, ha sido asociada con una disminución de los factores de riesgo tales como hipertension, hiperlipidemia e hiperglicemia.

Aunque la dieta y el ejercicio proven un procedimiento simple para disminuir el aumento de peso y promover la pérdida de peso, los individuos con sobrepeso y obesos a menudo no pueden controlar suficientemente estos factores para perder peso en forma eficaz. Se encuentra disponible farmacoterapia; varios fármacos para la pérdida de peso han sido aprobados por la Administración de Alimentos y Fármacos de Estados Unidos, que pueden usarse como parte de un programa integral para la pérdida de peso. Sin embargo, muchos de estos fármacos tienen serios efectos adversos. Un ejemplo de un supresor de apetito usado ampliamente es sibutramina (revisado por McNeely, W et al., Drugs, 1998, 56(6), 1093-1124). Los metabolitos primarios y secundarios de sibutramina son farmacológicamente activos y se cree que inducen a aumentar la saciedad y la termogénesis mediante la inhibición de serotonina y la reabsorción de noradrenalina. Cuando métodos menos invasivos han fracasado, y el paciente corre el riesgo de sufrir de obesidad relacionada con morbilidad o mortalidad, la cirugía para pérdida de peso es una opción en pacientes cuidadosamente seleccionados con obesidad clínicamente severa. Sin embargo estos tratamientos

son de alto riesgo y son únicamente apropiados para ser usados en una cantidad limitada de pacientes (Wolfe and Morton, JAMA, 2005, 294,1960-1963). No solamente los sujetos obesos desean perder peso. La gente con peso dentro del rango recomendado, por ejemplo, en la parte superior del rango recomendado, puede desear reducir su peso, para llevarlo más próximo al peso ideal.

La oxintomodulina (a continuación oxm) es un miembro peptídico de 37 amino ácidos de la superfamilia glucagon (Sherwood et al, Endocrine Reviews, 2000, 21(6): 619-670) que comprende la secuencia entera de 29 amino ácidos de glucagon, con una extensión terminal carboxi de 8 amino ácidos, resultante del procesamiento específico de tejido del precursor pre-pro-glucagon en el cerebro y el intestino (Holst, Ann Rev Physiol, 1997, 59:257-271). La administración de oxm a ratas a través de inyección intracerebroventricular e inyección dentro de los núcleos paraventriculares y arqueados del hipotálamo inhibe la realimentación después de un ayuno (Dakin et al, Endocrinology, 2001, 142:4244-4250; Dakin et al, Endocrinology, 2004, 145:2687-2695). Una administración central crónica dio como resultado un aumento de peso reducido, coherente con una reducción en la ingestión de comida (Dakin et al, Am J Physiol Endocrinol Metab, 2002, 283:E1173-E1177). Inyecciones periféricas dos veces por día dieron también como resultado reducción de la adiposidad y del aumento de peso corporal (Dakin et al, Endocrinology, 2004, 145:2687-2695).

La WO 03/022304 describe el uso de oxm en su forma natural y sus análogos como medicamento para ser usado en el control del apetito, alimentación, ingestion de comida, gasto de energía, e ingestión de calorias, particularmente en el campo de la obesidad. Los estudios en seres humanos han demostrado que oxm infusionado intravenosamente es un supresor eficaz del apetito (Cohen et al, J. Clin. Endocrinol Metab, 2003, 88(10): 4696-4701). En un estudio de los efectos de oxm sobre la pérdida de peso en seres humanos, se

descubrió que las inyecciones subcutáneas de 1,8 mg (aproximadamente 400 nmol) de oxm a voluntarios humanos tres veces por día (30 minutos antes de la comida) durante 28 días dieron como resultado una reducción significativa del peso corporal (Wynne et al, Diabetes, 2005, 54: 2390-2395).

Los péptidos han sido ampliamente usados en la práctica médica aunque cuando se han usado péptidos naturales o sus análogos en terapia, generalmente se halló que tenían una elevada tasa de aclaramiento y/o eran sensibles a la degradación. En particular, un aclaramiento elevado, o una degradación rápida de un agente terapéutico es inconveniente en casos en los cuales se desea mantener un nivel elevado en la sangre, por un período de tiempo prolongado, debido que serían necesarias administraciones repetidas, lo cual disminuye el cumplimiento del paciente y aumento del costo de la terapia.

Sigue habiendo necesidad de agentes que puedan usarse para efectuar pérdida de peso en sujetos obesos y con sobrepeso, y/o para tratar pacientes con otros trastornos que involucran exceso de peso, como por ejemplo, trastornos de diabetes y de alimentación. Hay una especial necesidad de agentes estructuralmente similares a oxm que muestren un mayor perfil de acción avanzado o terapéuticamente más útil y/o una tasa de aclaramiento más baja que la del oxm natural.

3. COMPENDIO DE LA INVENCION

Los compuestos de la invención son nuevos análogos peptídicos de oxm (a continuación "análogos de oxm") en los cuales uno o más amino ácidos o partes de la secuencia de oxm han sido reemplazados con uno o más amino ácidos o secuencias sustituyentes particulares. Por consiguiente la invención provee un péptido que comprende la secuencia de amino ácido:

Xaa1 Xaa2 Xaa3 Gly4 Thr5 Phe6 Thr7 Ser8 Asp9 Tyr10 Ser11 Lys12 Tyr13 Leu14

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Trp25 Leu26

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 Lys33 Asn34 Asn35 Ile36 Ala37;

donde:

Xaa1 es His1 o D-His1,
Xaa2 es Ser2 o Ala2,
Xaa3 es Gln3 o Asp3;

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

o Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24;

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 es:

Met27 Asn28 Thr29 Lys30 Arg31 Asn32,

Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,

o Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

o un péptido tal como se indicó anteriormente en el cual el residuo Asn34 es reemplazado con Asp34;

o un péptido tal como el indicado anteriormente en el cual Xaa3 es Glu3;

con la condición de que si
Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es
Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24,

entonces Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 no es
Met27 Asn28 Thr29 Lys30 Arg31 Asn32
(SEC ID NO: 356).

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En una realización, la invención provee un péptido que comprende la secuencia de amino ácido:

Xaa1 Xaa2 Xaa3 Gly4 Thr5 Phe6 Thr7 Ser8 Asp9 Tyr10 Ser11 Lys12 Tyr13 Leu14

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Trp25 Leu26

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 Lys33 Asn34 Asn35 Ile36 Ala37;

donde:

Xaa1 es His1 o D-His1,
Xaa2 es Ser2 o Ala2,
Xaa3 es Gln3 o Asp3;

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

o Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24;

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 es:

Met27 Asn28 Thr29 Lys30 Arg31 Asn32,

Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,

o Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

con la condición de que si:

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es

Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24,

entonces Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 no es

Met27 Asn28 Thr29 Lys30 Arg31 Asn32.

Los péptidos de la invención son potentes y prolongados supresores del apetito.

4. BREVE DESCRIPCION DE LAS FIGURAS

La Figura 1 describe 355 secuencias de péptidos específicas que entran dentro del alcance de la invención.

Las Figuras 2 a 41 muestran los resultados de los Ejemplos 1 a 19.

La Figura 2 se refiere al Ejemplo 1.

La Figura 3 se refiere al Ejemplo 2.

La Figura 4 se refiere al Ejemplo 3 (PÉPTIDO NO: 94).

La Figura 5 se refiere al Ejemplo 3 (PÉPTIDO NO: 82).

La Figura 6 se refiere al Ejemplo 3 (PÉPTIDO NO: 58).

La Figura 7 se refiere al Ejemplo 3 (PÉPTIDO NO: 52).

La Figura 8 se refiere al Ejemplo 4 (PÉPTIDO NO: 164).

La Figura 9 se refiere al Ejemplo 4 (PÉPTIDO NO: 167).

La Figura 10 se refiere al Ejemplo 5 (PÉPTIDO NO: 100).

La Figura 11 se refiere al Ejemplo 5 (PÉPTIDO NO: 148).

La Figura 12 se refiere al Ejemplo 6 (PÉPTIDO NO: 60).

La Figura 13 se refiere al Ejemplo 6 (PÉPTIDO NO: 178).

La Figura 14 se refiere al Ejemplo 7 (PÉPTIDO NO: 155).

La Figura 15 se refiere al Ejemplo 8 (PÉPTIDO NO: 142).

La Figura 16 se refiere al Ejemplo 8 (PÉPTIDO NO: 172).

La Figura 17 se refiere al Ejemplo 8 (PÉPTIDO NO: 184).

La Figura 18 se refiere al Ejemplo 9 (PÉPTIDO NO: 4).

La Figura 19 se refiere al Ejemplo 9 (PÉPTIDO NO: 108).

La Figura 20 se refiere al Ejemplo 9 (PÉPTIDO NO: 195).

La Figura 21 se refiere al Ejemplo 9 (PÉPTIDO NO: 136).

La Figura 22 se refiere al Ejemplo 10 (PÉPTIDO NO: 142).

La Figura 23 se refiere al Ejemplo 10 (PÉPTIDO NO: 22).

La Figura 24 se refiere al Ejemplo 10 (PÉPTIDO NO: 153).

La Figura 25 se refiere al Ejemplo 10 (PÉPTIDO NO: 199).

La Figura 26 se refiere al Ejemplo 11 (PÉPTIDO NO: 210).

La Figura 27 se refiere al Ejemplo 11 (PÉPTIDO NO: 211).

La Figura 28 se refiere al Ejemplo 11 (PÉPTIDO NO: 213).

La Figura 29 se refiere al Ejemplo 11 (PÉPTIDO NO: 214).

La Figura 30 se refiere al Ejemplo 12 (PÉPTIDO NO: 201).

La Figura 31 se refiere al Ejemplo 12 (PÉPTIDO NO: 202).

La Figura 32 se refiere al Ejemplo 13 (PÉPTIDO NO: 203).

La Figura 33 se refiere al Ejemplo 14 (PÉPTIDO NO: 204).

La Figura 34 se refiere al Ejemplo 14 (PÉPTIDO NO: 205).

La Figura 35 se refiere al Ejemplo 15 (PÉPTIDO NO: 206).

La Figura 36 se refiere al Ejemplo 15 (PÉPTIDO NO: 207).

La Figura 37 se refiere al Ejemplo 15 (PÉPTIDO NO: 209).

La Figura 38 se refiere al Ejemplo 16 (PÉPTIDO NO: 215).

La Figura 39 se refiere al Ejemplo 17 (PÉPTIDO NO: 216).

La Figura 40 se refiere al Ejemplo 18 (PÉPTIDO NO: 355).

La Figura 41 se refiere al Ejemplo 19 (PÉPTIDO NO: 130).

5. DEFINICIONES

Para facilitar una revisión de las varias realizaciones de esta descripción, se proveen las siguientes explicaciones de términos específicos:

Animal: Organismos vertebrados multicelulares vivos, una categoría que incluye por ejemplo mamíferos y aves. El término mamífero incluye tanto mamíferos humanos como no humanos. De manera similar "sujeto" incluye tanto sujetos humanos como no humanos, incluyendo sujetos veterinarios

Apetito: Deseo natural, o ansia de comida. En una realización, el apetito se mide mediante un estudio para verificar el deseo de comer. El aumento del apetito conduce generalmente al aumento del conductismo de alimentación.

Supresores de apetito: Compuestos que disminuyen el deseo de comer. Los supresores de apetito disponibles comercialmente incluyen, pero no están limitados a amfepramona (dietilpropion), fentermina, mazindol y fenilpropanolamina fenfluramina, dexfenfluramina, sibutramina, rimonabant y fluoxetina.

Indice de Masa Corporal (BMI): Una fórmula matemática para medir la masa corporal, denominada también algunas veces Indice de Quetelet. El BMI se calcula dividiendo el peso (en kg) por la altura^2 (en metros^2). La clasificación recomendada para el BMI en humanos, adoptada por un Panel de Expertos sobre la Identificación, Evaluación y Tratamiento de Sobrepeso y Obesidad en Adultos, y aprobado por destacadas organizaciones de profesionales de la salud, es la siguiente: Falta de Peso <18.5 kg/m^2; Peso Normal 18.5–24.9 kg/m^2; Sobrepeso 25–29.9 kg/m^2; Obesidad (Clase 1) 30–34.9 kg/m^2; Obesidad (Clase 2) 35–39.9 kg/m^2; Obesidad Extrema (Clase 3) ≥40 kg/m^2 (Guía Práctica para la Identificación, Evaluación y Tratamiento de Sobrepeso y Obesidad en Adultos, Asociación Norteamericana para el Estudio de la Obesidad (NAASO) y el Instituto Nacional del Corazón, Pulmones y Sangre (NHLBI) 2000). En una realización, un BMI de más de 25 kg/m^2 puede usarse para identificar un sujeto que necesita tratamiento para un exceso de peso u obesidad. El peso corporal ideal variará entre especies e individuos en base a la altura, la complexión corporal, la estructura ósea y el sexo.

Sustituciones Moderadas: El reemplazo de un residuo aminoácido por otro residuo similar en un polipéptido. Sustituciones moderadas típicas pero no limitativas son los reemplazos, uno por otro, entre los amino ácidos alifáticos Ala, Val, Leu y Ile; intercambio de residuos hidroxi que contienen Ser y Thr, intercambio de los residuos ácidos Asp y Glu, intercambio entre los residuos que contienen amida Asn y Gln, intercambio de los residuos básicos Lys y Arg, intercambio de los residuos aromáticos Phe y Tyr, e intercambio de los amino ácidos de tamaño pequeño Ala, Ser, Thr, Met y Gly. Sustituciones moderadas adicionales incluyen el reemplazo de un amino ácido por otro de configuración espacial o estérica similar, por ejemplo el intercambio de Asn por Asp, o Gln por Glu.

Tabla 1: Ejemplos no limitativos de sustituciones de amino ácido moderadas

Residuo Original	Sustituciones Moderadas
Ala	Gly, Val, Leu, Ile, Ser, Thr, Met
Arg	Lys
Asn	Asp, Gln, His
Asp	Glu, Asn
Cys	Ser
Gln	Asn, His, Lys, Glu
Glu	Asp, Gln
Gly	Ala, Ser, Thr, Met
His	Asn, Gln
Ile	Ala, Leu, Val, Met
Leu	Ala, Ile, Val, Met,
Lys	Arg

Met	Leu, Ile, Ala, Ser, Thr, Gly
Phe	Leu, Tyr, Trp
Ser	Thr, Cys, Ala, Met, Gly
Thr	Ser, Ala, Ser, Met, Gly
Trp	Tyr, Phe
Tyr	Trp; Phe
Val	Ala, Ile, Leu

Sustituciones no moderadas: El reemplazo, en un polipéptido, de un residuo amino ácido por otro residuo que no es biológicamente similar. Por ejemplo, el reemplazo de un residuo amino ácido por otro residuo que tienen una carga sustancialmente diferente, una hidrofobicidad sustancialmente diferente o una configuración espacial o estérica sustancialmente diferente.

La frase "amino ácido alternativo" abarca amino ácidos alternativos que son el resultado, tanto de sustituciones moderadas como de no moderadas. Además, de los 20 amino ácidos que ocurren comúnmente, que se encuentran típicamente en los polipéptidos naturales, amino ácidos raros, por ejemplo, canavanina, ornitina y 5-hidroxitriptofano, y amino ácidos artificiales, es decir, amino ácidos que no se encuentran normalmente *in vivo*, por ejemplo, t-butilglicina, pueden usarse como "amino ácidos alternativos" de acuerdo con la invención. Puede usarse cualquier forma quiral de un amino ácido.

Diabetes: Una falla de las células para transportar glucosa endógena a través de sus membranas que puede deberse a una deficiencia endógena de insulina y/o un defecto en la sensibilidad de la insulina. La diabetes es un síndrome crónico de un metabolismo de carbohidratos, proteínas y grasas deteriorado causado por una secreción insuficiente de insulina o de resistencia de la insulina al tejido

correspondiente. Ocurre en dos formas principales: diabetes mellitus insulino-dependiente (IDDM, tipo I), y diabetes mellitus no insulino dependiente (NIDDM, tipo II) que difieren en la etiología, patología, genética, edad de iniciación y tratamiento.

Las dos formas principales de diabetes están caracterizadas ambas, por una incapacidad de liberar insulina en una cantidad y con una programación precisa que es necesaria para controlar la homeostasis de glucosa. La diabetes de tipo I o diabetes mellitus insulino dependiente (IDDM) es causada por la destrucción de células beta pancreáticas, que da como resultado niveles insuficientes de insulina endógena. La diabetes de tipo II o diabetes no insulino dependiente, es el resultado de un defecto tanto en la sensibilidad del cuerpo a la insulina, como a una deficiencia relativa en la producción de insulina.

Ingestión de Comida: La cantidad de comida consumida por un sujeto individual. La ingestión de comida puede medirse por volumen o por peso. Por ejemplo, la ingestión de comida puede ser la cantidad total de comida consumida por un sujeto individual. O, la ingestión de comida puede ser la cantidad de proteínas, grasas, carbohidratos, colesterol, vitaminas, minerales o cualquier otro componente alimenticio del sujeto individual. "Ingestión de Proteínas" se refiere a la cantidad de proteína consumida por un individuo. De manera similar, "Ingestión de comida", "ingestión de carbohidrato", "ingestión de colesterol", "ingestión de vitamina" e "ingestión de mineral" se refiere a la cantidad de grasa, carbohidratos, colesterol y vitaminas o minerales consumidos por un sujeto individual respectivamente.

Dieta Diaria Normal: El promedio de ingestión de comida para un individuo de una especie determinada. Una dieta diaria normal puede expresarse en términos de ingestión calórica, ingestión de proteínas, ingestión de carbohidrato y/o ingestión de grasa. Una dieta diaria normal en seres humanos comprende

generalmente lo siguiente: aproximadamente 2000, aproximadamente 2400 o aproximadamente 2800 hasta significativamente más calorías. Además, una dieta diaria normal en seres humanos incluye generalmente aproximadamente 12 g hasta aproximadamente 45 g de proteína, aproximadamente 120 g hasta aproximadamente 610 g de carbohidrato, y aproximadamente 11 g hasta aproximadamente 90 g de grasa. Una dieta calórica baja no sería de más de aproximadamente 85%, y preferiblemente no más de aproximadamente 70%, de la ingestión calórica normal de un ser humano individual.

En animales, los requisitos calóricos y nutrientes varían dependiendo de la especie y el tamaño del animal. Por ejemplo, en gatos, la ingestión calórica total por libra (0,454 kg) así como también la distribución porcentual de proteína, carbohidrato y grasa varía con la edad del gato y el estado reproductor. Una guía general para gatos sin embargo es de 40 cal/lb/día (18.2 cal/kg/día). Aproximadamente 30% hasta aproximamente 40% debería ser proteína, aproximadamente 7% hasta aproximadamente 10% debería ser carbohidrato, y aproximadamente 50% hasta aproximadamente 62.5% debería derivar de ingestión de grasa. Un experto en la materia puede identificar fácilmente la dieta diaria normal de un individuo de cualquier especie.

Obesidad: Un estado en el cual el exceso de grasa corporal puede poner en peligro la salud de una persona (ver Barlow and Dietz, *Pediatrics* 102:E29, 1998; National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI), *Obes. Res.* 6 (suppl. 2):51S-209S, 1998). El exceso de grasa corporal es un resultado de un desquilibrio de la ingestión de energía y el gasto de energía. Por ejemplo, el índice de masa corporal (BMI) puede usarse para verificar la obesidad. En una convención comúnmente empleada, un BMI de 25.0 kg/m^2 a 29.9 kg/m^2 es sobrepeso, mientras que un BMI de 30 kg/m^2 o más es obesidad.

En otra convención, se usa a la circunferencia de la cintura para verificar la obesidad. El exceso de grasa abdominal es una verificación independiente, importante de los riesgos asociados con la obesidad o el sobrepeso. La medición de la circunferencia de la cintura es particularmente útil en pacientes que han sido categorizados como normales o con sobrepeso. Usualmente no es necesario medir la circunferencia de la cintura en individuos con BMIs ≥ 35 kg/m^2 debido a que agrega muy poco poder predictivo sobre la clasificación del riesgo de enfermedad por el BMI. Los hombres que tienen circunferencias de cintura mayores que 40 pulgadas (102 cm), y las mujeres que tienen circunferencias de cintura mayores que 35 pulgadas (90 cm), tienen mayores riesgos de diabetes, dislipidemia, hipertensión y enfermedad cardiovascular debido al exceso de grasa abdominal. Los individuos con circunferencias de cintura que superan estos valores deberían ser considerados dentro de la categoría de riesgo por arriba de la definida por su BMI

Existen fuertes evidencias que muestran que la obesidad afecta tanto la morbilidad como la mortalidad de los invididuos. Por ejemplo, un individuo obeso o con sobrepeso tiene un riesgo incrementado de sufrir cardiopatías, diabetes no insulino dependiente (tipo II), hipertensión, accidentes cerebrovasculares, cáncer, (por ejemplo, cáncer endometrial, de mama, de próstata y de colon), dislipidemia, colecistopatía, apnea del sueño, fertilidad reducida y osteoartritis entre otras (ver Lyznicki et al., *Am. Fam. Phys.* 63:2185, 2001).

Sobrepeso: Un individuo que pesa más que su peso corporal ideal. Un individuo con sobrepeso puede ser obeso pero no necesariamente obeso. Por ejemplo, un individuo con sobrepeso es cualqueir individuo que desea disminuir su peso. En una convención, un individuo con sobrepeso es un individuo con un BMI de 25,0 kg/m^2 a 29,9 kg/m^2.

Pegilación: El procedimiento de reacción de un poli(alquilen glicol), preferiblemente un poli(alquilen glicol) activado para formar un enlace covalente. Puede usarse un facilitador, por ejemplo, un amino ácido por ejemplo, lisina. Aunque la "pegilación" a menudo se lleva a cabo usando poli(etilen glicol) o sus derivados, tales como metoxi poli (etilen glicol), el término no está limitado aquí al uso de metoxi poli etilen glicol, sino que incluye también el uso de cualquier otro poli alquilen glicol útil, por ejemplo, polipropilen glicol. Pegilado se definirá de acuerdo a esto.

Administración Periférica: Administración fuera del sistema nervioso central. La administración periférica no incluye administración directa al cerebro. La administración periférica incluye pero no está limitada a administración intravascular, intramuscular, subcutánea, por inhalación, oral, rectal, transdérmica, bucal, sublingual o intranasal.

Polipéptido: Un polímero en el cual los monómeros son residuos amino ácidos que están unidos conjuntamente a través de enlaces amida. Cuando los amino ácidos son alfa-amino ácidos, pueden usarse cualquiera de los L-isómeros ópticos o D- isómeros ópticos, siendo preferidos los L-isómeros. A través de toda esta memoria, se asumirá que un alfa-aminoácido es un L-isómero sino se manifiesta explícitamente que es un D-isómero. Los términos "polipéptido" o "proteína" tal como se usan aquí abarcan cualquier secuencia de amino ácido e incluyen secuencias modificadas tales como glicoproteínas. El término "polipéptido" cubre las proteínas naturales así como también aquellas que se producen de manera recombinante o sintética. El término "fragmento polipeptídico" se refiere a una porción de un polipéptido, por ejemplo, un fragmento que exhibe por lo menos una secuencia útil en la adhesión de un receptor. El término "fragmentos funcionales

de un polipéptido" se refiere a todos los fragmentos de un polipéptido que retienen la actividad del polipéptido. Los péptidos biológicamente funcionales pueden incluir también proteínas de fusión, en las cuales el péptido de interés está fusionado a otros péptidos.

Cantidad terapéuticamente eficaz: Dosis suficiente para evitar el avance o para causar la regresión de un trastorno, o que tiene capacidad para aliviar una señal o síntoma de un trastorno o que es capaz de lograr un resultado deseado. En varias realizaciones, una cantidad terapéuticamente eficaz de un compuesto de la invención es una cantidad suficiente para inhibir o detener el aumento de peso, o una cantidad suficiente para disminuir el apetito, o una cantidad suficiente para reducir la ingestión calórica o la ingestión de comida o aumentar el gasto de energía o una cantidad suficiente para reducir el peso o para reducir el riesgo de mortalidad o morbilidad de estados asociados con el trastorno.

6. DESCRIPCION DETALLADA

Los inventores hallaron, sorprendentemente, que los análogos de oxm de la invención son eficaces supresores del apetito y/o que tienen un efecto más sostenido que el oxm natural sobre la ingestión de comida y/o que tienen un efecto más potente que el oxm natural en la ingestión de alimentos.

La secuencia de oxm humano (que es igual que el de la rata y hámster) es la siguiente:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn Arg Asn Asn Ile Ala (SEC ID NO: 357)

Los péptidos de la invención tienen también un tiempo de aclaramiento o vida media más prolongado o una resistencia mejorada a la degradación, en comparación con oxm. El aumento de la duración de la supresión del apetito puede ser particularmente importante para evitar el efecto conocido como "escape". Una corta duración del supresor de apetito puede reducir el apetito por el tiempo cubierto por una comida, en esa comida el sujeto come típicamente menos. Si, sin embargo, el supresor de apetito tiene un tiempo de aclaramiento rápido o una vida media corta, o si es luego metabolizado o removido de otra manera de la circulación del sujeto, entonces en el momento de la comida siguiente, el sujeto puede recuperar su apetito "normal". En vista de que el sujeto ha comido una comida frugal en el tiempo de comida previo, el sujeto puede experimentar en realidad un aumento del apetito en el momento de la comida subsiguiente. Si el sujeto satisface ese apetito, es posible que la ingestión de comida en las dos comidas en total no sea inferior a la ingestión de comida que hubiera ingerido sin el supresor de apetito. Es decir, que el sujeto puede haber "escapado" de los efectos del supresor de apetito. El "escape" puede reducirse usando dosis adicionales de supresor de apetito o usando un supresor de apetito con una duración de acción más prolongada. Si el sujeto tiene un apetito reducido durante más tiempo, entonces se reduce el grado hasta el cual puede recuperar el alimento perdido de una comida en la comida siguiente, debido a que hay un límite práctico en la capacidad total para recibir alimento en una comida particular. La administración repetida o continua de un compuesto por un período de tiempo, por ejemplo, un período de días o semanas, conducirá a una supresión de apetito extendida y reducirá el potencial para el escape de los efectos de la supresión de apetito.

La actividad y/o duración de acción mejorada de los análogos de oxm en comparación con oxm ofrece varias ventajas. Por ejemplo, se permitirá una supresión eficaz del apetito en dosis más bajas (una dosis menor y/o con niveles pico inferiores, lo cual ofrece la perspectiva de efectos secundarios reducidos (incluyendo náuseas) y una reducción en el costo del tratamiento), o el uso de dosis relativamente elevadas, será mejor tolerado por el paciente, lo cual permitirá lograr una pérdida de peso más rápida y/o mayor. Algunos de los compuestos de la invención usados en los ejemplos que se dan aquí, exhiben un modelo de supresión de apetito que es indicativo de un "estiramiento de la curva sanguínea", es decir, que tiene farmacocinética mejorada en virtud de exhibir cualquiera o ambos de (i) un inicio más gradual de la actividad supresora de apetito que con el oxm, y por lo tanto de evitar potencialmente un pico inicial brusco (que podría estar asociado con náuseas); y (ii) una duración de acción potencialmente más prolongada.

Otras ventajas de muchos compuestos de la invención incluyen el hecho de que los compuestos tienen características de almacenamiento mejoradas y pueden llevarse a síntesis a gran escala, por ejemplo, algunos compuestos de la invención no contienen motivos de secuencias asociados con la formación de especies de aspartimida, y/o son menos propensos a reducir la estabilidad.

En una realización, la invención provee un péptido en el cual

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

o Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24.

(SEC ID NO: 359).

En realizaciones particulares, un péptido de la invención es uno donde:

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es:

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

o Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24.

En una realización más, un péptido de la invención es uno donde:

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es:
Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24.

En una realización másl, un péptido de la invención comprende Xaa1 Xaa2 Xaa3 seleccionado del grupo que consiste en:

His1 Ser2 Gln3,
D-His1 Ser2 Gln3,
D-His1 Ala2 Gln3, y
D-His1 Ala2 Asp3.

(SEC ID NO: 360).

En una realización nás, un péptido de la invención es uno donde:

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 es:
Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,
Lys27 Asn28 Gly29 Gly30 Pro31 Ser32,
o Met27 Asn28 Thr29 Lys30 Arg31 Asn32.

En una realización más, un péptido de la invención es uno donde

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 is:

Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,
o Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

(SEC ID NO: 361).

En una realización, un péptido de la invención es uno donde

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 es:
Lys27 Asn28 Ala29 Gly30 Pro31 Ser32.

En particular, el péptido de la invención puede tener una secuencia de amino ácido seleccionada del grupo que comprende:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 1)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 2)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 3)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 4)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 5)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 6)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 7)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 8)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 9)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 10)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 11)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 12)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 13)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 14)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 15)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 16)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 17)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 18)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 19)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 20)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 21)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 22)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 23)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 24)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 25)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 26)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 27)

HisSer Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 28)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 29)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 30)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 31)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 32)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 33)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 34)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 35)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 36)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 37)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 38)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 39)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 40)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 41)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 42)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 43)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 44)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 45)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 46)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 47)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 48)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 49)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 50)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 51)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 52)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 53)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 54)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 55)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 56)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 57)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 58)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 59)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 60)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 61)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 62)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 63)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 64)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 65)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 66)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 67)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 68)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 69)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 70)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 71)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 72)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 73)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 74)

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D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 75)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 76)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 77)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 78)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 79)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 80)

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D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 82)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 83)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 84)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 85)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 86)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 87)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 88)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 89)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 90)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 91)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 92)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 93)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 94)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 95)

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D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 100)

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D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 102)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 103)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 104)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 105)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 106)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 107)

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D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 114)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 115)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 116)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 117)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 118)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 119)

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D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 121)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 122)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 123)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 124)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 125)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 126)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 127)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 128)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 129)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 130)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 131)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 132)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 133)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 134)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 135)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 136)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 137)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 138)

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D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 142)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 143)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 144)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 145)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 146)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 147)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 148)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 149)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 150)

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D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 152)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 153)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 154)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 155)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 156)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 157)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 158)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 159)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 160)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 161)

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D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 183)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 184)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 185)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 186)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 187)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 188)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 189)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 190)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 191)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 192)

Por ejemplo, el péptido de la invención puede tener la secuencia de amino ácido

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 193)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 194)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 195)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 196)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 197)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 198)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 199)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 200)

Opcionalmente, el péptido de la invención tiene una fracción de extension –A-B-C en el C-terminal. Por consiguiente, el péptido de la invención puede tener una fracción de extensión adicional de la secuencia -A-B-C,

donde:

A está ausente o 1, 2, 3 o 4 residuos Ala o 1, 2, 3 o 4 residuos Glu
B está ausente o 1, 2, 3 o 4 residuos Ala o 1, 2, 3 o 4 residuos Glu

con la condición de que A y B no comprendan ambos, residuos Ala, y que A y B no comprendan ambos, residuos Glu; y

C es Lys, o Lys con un ácido seleccionado entre ácido cáprico, ácido láurico, ácido mirístico, ácido palmítico, ácido esteárico y ácido araquídico, unido a través de su grupo –COOH al grupo $-NH_2$ de la cadena secundaria Lys por medio de un enlace peptídico.

En una realización, los grupos A o B o ambos A y B están ausentes. En una realización cuando A y B están ambos presentes, A es Glu y B es Ala. Por ejemplo, en una realización A es un residuo Glu, y B es un residuo Ala.

En una realización, C es un residuo Lys sin sustitución.

En una realización, C es un residuo Lys con un ácido graso unido a través de su grupo –COOH al grupo -NH2 de la cadena secundaria Lys por medio de un enlace peptídico. Por ejemplo, el ácido graso puede estar seleccionado de

- ácido cáprico
- ácido laúrico
- ácido mirístico,
- ácido palmítico,
- ácido esteárico, y
- ácido araquídico. (ácido icosanoico)

En otras realizaciones, la fracción de extension C-terminal –A-B-C es:

Lys38,
Lys38-caproilo,
Lys38-lauroilo,
Lys38-miristoilo,
Lys38-palmitoilo,
Lys38-estearoilo,
Lys38-araquidoilo,
Glu38 Ala39 Lys40,
Glu38 Ala39 Lys40-caproilo,

Glu38 Ala39 Lys40-lauroilo,

Glu38 Ala39 Lys40-miristoilo,

Glu38 Ala39 Lys40-palmitoilo,

Glu38 Ala39 Lys40-estearoilo,

o Glu38 Ala39 Lys40-araquidoilo.

El grupo araquidoilo es también conocido como el grupo icosanoilo.

Ejemplos de compuestos que comprenden la fracción de extensión C-terminal –A-B-C pueden seleccionarse del grupo que comprende:

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 201)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 202)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala Lys (SEC ID NO: 203)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 204)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 205)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-miristoilo (SEC ID NO: 206)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-palmitoilo (SEC ID NO: 207)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-estearoilo (SEC ID NO: 208)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-araquídoilo (SEC ID NO: 209)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys (SEC ID NO: 210)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-miristoilo (SEC ID NO: 211)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-miristoilo (SEC ID NO: 212)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-palmitoilo (SEC ID NO: 213)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-araquidoilo (SEC ID NO: 214)

Tal como se ha mencionado anteriormente, la secuencia oxm humana nativa (que es igual a la de rata y hámster) es la siguiente:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn Arg Asn Asn Ile Ala (SEC ID NO: 357)

La secuencia oxm bovina nativa (que es igual a la porcina) es la siguiente:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 358)

Es decir, que es la misma que la secuencia humana excepto que Arg33 en el péptido humano es reemplazado con Lys33 en el péptido bovino. La presente invención provee análogos de oxintomodulina tal como se indicó anteriormente. La invención provee además péptidos que son análogos en los cuales el residuo Lys33 del péptido mencionado anteriormente es reemplazdo con Arg33.

En una realización, la invención provee un péptido de la invención en el cual el residuo Asn34 es reemplazado con Asp34. Ciertos péptidos con el Asn34 reemplazado con Asp34 se muestran como péptidos No 215 a 292 en la Figura 1. En otra realización, la invención provee un péptido en el cual el residuo Gln3 o Asp3 es reemplazado con Glu3. Ciertos péptidos con Glu3 se muestran como péptidos No 293 a 355 en la Figura 1.

La invención comprende además realizaciones que incorporan la secuencia descrita en los ejemplos y/o figuras adjuntas.

Derivados

Un compuesto de la invención puede comprender una estructura indicada anteriormente, modificada por procedimientos bien conocidos que incluyen amidación, glicosilación, carbamilación, alquilación, acilación, por ejemplo, acetilación sulfatación, fosforilación, ciclación, lipidización, conjugación de proteínas (por ejemplo, albúmina) y pegilación. Los análogos de la invención pueden modificarse en posiciones aleatorias dentro de la molécula, o en posiciones pre-determinadas dentro de la molécula y pueden incluir, uno, dos, tres o cuatro fracciones químicas más, agregadas.

Un compuesto de la invención puede ser una proteína de fusión, donde el análogo de oxintomodulina está fusionado con otra proteína o polipéptido (el par de fusión) usando métodos recombinantes conocidos en la materia.

Alternativamente, dicha proteína de fusión puede sintetizarse sintéticamente por cualquier método conocido. Dicha proteína de fusión comprende el análogo de oxintomodulina. Cualquier péptido o proteína apropiados pueden usarse como par de fusión (por ejemplo, albúmina de suero, anhidrasa carbónica, glutationa S-transferasa, anticuerpos de cadena única, anticuerpos, fragmentos de anticuerpos o tioredoxina, etc). Por ejemplo, un compuesto de la invención podría fusionarse con un dominio variable de cadena liviana de inmunoglobulina que tiene especificidad de adhesión para albúmina de suero tal como se describió en la WO 05/118642. Los pares de fusión preferidos no tendrán actividad biológica adversa in vivo.

Dichas proteínas de fusión, incluyendo polipéptidos híbridos, pueden prepararse por enlace del carboxi terminal del par de fusión al amino terminal del análogo de oxintomodulina o viceversa, directamente o a través de un ligador que preferiblemente no involucra la pérdida de actividad de los componentes. Cuando está presente el ligador puede ser químicamente estable o lábil, por ejemplo, puede usarse un ligador disociable para ligar el análogo de oxintomodulina a uno o más pares de fusión. Una proteína de fusión disociable resultante puede disociarse in vivo de manera de liberar una forma activa de un compuesto de la invención. Ejemplos de dichos ligadores disociables, incluyen pero no están limitados a los ligadores D-D-D-D-Y, G-P-R, A-G-G y H-P-F-H-L, que pueden disociarse por enteroquinasa, trombina, enzima disociadora de ubiquitina y renina, respectivamente. Ver, por ejemplo, la Patente Norteamericana No. 6.410.707.

Alternativamente un compuesto de la invención puede ser una proteína de fusión, donde la estructura del compuesto de la invención está unido a un par de fusión a través de un enlace disulfuro lo cual da como resultado una unión covalente entre por lo menos un residuo Cys del compuesto de la invención y por lo menos un residuo Cys del par de fusión.

Cuando se usa una proteína como un par de fusión, se elige preferiblemente de manera que no exhiba antigenicidad indeseable. Puede evitarse la antigenicidad indeseable eligiendo una proteína que sea alogénica para el animal al cual se administrará el compuesto.

Un compuesto de la invención puede ser un derivado fisiológicamente funcional de un compuesto de la invención. el término "derivado fisiológicamente funcional" se usa para denotar un derivado químico de un compuesto de la invención que tiene la misma función fisiológica que el compuesto correspondiente no modificado de la invención. Por ejemplo, un derivado fisiológicamente funcional puede ser convertible en el cuerpo a un compuesto de la invención. De acuerdo con la presente invención, ejemplos de derivados fisiológicamente funcionales incluyen ésteres, amidas y carbamatos; preferiblemente ésteres y amidas.

Los ésteres y amidas farmacéuticamente aceptables de los compuestos de la invención pueden comprender alquilo C_{1-6}-, arilo C_{5-10}-, ar C_{5-10} -alquilo C_{1-6} -, o amino ácido -éster o -amida unidos en un sitio apropiado, por ejemplo, en un grupo ácido.

Las cadenas secundarias acilo pueden ser ventajosas por ejemplo, por su naturaleza lipofílica, haciendo que la fracción se una con la albúmina, causando de este modo una tasa de aclaramiento enormmemente reducida en un sujeto y aumentando de este modo la vida media y la duración del efecto. Aunque las cadenas secundarias acilo pueden ser acilo inferior, por ejemplo, acilo C_1- C_9, especialmente acilo C_{1-6}, se prefiere que sean C_{4-40}, en particular acilo C_{8-25}, especialmente acilo C_{16} o acilo C_{18}. El palmitoilo es especialmente preferido concadena secundaria acilo así como el lauroilo. Pueden agregarse cadenas

secundarias acilo en cualquier posición en el esqueleto peptídico. Un sustituyente acilo puede agregarse a un residuo amino ácido de tal manera que un grupo carboxilo del sustituyente acilo forme un enlace amida con un grupo amino del residuo amino ácido. Alternativamente, un sustituyente acilo puede estar unido a un residuo amino ácido de tal manera que un grupo amino del sustituyente acilo forme un enlace amida con un grupo carboxilo del residuo amino ácido. En un realización adicional preferida la presente invención se refiere a un derivado oxm en el cual un sustituyente acilo está unido al péptido principal mediante un espaciador. Por ejemplo, el sustituyente acilo puede estar unido a la fracción oxm por medio de un espaciador, de tal manera que un grupo carboxilo del espaciador forme un enlace amida con un grupo amino de la porción oxm. Se prefiere especialmente agregar una cadena secundaria acilo (opcionalmente a través de un espaciador) en una posición en el esqueleto peptídico donde se encuentra un residuo lisina. Esto es debido a que la lisina, que tiene una cadena secundaria de cuatro átomos de carbono que termina en un grupo epsilon-amino es particularmente apropiada para agregar fácilmente una cadena secundaria acilo. Puede ser necesario introducir un residuo lisina dentro de la secuencia únicamente con el propósito de proveer un sitio conveniente en el cual agregar una cadena secundaria acilo. Alternativamente, la cadena secundaria acilo puede agregarse al residuo lisina antes de la síntesis del péptido, por lo cual su incorporación en la etapa de síntesis relevante dará como resultado directamente una acilación. Esta metodología es ventajosa si la secuencia de péptidos contiene más de un residuo lisina debido a que evita la necesidad de usar condiciones selectivas que acilan únicamentel a lisina particular de interés. Preferiblemente, los derivados peptídicos tienen tres, más preferiblemente dos y más preferiblemente un sustituyente de cadena secundaria acilo. Ejemplos de acilo (y otros sustituyentes lipofílicos), realizaciones y métodos de síntesis para agregar

dichos péptidos (con o sin uso de espaciadores) han sido descritos en la Patente Norteamericana N°. 6.268.343; y la Patente Norteamericana N°: 6.458.924. Otros ejemplo de ácidos grasos saturados apropiados para la derivatización acilo de compuestos de la invención son butírico (ácido butanoico): $CH_3(CH_2)_2COOH$; caproico (ácido hexanoico): $CH_3(CH_2)_4COOH$; caprílico (ácido octanoico): $CH_3(CH_2)_6COOH$; cáprico (ácido decanoico): $CH_3(CH_2)_8COOH$; laurico (ácido dodecanoico): $CH_3(CH_2)_{10}COOH$; mirístico (ácido tetradecanoico): $CH_3(CH_2)_{12}COOH$; palmítico (ácido hexadecanoico): $CH_3(CH_2)_{14}COOH$; esteárico (ácido octadecanoico): $CH_3(CH_2)_{16}COOH$; araquídico (ácido eicosanoico): $CH_3(CH_2)_{18}COOH$; behénico (ácido docosanoico): $CH_3(CH_2)_{20}COOH$.

De acuerdo con ciertas realizaciones preferidas, las cadenas secundarias acilo pueden agregarse en la posición 30 y/o en la posición 33 y/o posiciones 38 a 46 del esqueleto peptídico.

Las amidas y carbonatos farmacéuticamente aceptables de los compuestos de fórmula (I) pueden comprender alquilo C_{1-6}-, arilo C_{5-10}-, ar C_{5-10} -alquilo C_{1-6} -, o amino ácido- éster o -amida, o -carbamato unido a un sitio apropiado, por ejemplo, a un grupo amino.

Los métodos para lipidización de compuestos que contienen sulfhidrilo con derivados ácido graso han sido descritos en la Patente Norteamericana No. 5.936.092; Patente Norteamericana No. 6.093.692; y Patente Norteamericana No. 6.225.445. Los derivados de ácido graso de un compuesto de la invención que comprenden un compuesto de la invención ligado al ácido graso a través de un enlace disulfuro pueden usarse para liberar un compuesto de la invención a las células y tejidos neuronales. La lipidización aumenta notablemente la absorción de los compuestos con relación al régimen de absorción de los compuestos no lipidizados correspondientes, al mismo tiempo que prolonga la retención de sangre y tejido de los compuestos. Además, el enlace disulfuro en el derivado

lipidizado es relativamente lábil en las células y por lo tanto facilita la liberación intracelular de la molécula desde las fracciones de ácido graso. Las fracciones que contienen lípidos apropiadas son sustituyentes hidrofóbicos con cuatro a veintiséis átomos de carbono preferiblemente, cinco a diecinueve átomos de carbono. Los grupos lípidos apropiados incluyen pero no están limitados a los siguientes: palmitoilo ($C_{15}H_{31,}$), oleoilo ($C_{15}H_{29}$), estearoilo ($C_{17}H_{35}$), colato; y desoxicolato.

Los expertos en la materia apreciarán que pueden introducirse residuos amino ácido particulares a la secuencia oxm para facilitar una o más de las modificaciones que se describen aquí.

Los métodos de ciclación incluyen ciclación a través de la formación de un enlace disulfuro y ciclación de cabeza a cola usando una resina de ciclación. Los péptidos ciclados pueden tener estabilidad mejorada, incluyendo resistencia incrementada a la degradación enzimática como resultado de sus restricciones configurativas. La ciclación puede ser conveniente en particular cuando el péptido no ciclado incluye un grupo cisteína N-terminal. Los péptidos ciclados apropiados incluyen estructuras de cabeza a cola monoméricas y diméricas. Los péptidos ciclados pueden incluir uno o más residuos adicionales, especialmente una cisteína adicional incorporada con el propósito de formar un enlace disulfuro o una cadena secundaria incorporada con el propósito de una ciclación basada en resina.

Un compuesto de la invención puede estar pegilado. Los compuestos pegilados de la invención pueden proveer ventajas adicionales tales como un aumento de la solubilidad, estabilidad y el tiempo de circulación del polipéptido, o una inmunogenicidad disminuida (ver Patente Norteamericana No. 4.179.337). La WO 2006/082517 y la Patente Norteamericana 2006/171920, que se

incorporan aquí como referencia, proveen ejemplos y métodos asociados de pegilación de péptidos y análogos y derivados de éstos.

Las fracciones químicas para la derivatización de un compuesto de la invención pueden seleccionarse también a partir de polímeros solubles en agua, tales como polietilen glicol, copolímeros de etilen glicol/propilen glicol, carboximetilcelulosa, dextrano, alcohol polivinílico y similares. Una fracción polimérica para la derivatización de un compuesto de la invención puede ser de cualquier peso molecular y puede ser ramificada o no ramificada. Para facilitar la manipulación y manufactura el peso molecular preferido de un polietilen glicol para la derivatización de un compuesto de la invención es de desde aproximadamente 1 kDa hasta aproximadamente 100 kDa; el término "aproximadamente" indica que en las preparaciones de polietilen glicol, algúnas moléculas pesarán más, algunas menos, que el peso molecular manifestado. Pueden usarse polímeros de otros pesos moleculares, dependiendo del perfil terapéutico deseado, por ejemplo, la duración de la liberación sostenida deseada, los efectos, si hay alguno, sobre la actividad biológica, la facilidad de manipulación, el grado o falta de antigenicidad y otros efectos conocidos del polietilen glicol para una proteína terapéutica o análoga. Por ejemplo, el polietilen glicol puede tener un peso molecular promedio de aproximadamente 200, 500, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11,000, 11,500, 12,000, 12,500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18,500, 19,000, 19,500, 20,000, 25,000, 30,000, 35,000, 40,000, 50,000, 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, 95,000, o 100,000 kDa.

Sales y solvatos de los compuestos de la invención que son apropiadas para ser usadas en un medicamento son aquellas en las cuales un contraion o un

solvente asociado es farmacéuticamente aceptable. Sin embargo, sales y solvatos que tienen contraiones no farmacéuticamente aceptables o solventes asociados están dentro del alcance de la presente invención, por ejemplo, para ser usados como intermediarios en la preparación de los compuestos de la invención y sus sales o solvatos farmacéuticamente aceptables.

Las sales apropiadas de acuerdo con la invención incluyen aquellas formadas con ácidos orgánicos o inorgánicos o bases. Las sales de adición de ácido farmacéuticamente aceptables incluyen aquellas formadas con ácido clorhídrico, bromhídrico, sulfúrico, nítrico, cítrico, tartárico, acético, fosfórico, láctico, pirúvico, acético, trifluoracético, succínico, perclorico, fumárico, maleico, glicólico, láctico, salicílico, oxaloacético, mentánsulfónico, etánsulfónico, p-toluensulfónico, fórmico, benzoico, malónico, naftalen-2-sulfónico, benzensulfónico e isetiónico. Otros ácidos tales como oxálico; aunque no son por sí mismos farmacéuticamente aceptables, pueden ser útiles como intermediarios para obtener los compuestos de la invención y sus sales farmacéuticamente aceptables. Las sales farmacéuticamente aceptables con bases incluyen sales de amonio, sales de metales alcalinos por ejemplo, sales de potasio y sodio, sales de metales alcalino térreos, por ejemplo, sales de calcio y magnesio, y sales con bases orgánicas, por ejemplo, diciclohexilamina y N-metil-D-glucamina.

Los expertos en química orgánica apreciarán que muchos compuestos orgánicos pueden formar complejos con solventes en los cuales reaccionan o a partir de los cuales precipitan o cristalizan. Dichos complejos se conocen como "solvatos". Por ejemplo, un complejo con agua se conoce como un "hidrato" la presente invención provee solvatos de compuestos de la invención.

Los péptidos de la invención pueden prepararse mediante cualquier técnica apropiada para preparar péptidos incluyendo pero sin limitarlo a metodología convencional, por ejemplo, síntesis a partir de amino ácidos individuales

especialmente sintésis en etapas usando un sintetizador de péptidos automático; modificación de péptidos naturales; o técnicas de manufactura recombinante.

Condiciones

La invención provee una composición farmacéutica que comprende un péptido de acuerdo con la invención y uno o más portadores farmacéuticamente aceptables. La invención provee también una composición farmacéutica para ser usada en el control del apetito, la comida, la ingestión de comida, el gasto de energía y la ingestión de calorías, donde dicha composición comprende una cantidad eficaz de un compuesto de acuerdo con la invención. Más particularmente, la invención provee una composición farmacéutica para ser usada en el tratamiento de la obesidad, para ser usada en el tratamiento de trastornos de la alimentación, o para ser usada en el tratamiento de diabétes o un síntoma de diabétes o para ser usada en el tratamiento o prevención de co-morbilidades asociadas con obesidad o exceso de peso.

Además, la invención provee un método para reducir el exceso de peso, por ejemplo, exceso de peso cosmético que comprende administrar a un paciente que desea reducir su peso, una cantidad eficaz de un compuesto o de una composición farmacéutica de acuerdo con la invención.

Además, la invención provee un método para el tratamiento o prevención de la obesidad o diabetes u otra co-morbilidad de la obesidad en un sujeto que lo necesita, que comprende administrar al sujeto una cantidad eficaz de un compuesto o de una composición farmacéutica de acuerdo con la invención.

La invención provee también un método para reducir el apetito en un sujeto, reducir la ingestión de comida en un sujeto o reducir la ingestión de calorías en un sujeto, reducir el peso corporal en un sujeto, reducir el aumento de peso corporal en un sujeto o aumentar el gasto de energía en un sujeto que lo

necesita, que comprende administrar al sujeto un péptido o una composición farmacéutica de acuerdo con la invención.

La invención provee también un método para provocar pérdida de peso o para evitar aumento de peso con propósitos cosméticos, que comprende administrar al sujeto un péptido o una composición farmacéutica de acuerdo con la invención.

La invención provee también un péptido de la invención para ser usado como medicamento. Puede usarse como medicamento para el tratamiento de la obesidad o diabetes o de una co-morbilidad de la obesidad. Puede ser para usar como medicamento para reducir el apetito en un sujeto, reducir la ingestión de comida en un sujeto o reducir la ingestión calórica en un sujeto, reducir el peso corporal en un sujeto, reducir el aumento de peso corporal en un sujeto o aumentar el gasto de energía en un sujeto.

La invención provee también el uso de un compuesto de acuerdo con la invención para la manufactura de un medicamento para ser usado en el tratamiento de un trastorno seleccionado entre obesidad, trastornos de la alimentación, diabetes, cardiopatía, hipertensión, enfermedad de lípidos, y trastornos de la actividad intestinal y de la actividad motora gástrica y otros aspectos del intestino y de la función intestinal, por ejemplo, absorción de agua y manipulación del fluido o la función pancreática que incluye el páncrea endocrino o trastornos de la función hepato-biliar o prevención del cáncer. En particular la invención provee el uso de un péptido de la invención para la manufactura de un medicamento para el tratamiento de la obesidad o diabetes o de una co-morbilidad de la obesidad. Además, la invención provee el uso de un compuesto de acuerdo con la invención para la manufactura de un medicamento para ser usado en el control de una o más de apetito, comida, ingestión de comida, gasto de energía e ingestión de calorías. En particular la invención provee el uso de un

péptido de la invención para la manufactura de un medicamento para reducir el apetito en un sujeto, reducir la ingestión de alimento en un sujeto o reducir la ingestión de calorías en un sujeto, reducir el peso corporal en un sujeto, reducir el aumento de peso corporal en un sujeto o aumentar el gasto de energía en un sujeto.

El sujeto al cual se administra el compuesto puede tener sobrepeso, por ejemplo, ser obeso. Alternativamente, o adicionalmente el sujeto puede ser diabético, por ejemplo, puede tener resistencia a la insulina o intolerancia a la glucosa o ambos. El sujeto puede tener diabetes mellitus por ejemplo, el sujeto puede tener diabetes de tipo II. El sujeto puede tener sobrepeso, por ejemplo, obesidad y puede tener diabetes mellitus por ejemplo, diabetes de tipo II.

Además, el sujeto puede tener o corre el riesgo de tener un trastorno en el cual la obesidad o el sobrepeso es un factor de riesgo. Dichos trastornos incluyen pero no están limitados a enfermedades cardiovasculares por ejemplo, hipertensión, ateroesclerosis, insuficiencia cardíaca congestiva y dislipidemia; accidentes cerebrovasculares, enfermedad de la vesícula; osteoartritis, apnea del sueño, trastornos de reproducción, por ejemplo, síndrome de ovario poliquístico de, cánceres, por ejemplo, de mama, próstata, colon, endometrio, riñón y esófago; venas varicosas; acantosis nigricans; excema; intolerancia al ejercicio; resistencia a la insulina; hipertensión o hipercolesterolemia, colitiasis, osteoartritis, lesiones ortopédicas; resistencia a la insulina, por ejemplo diabetes de tipo II y síndrome X; síndrome metabólico; y enfermedad tromboembólica (ver Kopelman (2000), Nature 404:635-43; Rissanen et al., British Med. J. 301, 835, 1990).

Otros trastornos asociados con la obesidad incluyen depresión, ansiedad, ataque de pánico, migraña, dolores de cabeza, PMS, estados de dolor crónico, fibromialgia, insomnio, impulsividad, trastorno obsesivo compulsivo, síndrome de intestino irritable (IBS), y mioclonia. Además, la obesidad es un factor de riesgo

reconocido porque aumenta la incidencia de las complicaciones de la anestesia general. (Ver por ejemplo, Kopelman, Nature 404:635-43, 2000). En general, la obesidad reduce los años de vida y significa un serio riesgo de co-morbilidades tales como las enumeradas anteriormente.

Otras enfermedades o trastornos asociados con la obesidad son defectos de nacimiento, estando asociada la obesidad maternal con el aumento de la incidencia de defectos del tubo neural, síndrome del tunel carpiano (CTS); insuficiencia venosa crónica (CVI); somnolencia diurna; trombosis de vena profunda (DVT); enfermedad renal de etapa terminal (ESRD); gota, trastornos cardíacos; respuesta de inmunidad alterada; función respiratoria alterada; infertilidad; enfermedad del hígado; lumbalgia; complicaciones obstétricas y ginecológicas; pancreatitis; así como también hernias abdominales; acantosis nígrica; anormalidades endócrinas; hipoxia crónica e hipercapnia; efectos dermatológicos; elefantitis; reflujo gastro esofágico; espolón calcaneo; edema de extremidad inferior; mamegalia que causa considerables problemas tales como dolor al sujetar la tira del corpiño, lesiones en la piel, dolor cervical, dolores crónicos en infecciones en los pliegues de la piel por debajo de las mamas, etc,; masas de la pared abdominal anterior gruesa, por ejemplo, panniculitis abdominal con paniculitis frecuente, impedimento para caminar, que causa frecuentes infecciones, dificultades para vestirse, lumbalgia; enfermedad musculoesqueletal; pseudo tumor cerebri (o hipertensión intracraneal benigna), y hernia de hiato deslizante.

Wynne et al (Intenational Journal of Obesity 12: 1729-1736, 2006) describieron como administrando 400 nmoles de oxintomodulina pre-prandial, tres veces por día, durante cuatro días, aumento el gasto de energía relacionado con la actividad en 143+/-109 kcal/día o 26.2+/-9.9% (P=0.0221); el gasto de energía

total en 9.4+/-4.8% (P=0.0454) y el nivel de actividad física en 9.5+/-4.6% (P=0.0495). Por consiguiente, la presente invención provee además un método para aumentar el gasto de energía en un sujeto. El método incluye por ejemplo administrar periféricamente una cantidad terapéuticamente eficaz de un compuesto de la invención al sujeto, alterando de este modo el gasto de energía. La energía se quema en todos los procesos fisiológicos. El cuerpo puede alterar la tasa de gasto de energía directamente, modulando la eficiencia de aquellos procesos, o cambiando la cantidad y naturaleza de procesos que ocurren. Por ejemplo, durante la digestión el cuerpo gasta energía para mover el alimento da través del intestino, y digerir la comida y dentro de las células, la eficiencia del metabolismo celular puede alterarse para producir más o menos calor.

En un aspecto el método de la invención involucra la manipulación del circuito arqueado que altera coordinadamente la ingestión de alimento, y altera recíprocamente el gasto de energía. El gasto de energía es un resultado del metabolismo celular, de la síntesis de proteína, de la tasa metabólica y de la utilización calórica. Por lo tanto en este aspecto de la invención la administración de un compuesto de la invención puede dar como resultado un gasto de energía incrementado y puede disminuir la eficiencia de la utilización de calorías.

La invención provee también un método para mejorar un perfil de lípidos en un sujeto. La invención provee también un método para aliviar una alteración o trastorno que puede ser aliviado mediante la reducción de la disponibilidad de nutrientes. El apetito puede medirse mediante cualquier medio conocido por un experto en la materia. Por ejemplo, puede verificarse la disminución del apetito mediante una verificación psicológica. Por ejemplo, la administración de un compuesto de la invención da como resultado un cambio en el hambre percibido, la saciedad y/o la distención. El hambre puede verficarse mediante cualquier método por un experto en la materia. Por ejemplo, el hambre se verifica usando

ensayos psicológicos tales como por verificación de una sensación de hambre y una percepción sensorial usando un cuestionario tal como pero sin limitarlo al cuestionario. Visual Analog Score (VAS). En un ejemplo específico, no limitativo el hambre se verifica contestando preguntas relacionadas con el deseo de comida, bebida, presunto consumo de comida, náuseas, y percepciones relacionadas con el olor o sabor.

Puede usarse un compuesto de la invención para controlar el peso y como tratamiento, por ejemplo, para la reducción o prevención de la obesidad en particular cualquiera de una o más de las siguientes: prevenir y reducir el aumento de peso; inducir o promover la pérdida de peso; y reducir la obesidad midiéndola mediante el Indice de Masa Corporal. Un compuesto de la invención puede usarse para el control de uno o más de apetito, saciedad y hambre, en particular cualquiera o más de los siguientes: reducción, supresión en inhibición del apetito; inducción, incremento, aumento y promoción de la saciedad y de las sensaciones de saciedad; y reducción, inhibición y supresión del hambre y las sensaciones de hambre. Un compuesto de la invención puede usarse para mantener uno o más de un peso corporal deseado, un índice de masa corporal deseado, una apariencia deseada y buena salud.

Un sujeto puede ser un sujeto que desea perder peso, por ejemplo, mujeres y hombres que desean un cambio en su apariencia. Un sujeto puede desear disminuir la sensación de hambre, por ejemplo, el sujeto puede ser una persona involucrada en una larga tarea que requiere un nivel de concentración elevado, por ejemplo, soldados en actividad, controladores de tráfico, o conductores de camiones en vías de larga distancia, etc.

La presente invención puede usarse también para tratar, prevenir, mejorar o aliviar alteraciones o trastornos causados, complicados, o agravados por una disponibilidad de nutrientes relativamente elevada. El término "alteración" o

trastorno que puede ser aliviado mediante la reducción de la disponibilidad calórica (o nutrientes) se usa aquí para denotar cualquier alteración o trastorno en un sujeto que sea causado por, que se complique por o que se agrave por una disponibilidad de nutrientes relativamente elevada o que puede aliviarse reduciendo la disponibilidad de nutrientes, por ejemplo, disminuyendo la ingestión de comida. Los sujetos que son resistentes a la insulina, intolerantes a al glucosa o que tienen cualquier forma de diabetes mellitus, por ejemplo, diabetes de tipo I, de tipo II o gestacional, pueden beneficiarse también de los métodos de acuerdo con la presente invención.

Las alteraciones o trastornos asociados con el aumento de la ingestión de calorías incluyen pero no están limitados a resistencia a la insulina, intolerancia a la glucosa, obesidad, diabetes, incluyendo diabetes de tipo II, trastornos de la alimentación, síndrome de resistencia a la insulina y enfermedad de Alzheimer,.

De acuerdo con la presente invención, un compuesto de la invención se usa preferiblemente en el tratamiento de un ser humano. Sin embargo aunque los compuestos de la invención se usarán típicamente para tratar sujetos humanos, también pueden usarse para tratar trastornos similares o idénticos en otros vertebrados, por ejemplo, en otros primates; animales de granja, por ejemplo, cerdos, ganado y aves; animales que se usan para deportes, por ejemplo caballos; animales de compañía, por ejemplo, perros y gatos.

Resumiendo, la invención provee también un péptido de la invención para ser usado como medicamento para la prevención o tratamiento de la obesidad. Además, se provee un péptido de la invención para ser usado como medicamento para reducir el apetito en un sujeto, reducir la ingestión de comida en un sujeto o reducir la ingestión de calorías en un sujeto, reducir el peso corporal en un sujeto, reducir, el aumento de peso corporal en un sujeto o aumentar el gasto de energía en un sujeto.

La invención provee también un método para tratar o prevenir la obesidad en un sujeto que lo necesita que comprende administrar al sujeto un péptido de acuerdo con la invención. También se provee un método para el tratamiento o prevención de diabetes o de una co-morbilidad de obesidad en un sujeto que lo necesita, que comprende administrar al sujeto un péptido de acuerdo con la invención. Además, se provee un método para reducir el apetito en un sujeto, reducir la ingestión de comida en un sujeto o reducir la ingestión de calorías en un sujeto, reducir el peso corporal en un sujeto, reducir el aumento de peso corporal en un sujeto o aumentar el gasto de energía en un sujeto que lo necesita, que comprende administrar al sujeto un péptido de acuerdo con la invención o una composición farmacéutica de acuerdo con la invención.

Composiciones

Aunque es posible administrar el ingrediente activo solo, es preferible que esté presente en una formulación o composición farmacéutica. Por consiguiente la invención provee una formulación farmacéutica que comprende un compuesto de la invención o una variante o derivado de ésta o una sal o solvato de ésta tal como se definió anteriormente y un excipiente farmacéuticamente aceptable. Las composiciones farmacéuticas de la invención pueden tener la forma de una formulación farmacéutica tal como se describe a continuación.

Las formulaciones farmacéuticas de acuerdo con la invención incluyen aquellas que son apropiadas para administración oral, parenteral (incluyendo subcutánea, intradérmica, intramuscular, intravenosa e intraarticular), inhalación (incluyendo polvos o nieblas de partículas finas que pueden generarse por medio de varios tipos de dosis medidas, aerosoles presurizados, nebulizadores o insufladores, incluyendo en forma intranasal o a través de los pulmones),

administración rectal y tópica (incluyendo dérmica, transdérmica, transmucosal, bucal, sublingual e intraocular), aunque la vía más apropiada puede depender por ejemplo del estado y el trastorno del que lo recibe.

Las formulaciones pueden presentarse convenientemente en forma de dosificación unitaria y pueden prepararse mediante cualquiera de los métodos que son bien conocidos en farmacia. Todos los métodos incluyen la etapa de poner el ingrediente activo en asociación con un portador farmacéutico que consituye uno o más ingredientes accesorios. en general, las formulaciones se preparan teniendo uniformemente e íntimamente en asociación el ingrediente activo con los portadores líquidos o portadores sólidos finamente divididos o ambos y luego si es necesario configurar el producto en la formulación deseada.

Las formulaciones de la presente invención apropiadas para administración oral pueden presentarse en forma de unidades discretas tales como cápsulas, sellos o tabletas, donde cada una contiene una cantidad pre-determinada de ingrediente activo; en forma de polvo o gránulos; en forma de una solución o una suspensión en un líquido acuoso o un líquido no acuoso; o en forma de una emulsión líquida de aceite en agua o una emulsión líquida de agua en aceite. El ingrediente activo puede estar también presente en forma de un bolo, un electuario o pasta. Varios portadores farmacéuticamente aceptables y sus formulaciones se describen en tratados de formulaciones convencionales, por ejemplo, en Remington's Pharmaceutical Sciences by E. W. Martin. Ver también, Wang, Y. J. and Hanson, M. A., Journal of Parenteral Science and Technology, Technical Report No. 10, Supp. 42:2S, 1988.

Puede prepararse una tableta por compresión o moldeo, opcionalmente con uno o más ingredientes accesorios. Pueden prepararse tabletas comprimidas comprimiendo en una máquina apropiada el ingrediente activo en forma fluida tal como polvo o gránulos, y mezclando opcionalmente con un aglutinante o

lubricante, un diluyente inerte, un lubricante, un agente dispersante o tensoactivo. Las tabletas moldeadas pueden prepararse moldeando en una máquina apropiada una mezcla del compuesto en polvo humedecida con un diluyente líquido inerte. las tabletas pueden estar opcionalmente recubiertas o ranuradas y pueden formularse de manera de proveer liberación lenta o controlada del ingrediente activo del mismo. Los presentes compuestos pueden administrarse por ejemplo en una forma apropiada para liberación inmediata o liberación demorada. Puede lograrse una liberación inmediata o una liberación demorada mediante el uso de composiciones farmacéuticas apropiadas que comprenden los presentes compuestos o particularmente en el caso de liberación demorada mediante el uso de dispositivos tales como implantos subcutáneos o bombas osmóticas. Los compuestos pueden formularse para administración oral con agentes liberadores o portadores que facilitan el transporte de las macromoléculas terapéuticas y compuestos altamente cargados a través de las membranas celulares, especialmente en el intestino delgado. Dichos agentes liberadores o portadores pueden inhibir además la degradación enzimática de los péptidos durante el pasaje a través del tracto gastrointestinal (GI) y/o la formulación puede incluir agentes adicionales que protegen contra dicha degradación. Los presentes compuestos pueden administrarse también liposomáticamente.

Ejemplos de composiciones para administración oral incluyen suspensiones que pueden contener por ejemplo, celulosa microcristalina para impartir volumen, ácido algínico o alginato de sodio como agentes de suspensión, metilcelulosa como mejorador de viscosidad y edulcorantes o agentes saborizantes tales como los que se conocen en la materia; y tabletas de liberación inmediata que pueden contener por ejemplo, celulosa microcristalina, fosfato dicálcico, almidón, estearato de magnesio y/o lactosa y/o excipientes,

aglutinantes, extendedores, desintegrantes, diluyentes, lubricantes tales como los conocidos en la materia. Los compuestos de la invención, pueden ser también liberados a través de la cavidad oral mediante administración sublingual y/o bucal. Ejemplos de formas que pueden usarse son tabletas moldeadas, tabletas comprimidas o tabletas secadas por congelación. Ejemplos de composiciones incluyen aquellas en las que se formulan los presentes compuestos con diluyentes de rápida disolución tales como manitol, lactosa, sucrosa y/o ciclodextrona. Asimismo, se incluyen en dichas formulaciones, excipientes de alto peso molecular, tales como celulosa (Avicel) o polietilen glicoles (PEG). Dichas formulaciones pueden incluir un excipiente para ayudar a la adhesión mucosal tal como hidroxi propil celulosa (HPC), hidroxi propil metil celulosa (HPMC), carboxi metil celulosa de sodio (SCMC), copolímero de anhídrido maleico (por ejemplo., Gantrez), y agentes para controlar la liberación tales como copolímero poliacrílico (pro ejemplo. Carbopol 934). Pueden agregarse también para faciliar la fabricación y uso lubricantes, deslizantes, saborizantes, agentes colorantes y estabilizadores.

Las formulaciones para administración parenteral incluyen soluciones acuosas y no acuosas estériles para inyección que pueden contener antioxidantes, buffer, bacteriostatos y solutos que convierten a la formulación en isotónica con la sangre del receptor determinado, y suspensiones estériles acuosas y no acuosas que pueden incluir agentes de suspensión y agentes espesantes. Las formulaciones pueden estar presentes en contenedores de dosis unitarias y de multidosis, por ejemplo, ampollas y frascos sellados y pueden almacenarse en estado congelado (liofilizado) que require únicamente la adición del portador líquido estéril, por ejemplo, en solución salina o agua para inyección, inmediatamente antes del uso. Pueden prepararse soluciones y suspensiones para inyección extemporánea a partir de polvos, gránulos y tabletas estériles de la

clase descrita previamente. Ejemplos de composiciones para administración parenteral incluyen soluciones o suspensiones inyectables que pueden contener por ejemplo, diluyentes o solventes apropiados no tóxicos parenteralmente aceptables tales como manitol, 1,3-butanodiol, agua, solución de Ringer, una solución isotónica de cloruro de sodio u otros agentes de suspensión y humectación o dispersantes apropiados, que incluyen mono- y diglicéridos sintéticos y ácidos grasos incluyendo ácido oleico o Cremafor. Un portador acuoso puede ser por ejemplo una solución buffer isotónica a un pH de desde aproximadamente 3.0 hasta aproximadamente 8.0, preferiblemente a un pH de desde aproximadamente 3.5 hasta aproximadamente 7.4, por ejemplo desde 3.5 a 6.0, por ejemplo desde 3.5 hasta aproximadamente 5.0. Buffers útiles incluyen citrato de sodio - ácido cítrico y fosfato de sodio - ácido fosfórico y buffers de acetato de sodio/ ácido acético. La composición no incluye preferiblemente agentes oxidantes y otros compuestos que se sabe que son perjudiciales para oxm y agonistas de oxm.

Los excipientes que pueden incluirse son por ejemplo, otras proteínas tales como albúmina de suero humano o preparaciones de plasma. Si se desea la composición farmacéutica puede contener también cantidades menores de sustancias auxiliares no tóxicas tales como agentes humectantes o emulsionantes, preservadores y agentes reguladores del pH y similares, por ejemplo, acetato de sodio o monolaurato de sorbitan.

Composiciones que son ejemplos para aerosol nasal o para administración por inhalación incluyen soluciones salinas que pueden contener por ejemplo alcohol bencílico u otros preservadores apropiados, promotores de absorción para mejorar la biodisponibilidad y/o otros agentes solubilizantes o dispersantes tales como los conocidos en la materia. Convenientemente las composiciones en aerosol para administración nasal o para inhalación del compuesto de la

invención, son liberadas en forma de presentación de rocío en aerosol desde un envase presurizado o un nebulizador, usando un propulsor apropiado, por ejemplo, diclorodifluor-metano, triclorofluormetano, diclorotetrafluoretano, dióxido de carbono u otro gas apropiado. En el caso de un aerosol presurizado, la unidad de dosificación puede determinarse para proveer una válvula para liberar una cantidad dosificada. Las cápsulas y cartuchos de por ejemplo, gelatina para ser usadas en un inhalador o insuflador pueden formularse de manera de contener una mezcla del compuesto en polvo y una base de polvo apropiada, por ejemplo, lactosa o almidón. En un ejemplo específico no limitativo, se mezcla un compuesto de la invención en forma de un aerosol desde una válvula de dosis medida, a través de un adaptador de aerosol conocido también como accionador.Opcionalmente se incluye también un estabilizador y/o partículas porosas para liberación profunda en el pulmón (por ejemplo, ver la Patente Norteamericana No. 6.447.743). Las formulaciones intranasales pueden incluir agentes de liberación para abrir reversiblemente la unión nasal hermética aumentado de este modo la permeabilidad del fármaco (ver por ejemplo, la Solicitud de Patente Norteamericana 10/322,266).

Las formulaciones para administración rectal pueden presentarse en forma de un enema de retención o un supositorio con los portadores usuales tales como manteca de cacao, ésteres glicéridos sintéticos o polietilen glicol. Dichos portadores son típicamente sólidos a temperaturas comúnes pero se licuan y/o disuelven en la cavidad rectal para liberar el fármaco. Las formulaciones para administración tópica en la boca, por ejemplo, bucalmente o sublingüalmente incluyen caramelos que comprenden el ingrediente activo en una base aromatizada, tal como sucrosa y acacia o atragacanto, y pastillas que comprenden el ingrediente activo en una base tal como gelatina y glicerina o

sucrosa y acacia. Ejemplos de composiciones para administración tópica incluyen un portador tópico tal como Plastibase (aceite mineral gelificado con polietileno).

Las formulaciones de dosis unitaria preferida, son aquellas que contienen una dosis eficaz tal como se indicó anteriormente, o una fracción apropiada de ésta, del ingrediente activo.

Cabe observar que además de los ingredientes mencionados particularmente anteriormente, las formulaciones de esta invención pueden incluir sus agentes convenionales en la materia que tienen en cuenta el tipo de formulación en cuestión, por ejemplo, aquellos que son apropiados para administración oral, pueden incluir agentes saborizantes.

Los compuestos de la invención son también administrados convenientemente en forma de sistemas de liberación demorada. Ejemplos apropiados de sistemas de liberación demorada de acuerdo con la invención incluyen materiales poliméricos adecuados, por ejemplo, matrices poliméricas impermeables en forma de artículos configurados, por ejemplo, películas o microcápsulas, materiales hidrofóbicos apropiados por ejemplo, en forma de una emulsión en un aceite aceptable; o resinas de intercambio iónico; y derivados escasamente solubles del compuesto de la invención, por ejemplo, una sal escasamente soluble. Los sistemas de liberación demorada pueden administrarse por vía oral, rectal, parenteral; intracisternal; intravaginal; intraperitoneal; tópica, por ejemplo, en forma de un polvo, ungüento, gel, gotas o parche transdérmico; bucal; o como un rocío oral o nasal.

Las preparaciones para administración puede formularse convenientemente para proporcionar una liberación controlada de los compuestos de la invención. Por ejemplo, las composiciones farmacéuticas pueden estar en forma de partículas que comprenden uno o más polímeros biodegradables, polisacáridos gelificables y/o polímeros bioadhesivos, polímeros anfifílicos,

agentes capaces de modificar las propiedades de interfase de las partículas del compuesto de la invención. Estas composiciones exhiben ciertas características de biocompatibilidad que permiten una liberación controlada de la sustancia activa. Ver Patente Norteramericana No. 5.700.486.

Un compuesto de la invención puede ser liberado mediante bombeo (ver Langer, Science 249:1527-1533, 1990; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201, 1987; Buchwald et al., Surgery 88:507, 1980; Saudek et al., N. Engl. J. Med. 321:574, 1989) o por infusiones subcutáneas continuas, por ejemplo, usando una mini-bomba. Puede emplearse también una solución en una bolsa intravenosa. El factor clave para seleccionar una dosis apropiada es el resultado obtenido medido por la disminución de peso corporal total o la relación de masa grasa a magra, o mediante otros criterios para medcir, controlar o prevenir la obesidad o para la prevención de trastornos relacionados con la obesidad, según lo estime apropiado el practicante. Otros sistemas de liberación controlada se discuten en la revisión de Langer, supra. En otro aspecto de la descripción, los compuestos de la invención se liberan mediante una bomba implantada, descrita por ejemplo en Patent No. 6.436.091; Patente Nortemericana No. 5,939,380; U.S. Patent No. 5.993.414.

Se usan dispositivos de infusión de fármaco implantables para proveer a los pacientes una dosis o infusión constante y a largo término de un fármaco o cualquier otro agente terapéutico. Esencialmente, dicho dispositivo puede categorizarse como activo o pasivo. Puede formularse un compuesto de la invención como una preparación de acción prolongada. Dicha formulaciónd e acción prolongada puede administrarse por implantación; por ejemplo, subcutáneamente o intramuscularmente o por inyección intramuscular. Por lo tanto, por ejemplo, los compuestos pueden formularse con materiales poliméricos o hidrofóbicos apropiados, por ejemplo, en forma de una emulsión en un aceite

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aceptable; o por resinas de intercambio iónico; o como derivados escasamente solubles, por ejemplo, una sal escasamente soluble.

Una cantidad terapéuticamente eficaz de un compuesto de la invención puede administrarse en forma de una dosis de pulso único, como una dosis de un bolo o pueden administrarse dosis pulsátiles a lo largo del tiempo. Por lo tanto en dosis pulsátiles, se provee la administración de un bolo de un compuesto de la invención seguido de un período de tiempo en el cual se administra el compuesto de la invención al sujeto, seguido de una administración de un segundo bolo. En ejemplos específicos no limitativos, las dosis pulsátiles de un compuesto de la invención se administran durante el curso de un día, durante el curso de una semana o durante el curso de un mes.

En una realización, se administra una cantidad terapéuticamente eficaz de un compuesto de la invención con una cantidad terapéuticamente eficaz de otro agente, por ejemplo, un agente adicional supresor de apetito, un agente reductor de ingestión de comida, un agente inhibidor de dipeptidil peptidasa IV (DPP-IV), un agente que disminuye la glucosa del plasma o un agente que altera los lípidos del plasma. Ejemplos específicos no limitativos de un supresor de apetito adicional incluye amfepramona (dietilpropion), fentermina, mazindol y fenilpropanolamina, fenfluramina, dexfenfluramina, sibutramina, rimonabant, y fluoxetina. Ejemplos no limitativos no específicos de inhibidores DPP-IV incluye Januvia (fosfato de sitagliptina), y Galvus (vildagliptina). El compuesto de la invención puede administrarse simultáneamente con el agente adicional o puede administrarse consecutivamente. Por lo tanto, en una realización, el compuesto de la invención se formula y administra con un agente adicional en forma de una sola dosis.

En otra realización, se administra una cantidad terapéuticamente eficaz de un compuesto de la invención en combinación con una cantidad terapéuticamente

eficaz de otro agente para el tratamiento de enfermedades distintas de la obesidad, por ejemplo diabetes, donde ejemplos específicos no limitativos de un agente terapéutico adicional son GLP-1 o un análogo de éste, exenatida y pramlintida.

Un compuesto de la invención puede administrarse siempre que se desee el efecto de, por ejemplo, supresión del apetito, disminución de la ingestión de comida o disminución de la ingestión calórica, o poco antes de cuando se desee el efecto deseado, tal como pero sin limitarlo a aproximadamente 10 minutos, aproximadamente 15 minutos, aproximadamente 30 minutos, aproximadamente 60 minutos, aproximadamente 90 minutos, aproximadamente 120 minutos, aproximadamente 4 horas, aproximadamente 8 horas, o aproximadamente 12 horas, antes del tiempo en el que se desee el efecto.

Puede administrarse un compuesto de la invención en combinación con cualquiera de los efectos que se deseen, por ejemplo, supresión del apetito, disminución de la ingestión de comida o disminución de la ingestión calórica, o poco tiempo antes de cuando se desea el efecto deseado, tal como pero sin limitarlo a aproximadamente aproximadamente 10 minutos, aproximadamente 15 minutos, aproximadamente 30 minutos, aproximadamente 60 minutos, aproximadamente 90 minutos, aproximadamente 120 minutos, aproximadamente 4 horas, aproximadamente 8 horas, o aproximadamente 12 horas, antes del tiempo en que se desea el efecto.

Dosis

La cantidad terapéuticamente eficaz de un compusto de la invención dependerá de la molécula utilizada del sujeto tratado, de la gravedad y tipo de enfermedad, y de la forma y vía de administración. Por ejemplo, una cantidad terapéuticamente eficaz de un compuesto de la invención puede variar en desde aproximadamente 0,01 µg por kilogramo (kg) de peso corporal hasta

aproximadamente 1 g por kg de peso corporal, por ejemplo, aproximadamente .0.1 µg hasta aproximadamente 5 mg por kg de peso corporal, o aproximadamente 1 µg hasta aproximadamente 1 mg por kg de peso corporal por día. Un compuesto de la invención puede administrarse a un sujeto a 0.5 hasta 200 picomoles (pmol) por kg de peso corporal, o aproximadamente 20 pmol por kg de peso corporal. Para compuestos especialmente activos o compuestos administrados por una vía especialmente eficiente, en un ejemplo específico, no limitativo, se administra un compuesto de la invención en una dosis de aproximadamente 1 nmol o más, 2 nmol o más, 5 nmol o más, o 10 nmol o más y la dosis del compuesto de la invención generalmente no es de más de 100 nmol, por ejemplo, la dosis es de 90 nmoles o menos, 80 nmoles o menos, 70 nmoles o menos, 60 nmoles o menos, 50 nmoles o menos, 40 nmoles o menos, 30 nmoles o menos, 20 nmoles o menos, o 10 nmoles o menos. Para un compuesto menos activo o un compuesto administrado por una vía menos eficiente, en otro ejemplo específico no limitativo, se administra un compuesto de la invención en una dosis de aproximadamente 100 nmol o más, 200 nmol o más, 300 nmol o más, 400 nmol o más, 500 nmol o más, 600 nmol o más, 700 nmol o más, 800 nmol o más, 900 nmol o más, o 1 µmol o más y la dosis del compuesto de la invención generalmente no es de más de 10 µmoles, por ejemplo, la dosis es de 9 µmoles o menos, 8 µmoles o menos, 7 µmoles o menos, 6 µmoles o menos, 5 µmoles o menos, 4 µmoles o menos, 3 µmoles o menos, 2 µmoles o menos, 1 µmol o menos. Por ejemplo, un rango de dosis puede comprender cualquier combinación de cualquiera de los límites de dosis inferiores especificados, con cualquiera de los límites de dosis superiores especificados. Por lo tanto, ejemplos de rangos de dosis no limitativos de compuestos de la invención están dentro del rango de desde 1 nmol a 1 µmol, desde1 a 900 nmols, o desde 1 a 800 nmoles. Para compuestos especialmente activos o compuestos administrados mediante una vía

especialmente eficiente la dosis puede ser de desde 1 nmol hasta 100 nmol, desde 2 a 80 nmoles, o desde 5 a 60 nmoles. Para un compuesto menos activo o un compuesto administrado por una vía menos eficiente, la dosis puede ser de desde 100 nmol a 10 μmol, from 200 nmol to 5 μmols, o desde 500 nmoles a 2 μmoles.

En un ejemplo no limitativo, específico, se administra desde aproximadamente 0.5 hasta aproximadamente 50 nmol de un compuesto de la invención, por ejemplo, se administra como inyección subcutánea desde aproximadamente 1 hasta aproximadamente 20 nmol, por ejemplo, aproximadamente 2 nmol. La dosis exacta es fácilmente determinada por un experto en la materia en base a la potencia del compuesto específico utilizado, la edad, el sexo y el estado fisiológico del sujeto.

En otro ejemplo específico no limitativo, se administra un compuesto de la invención a un sujeto en una dosis de aproximadamente 1 μg hasta aproximadamente 2 mg por dosis, aproximadamente una vez, aproximadamente dos veces, aproximadamente tres veces, o aproximadamente cuatro veces por día. Una cantidad terapéuticamente eficaz de un compuesto de la invención puede variar en desde aproximadamente 0.01 μg por kilogramo (kg) de peso corporal hasta aproximadamente 1 g por kg de peso corporal, por ejemplo, aproximadamente 0.1 μg hasta aproximadamente 5 mg por kg de peso corporal, o aproximadamente 5 μg hasta aproximadamente 1 mg por kg de peso corporal por día. Teniendo en cuenta que un análogo típico de oxintommudilina de la invención tiene un peso molecular de alrededor de 4500, un compuesto de la invención puede administrarse a un sujeto a 2.25 a 900 ng por kg de peso corporal, o aproximadamente 90 ng por kg de peso corporal. Para compuestos especialmente activos o compuestos administrados por una vía especialmente eficiente, en un ejemplo específico, no limitativo, se administra un compuesto de

la invención en una dosis de aproximadamente 4.5 μg o más, 9 μg o más, 22.5 μg o más, o 45 μg o más y la dosis del compuesto de la invención generalmente es de no más de 450μg, por ejemplo, la dosis es de 405μg o menos, 360μg o menos, 315μg o menos, 270μg o menos, 225μg o menos, 180μg o menos, 135μg o menos, 90μg o menos, o 45μg o menos. Para un compuesto menos específico o para un compuesto administrado por una vía menos eficiente, en otro ejemplo específico no limitativo, se administra un compuesto de la invención en una dosis de aproximadamente 450μg o más, 900 μg o más, 1350μg o más, 1800 μg o más, 2250μg o más, 2700μg o más, 3150μg o más, 3600μg o más, 4050μg o más, o 4500μg o más y la dosis del compuesto de la invención generalmente es de no más de 45000 μg , por ejemplo, la dosis es de 40500 μg o menos, 36000μg o menos, 31500 μg o menos, 27000 μg o menos, 22500 μg o menos, 18000 μg o menos, 13500 μg o menos, 9000 μg o menos, 45000 μg o menos. Por ejemplo, un rango de dosis puede comprender cualquier combinación de cualquiera de los límites de dosis especificados con cualquiera de los límites de dosis más altos específicados. Por lo tanto, ejemplos de rangos de dosis no limitativos de compuestos de la invención están dentro del rango de menos de 4.5μg a 4500μg, desde 4.5 a 4050μg , o desde 4.5 a 3600μg. Para compuestos especialmente activos o compuestos administrados por una vía especialmente eficiente la dosis puede ser de desde 4.5μg a 450μg, desde 9 a 360μg, o desde 22.5 a 270 μg. Para un compuesto menos activo o un compuesto administrado por una vía menos eficiente, la dosis puede ser de desde 450μg a 45000μg, desde 900μg a 22500μg, o desde 2250 a 9000μg.

Dosis apropiadas de compuestos de la invención incluyen también aquellas que dan como resultado una reducción de la ingestión calórica, de la ingestión de comida o del apetito, o del aumento en el gasto de energía que es equivalente a la reducción de la ingestión calórica, ingestión de comida o apetito, o el aumento

del gasto de energía causado por niveles de oxm que han sido observados en el hombre. Ejemplos de dosis incluyen pero no están limitadas a dosis que producen el efecto de mostrado cuando los niveles de oxm en el suero son de desde aproximadamente 800 pM hasta aproximadamente 1300 pM, o desde aproximadamente 900 pM hasta aproximadamente 1000 pM, o aproximadamente 950 pM.

Las dosis apropiadas de compuestos de la invención incluyen también aquellos que son equivalentes a niveles de oxm que se observan en sujetos que experimentan trastornos asociados con apetito reducido, por ejemplo, by pass del yeyuno ileo (Sarson *et al., Int J Obes*, 1981, 5:471–480; Holst *et al., Scand J Gastroenterol*, 1979, 14:205–207).

En un estudio de los efectos de oxintomodulina en la supresión de apetito y en la reducción de ingestión de comida en seres humanos (Cohen *et al.*, *J. Clin. Endocrinol. Metab.*, 2003, 88(10), 4696-4701) se halló que una infusión de oxintomodulina en voluntarios humanos a 3,0 pmol/kg.min durante 90 minutos condujo a una ingestión de energía *ad libitum* significativamente reducida (19.3 +/- 5.6%; P<0.01). La oxintomodulina total infusionada fue de 270 pmol/kg de peso corporal. La inmunoreactividad de tipo de oxintomodulina observada en la sangre de los sujetos se elevó hasta alrededor de 800 pmol/L durante la infusión.

En un estudio de los efectos de oxintomodulina sobre la pérdida de peso en seres humanos (Wynne *et al., Diabetes.*, 2005, 54(Aug), 2390-2395) se halló que inyecciones subcutáneas de oxintomodulina a voluntarios humanos dieron como resultado una reducción significativa del peso corporal. En un período de estudio de 28 días, en peso corporal del grupo de tratamiento se redujo en 2.3 ± 0.4 kg en el grupo de tratamiento en comparación con 0.5 ± 0.5 kg en el grupo de control (P = 0.0106). 1.8 mg (aproximadamente 400 nmol) de oxintomodulina se administraron tres veces por día 30 minutos antes de la comida. En promedio, el

grupo de tratamiento tuvo una pérdida de peso adicional de 0.45kg por semana. La ingestión de energía en el grupo de tratamiento se redujo significativamente de 170 ± 37 kcal (25 ± 5%) en la comida del estudio inicial dentro del período de estudio de 28 días (P = 0.0007) y en 250 ± 63 kcal (35 ± 9%) en la comida del día de estudio final durante el período de estudio de 28 días (P = 0.0023), sin ningún cambio en la aceptabilidad en cuanto al sabor de la comida subjetiva. El tratamiento con oxintomodulina dió como resultado una pérdida de peso y un cambio en los niveles de hormonas adiposas coincidente con una pérdida de tejido adiposo. El efecto anoréxico se mantuvo por un período de cuatro semanas.

Los compuestos de la invención demostraron ser más activos y/o menos duraderos que la oxintomodulina natural usada en estudios en seres humanos actualmente (Cohen *et al.* (2003) y Wynne *et al.* (2005) *Diabetes* 54(Aug), 2390-2395). La dosis requerida para un compuesto de la invención puede ser un poco inferior a la requerida para la oxintomodulina natural. La dosis de péptidos de la invención requerida para observar un efecto en seres humanos puede esperarse que sea inferior, por ejemplo, 2.5 veces, 200 veces, 400 veces, y 1-4000 veces menos que la dosis de la oxintomodulina natural. La magnitud de la potencia de los péptidos de la invención con comparación con el péptido de oxintomodulina natural permite también la administración de un compuesto de la invención con menos frecuencia que la requerida para la oxintomodulina natural.

La descripción se ilustra en los ejemplos siguientes no limitativos.

EJEMPLOS

Materiales y Métodos

Animales: Todos los procedimientos en animales fueron aprobados por British Home Office Animals (Scientific Procedures) Act 1986 (Project License number 70/5516). 6 ratones macho C57BL/6 y ratas macho Wistar se mantuvieron en

jaulas individuales bajo temperatura controlada (21-23 °C) con acceso *ad libitum* a comida standard (dieta RM1, SDS Ltd, Witham, Essex, UK) y agua. El ciclo de luz fue de 12 horas de luz y 12 horas de oscuridad con "apagado" a 07:00, luces prendidas a las 07:30, "oscureciendo" a las 19:00 con luces apagadas a las 19:30. Estos tiempos se fijaron en las instalaciones donde están los animales. Todos los animales se manipularon casi diariamente en un promedio de 9 día antes del primer estudio. Durante el período de aclimatización, los ratones recibieron dos inyecciones salinas, por lo menos con dos días de diferencia para aclimatarlos adicionalmente al procedimiento en los días de estudio. Se halló en las latas que minimizando la cantidad de inyecciones se obtenía una respuesta óptima, de modo que no se usaron inyecciones para aclimatación.

Inyecciones Intra-peritoneales (IP): Se administaron inyecciones IP a ratones a través de una jeringa de 0,5 ml con un aguja de calibre 29 (volumen máximo de la inyección 0.1 ml). El volumen máximo administrado por IP fue de 0,1 ml.

Inyecciones Subcutáneas (SC): Se administaron inyecciones SCIP a ratas a través de una jeringa de 05, ml con un aguja de calibre 29 (volumen máximo de la inyección 0.2 ml) en un volumen de 0,1 ml si se administraba en la piel del muslo, o 0,2 ml si se administraba en el cogote.

Protocolo de estudio: ratones C57BL/6 (20-35 g) fueron inyectados con el péptido bajo investigación después de 20 horas de ayuno. Se inyectaron ratas Wistar después de 24 horas de ayuno, típicamente se usaron 6 a 10 roedores por grupo experimental. Las inyecciones se administraron típicamente a 9:00. Se presentó una cantidad pre-pesada de comida inmediatamente después de la inyección. La comida restante se midió a intervalos regulares (por ejemplo, 1, 2, 3,4, 6, 8, 24, 32 y 48 horas después de la inyecicón) y se calculó la ingestión de comida.

Síntesis de Péptidos

Síntesis de péptidos

Se produjeron péptidos por síntesis en etapas de fase sólida (SPSS) usando la estrategia de protección N-terminal Fmoc. Se llevó a cabo un ensamblado de cadena con sintetizadores automáticos Applied Biosystems 431, 433 o Pioneer. Se usaron resinas de fase sólida con amino ácido C-temrinal pre-cargado en factoria o con un ligador amida según fuera apropiado. Se usaron los siguientes grupos protectores de cadena secundaria: Asn(Trt), Gln(Trt), Cys(Trt), His(Trt), Asp(tBu), Glu(tBu), Ser(tBu), Thr(tBu), Tyr(tBu), Arg(Pbf), Lys(Boc), Trp(Boc). En algunos casos, cuando se anticipaban dificultades en las síntesis, se usaron di-péptidos de oxazolidina pre-formados en lugar de los monómeros respectivos. Todos los productos químicos (de varios proveedores incluyendo Applied Biosystems, Merck Biosciences and AGCT) fueron de calidad de síntesis. Se empleó en todos los instrumentos monitoreo de retroalimentación para optimizar la síntesis.

Recuperación de péptidos

Después de la síntesis, los péptidos fueron disociados del soporte de resina de fase sólida y fueron desprotegidos en la cadena completamente secundaria. Esto se logro por tratamiento durante dos horas con ácido

trifluoracético (TFA) que contenía 4% de agua y 2,5% de tri-isopropilsilano para el barrido de los grupos protectores de cadena secundaria. Las soluciones de péptido-TFA se filtraron desde las resinas y los péptidos precipitaron con éter ter-butilmetílico (MTBE). Los péptidos fueron aislados por centrifugación, lavados en MTBE y secados al vacío.

Análisis y purificación de péptidos

Se disolvieron los péptidos en agua desionizada con adición de ácido acético cuando era necesario. Las soluciones de péptidos se clarificaron por centrifugación o filtración (Filtro de jeringa Whatman GD/X) antes del análisis y purificación.

Todos los productos de péptidos fueron analizados por HPLC de fase inversa en un instrumento Applied Biosystems BioCad usando una columna analítica Brownlee Aquapore RP300 C8 o Phenomenex Synergi Hydro C18. La purificación se llevó a cabo por HPLC de fase inversa usando columnas preparativas de los tipos anteriores. Se usaron gradientes de acetonitrilo - agua (con TFA como contra-ión) para la elución de los productos. Se llevó a cabo Electrofóresis de Zona Capilar (CZE) en péptidos crudos y purificados usando un instrumento Hewlett Packard 3DCE. La determinación del peso molecular se llevó a cabo en un espectrógrafo de masa MALDI –R.

Los péptidos purificados se secaron por congelación en frascos de vidrio de calidad farmacéutica (Adelphi Vials) y se cerraron al vacío.

Cadenas secundarias derivatizadas

Los péptidos que tenían cadena secundaria derivatizada con un grupo acilo o alquilo se prepararon por métodos convencionales.

Solubilidad de los péptidos derivatizados

Los polipéptidos derivatizados deberían estar completamente disueltos antes de la administración. Para lograr la solubilidad puede ser necesario disolver los polipéptidos en una pequeña cantidad de álcali diluido (por ejemplo, 50 µl 0.01 NaOH) y luego diluir los p´petidos en solución salina.

Inhibición de los experimentos de ingestión de comida.

Ejemplo 1 (ejemplo comparativo).

El efecto de alimentación de oxintomodulina natural (humana) se investigó por inyección intraperitoneal de 1400 nmoles/kg a grupos de ratones en ayunas. Se administró otro grupo de solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en comparación con la solución salina en la Figura 2. Debido a la actividad realtivamente baja de la oxintomodulina natural se administró una dosis elevada. Se observaron resultados menos significativos con dosis inferiores.

Ejemplo 2 (ejemplo comparativo)

El efecto de alimentación de oxintomodulina natural (humana) se investigó por inyección subcutánea de 1400 nmoles/kg a grupos de ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 6 horas se muestra en comparación con la de solución salina en la Figura 3. Puede observarse que incluso en una dosis elevada de 1400 mmoles/kg, oxintomodulina natural no es capaz de reducir la ingestión de comida en ratas en ayunas bajo estas condiciones. En dosis más bajas se observó la misma falta de eficacia.

Ejemplo 3.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados: PÉPTIDO NO: 178 [SEC. ID NO:178]; PÉPTIDO NO: 82

[SEC ID NO:82]; PÉPTIDO NO: 58 [SEC ID NO:58]; and PÉPTIDO NO: 52 [SEC ID NO:52]. Los análogos se administraron en una dosis de 10 (PÉPTIDO NO: 178 [SEC ID NO:178]) y 10 (PÉPTIDO NO: 82 [SEC ID NO:82]; PÉPTIDO NO: 58 [SEC ID NO:58]; y PÉPTIDO NO: 52 [SEC ID NO:52]) nmoles/kg por inyecicón subcutánea a grupos de ratas en ayunas. Otro grupo recibió solución salina (control). Se mostró la ingestión de comida acumualtiva promedio en el curso de 24 horas, en comparación con la de solución salina en las figuras 4 a 7. Los análogos demostraron una supresión de acción potente y prolongada de comida en comparación con el control salino. La supresión de ingestión de comida continua durante el período de 24 horas completo; es decir, que la ingestión de comida en el período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 4.

Se investigaron los efectos de la alimentación de los análogos siguientes de oxintomodulina: PÉPTIDO NO: 164 [SEC ID NO:164]; y PÉPTIDO NO: 167 [SEC ID NO:167]. Los análogos se administraron en una dosis de 4 y 5 mmoles/kg respectivamente por inyección subcutánea a grupos de ratas en ayunas. A un grupo se le administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 48 horas (PÉPTIDO NO: 164 [SEC ID NO:164]) y y 32 horas (PÉPTIDO NO: 167 [SEC ID NO:167]; se muestra en comparación con la solución salina de las figuras 8 y 9. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 48 horas completo; (PÉPTIDO NO: 164 [SEC ID NO:164]) y y 32 (PÉPTIDO NO: 167 [SEC ID NO:167];es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino y continúa permaneciendo por debajo de éste en las 24 horas siguientes (PÉPTIDO NO: 164

[SEC ID NO:164]) y 8 horas (PÉPTIDO NO: 167 [SEC ID NO:167];. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 5.

Se investigaron los efectos de alimentación de los análogos de oxintomodulina siguientes: PÉPTIDO NO: 100 [SEC ID NO:100]; y PÉPTIDO NO: 148 [SEC ID NO:148]. Los análogos se administraron en una dosis de 20 y 10 mmoles/kg respectivamente, por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se le administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en comparación con la solución salina de las figuras 10 y 11. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 24 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 6.

Se investigaron los efectos de la alimentación de los análogos de oxintomodulina siguientes: PÉPTIDO NO: 60 [SEC ID NO:60]; y PÉPTIDO NO: 94 [SEC ID NO:94]. Los análogos se administraron en una dosis de 100 y 5 mmoles/kg respectivamente, por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se le administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en comparación con la solución salina de las figuras 12 y 13. Los análogos demostraron una supresión de ingestión de comida potente y de acción

prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 24 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 7.

Se investigaron los efectos de la alimentación de los análogos de oxintomodulina siguientes: PÉPTIDO NO: 155 [SEC ID NO:155]. El análogo se administró en una dosis de 4 mmoles/kg, por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se le administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 32 horas se muestra en comparación con la solución salina de la figura 14. El análogo demuestra una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 32 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino y continua permaneciendo por debajo en las 8 horas siguientes. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 8.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados: PÉPTIDO NO: 142 [SEC ID NO:142]; PÉPTIDO NO: 184 [SEC ID NO:184]; y PÉPTIDO NO: 172 [SEC ID NO:172]. Los análogos se administraron en una dosis de 3 mmoles/kg, por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en

comparación con la solución salina de las figuras 15 a 17. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 24 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural

Ejemplo 9.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados: PÉPTIDO NO: 4 [SEC ID NO:4]; PÉPTIDO NO: 195 [SEC ID NO:195]; PÉPTIDO NO: 136 [SEC ID NO:136] y PEPTIDO NO: 108 [SEC ID NO: 108]. Los análogos se administraron en una dosis de 5, 800, 5 y 100 mmoles/kg, respectivamente, por inyección intraperitoneal a grupos de subcutánea a grupos de ratones en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en comparación con la solución salina de las figuras 18 a 21. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 24 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 10.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados: PÉPTIDO NO: 142 [SEC ID NO:142]; PÉPTIDO NO: 22 [SEC

ID NO:22]; PÉPTIDO NO: 153 [SEC ID NO:153]; y PÉPTIDO NO: 199 [SEC ID NO:199]. Los análogos se administraron a dosis de 3 nmoles/kg, 200 nmoles/kg (PÉPTIDO NO: 153 [SEC ID NO:153]), y 500 nmoles/kg (PÉPTIDO NO: 199 [SEC ID NO:199]) por inyección subcuténa a grupos de subcutánea a grupos de ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en comparación con la solución salina de las figuras 22 a 25. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 24 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 11.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados: PÉPTIDO NO: 210 [SEC ID NO:210]; PÉPTIDO NO: 211 [SEC ID NO:211]; PÉPTIDO NO: 213 [SEC ID NO:213]; y PÉPTIDO NO: 214 [SEC ID NO:214]. Los análogos se administraron a dosis de 20, 200, 400 y 400 nmoles/kg respectivamente, por inyección intraperitoneal a grupos de subcutánea a grupos de ratones en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 48 horas se muestra en comparación con la solución salina de las figuras 26 a 29. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 48 horas completo; es decir, que la

ingestión de comida en el primer período de 24 horas es menor que en el de control salino y continua siendo bajo en las siguientes 24 horas. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 12.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados: PÉPTIDO NO: 201 [SEC ID NO:201]; PÉPTIDO NO: 202. Los análogos se administraron a dosis de 5 nmoles/kg, por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 48 horas se muestra en comparación con la solución salina de las figuras 30 y 31. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 48 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino y continua siendo bajo en las siguientes 24 horas. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 13.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados PÉPTIDO NO: 203 [SEC ID NO:203]. Los análogos se administraron a dosis de 100 nmoles/kg por inyección subcutánea a ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 48 horas se muestra en comparación con la solución salina de la figura 32. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el

período de 48 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 14.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados PÉPTIDO NO: 204 [SEC ID NO:204]; y PÉPTIDO NO: 205 [SEC ID NO:205]. Los análogos se administraron a dosis de 5 nmoles/kg por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 32 horas se muestra en comparación con la solución salina de las figuras 33 y 34. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 32 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino y continua siendo bajo en las siguientes 8 horas. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 15.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados PÉPTIDO NO: 206 [SEC ID NO:206]; PÉPTIDO NO: 207 [SEC ID NO:207] y PÉPTIDO NO: 209 [SEC ID NO:209]. Los análogos se administraron a dosis de 80 nmoles/kg por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 48 horas se muestra en comparación con la solución salina de las figuras 35 a 37. Los análogos demostraron una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de

comida continúa durante el período de 48 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino y continua siendo bajo en las siguientes 24horas. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 16.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados PÉPTIDO NO: 215 [SEC ID NO:215];. El análogo se administró a dosis de 5 nmoles/kg por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en comparación con la solución salina de la figura 38. El análogo demostró una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 24 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 17.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados PÉPTIDO NO: 216 [SEC ID NO:216];. El análogo se administraró a dosis de 10 nmoles/kg por inyección subcutánea a grupos de ratas en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en comparación con la solución salina de la figura 39. El análogo demostró una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el

período de 24 horas completo; es decir, que la ingestión de comida en el primer período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 18.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados PÉPTIDO NO: 355 [SEC ID NO:355];. El análogo se adminsitró a dosis de 5 nmoles/kg por inyección subcutánea a grupos de ratones en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 4 horas se muestra en comparación con la solución salina de la figura 40. El análogo demostró una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 4 horas completo; es decir, que la ingestión de comida en el primer período de 4 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Ejemplo 19.

Los efectos de alimentación de los análogos siguientes de oxintomodulina fueron investigados PÉPTIDO NO: 130 [SEC ID NO:130];. El análogo se adminsitró a dosis de 20 nmoles/kg por inyección subcutánea a grupos de ratones en ayunas. A otro grupo se administró solución salina (control). La ingestión de comida acumulativa promedio en el curso de 24 horas se muestra en comparación con la solución salina de la figura 41. El análogo demostró una supresión de ingestión de comida potente y de acción prolongada en comparación con el control salino. La supresión de ingestión de comida continúa durante el período de 24 horas completo; es decir, que la ingestión de comida en el primer

período de 24 horas es menor que en el de control salino. También es más bajo que en el grupo de control tratado con oxintomodulina natural.

Se apreciará a través de todos los ejemplos anteriores, que los compuestos de la invención son capaces de inhibir la ingestión de comida en dosis marcadamente más bajas que las del péptido natural usado en los experimentos de comparación.

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<120> NUEVOS COMPUESTOS Y SUS EFECTOS SOBRE EL CONDUCTISMO DE LA ALIMENTACION

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Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 38

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 39

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln

1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 41

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser

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Lys Asn Asn Ile Ala
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
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<400> 43

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala

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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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<400> 46

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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<400> 47

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 48

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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<400> 50

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Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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<400> 51

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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<400> 52

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 53

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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<400> 54

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 56

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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<400> 58

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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<400> 68

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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<400> 70

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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<400> 71

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
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<400> 73

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 74

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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<400> 75

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
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<400> 76

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 78

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 81

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
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<400> 82

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 83

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<400> 84

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
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<400> 85

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

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<400> 86

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

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<400> 87

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
35

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Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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Lys Asn Asn Ile Ala
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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Lys Asn Asn Ile Ala
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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Xaa Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala Lys
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Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala Lys
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Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asn Asn Ile Ala Lys
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Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala Lys
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Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala Lys
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Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala Ala Ala Xaa
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala Ala Ala Xaa
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala Ala Ala Xaa
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Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asn Asn Ile Ala Ala Ala Xaa
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu

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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala Glu Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Xaa
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His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala Glu Ala Xaa
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Xaa Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu
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Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro
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Ser Lys Asn Asn Ile Ala Glu Ala
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asn Asn Ile Ala Glu Ala Xaa
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Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asp Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asp Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Lys Asp Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asp Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
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Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Xaa Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asp Asn Ile Ala
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Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
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Lys Asp Asn Ile Ala
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Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
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Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
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Lys Asp Asn Ile Ala
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Lys Asp Asn Ile Ala
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Lys Asp Asn Ile Ala
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Lys Asp Asn Ile Ala
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Lys Asp Asn Ile Ala
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Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Lys Asp Asn Ile Ala
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
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Lys Asp Asn Ile Ala
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Lys Asp Asn Ile Ala Lys
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Lys Asp Asn Ile Ala Lys
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Lys Asp Asn Ile Ala Lys
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Lys Asp Asn Ile Ala Lys
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<400> 245

Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Lys
35

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<223> Xaaen la posición 40 es Lys-miristoilo

<400> 246

Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Ala Ala Xaa
35 40

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<223> Xaaen la posición 40 es Lys-palmitoilo

<400> 247

Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Ala Ala Xaa
35 40

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<223> Xaaen la posición 40 es Lys-estearoilo

<400> 248

Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Ala Ala Xaa
35 40

<210> 249
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<400> 249

Xaa Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Ala Ala Xaa
35 40

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<400> 250

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Glu Ala Lys
35 40

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<223> Xaaen la posición 40 es Lys-miristoilo

<400> 251

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Glu Ala Xaa
35 40

<210> 252

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<400> 252

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Glu Ala Xaa
35 40

<210> 253
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<223> Xaaen la posición 40 es Lys-araquidoilo

<400> 253

Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Glu Ala Xaa
35 40

<210> 254
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<220>
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<400> 254

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 255
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<220>
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<400> 255

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 256
<211> 37
<212> PRT
<213> Artificial

<220>
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<400> 256

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 257
<211> 37
<212> PRT
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<220>
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<400> 257

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 258
<211> 37
<212> PRT
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<220>
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<400> 258

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 259
<211> 37
<212> PRT
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<220>
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<400> 259

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 260
<211> 37
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<220>
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<400> 260

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 261
<211> 37
<212> PRT
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<220>
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<400> 261

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asp Asn Ile Ala
35

<210> 262
<211> 37
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<220>
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<400> 262

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 263
<211> 37
<212> PRT
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<400> 263

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 264
<211> 37
<212> PRT

<213> Artificial

<220>
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<400> 264

His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 265
<211> 37
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<400> 265

His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asp Asn Ile Ala
35

<210> 266
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<400> 266

His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 267
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<400> 267

His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 268
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<220>
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<400> 268

His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln

1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 269
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<400> 269

His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 270
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<400> 270

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser

20 25 30

Lys Asp Asn Ile Ala
35

<210> 271
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<400> 271

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asp Asn Ile Ala
35

<210> 272
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<400> 272

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala

35

<210> 273
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<400> 273

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 274
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<400> 274

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

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<211> 37
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<400> 275

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 276
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<400> 276

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 277
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<400> 277

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 278
<211> 37
<212> PRT
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<220>
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<400> 278

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

<210> 279
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<400> 279

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala
35

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<400> 280

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Lys
35

<210> 281
<211> 38
<212> PRT
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<400> 281

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Lys
35

<210> 282
<211> 38
<212> PRT
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<400> 282

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asp Asn Ile Ala Lys
35

<210> 283
<211> 38
<212> PRT
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<400> 283

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Lys
35

<210> 284
<211> 38
<212> PRT
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<400> 284

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Lys
35

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<223> Xaaen la posición 40 es Lys-miristoilo

<400> 285

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser

20 25 30

Lys Asp Asn Ile Ala Ala Ala Xaa
35 40

<210> 286
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<223> Xaaen la posición 40 es Lys-palmitoilo

<400> 286

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Ala Ala Xaa
35 40

<210> 287
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<223> Xaaen la posición 40 es Lys-estearoilo

<400> 287

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Ala Ala Xaa
35 40

<210> 288
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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-araquidoilo

<400> 288

His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Ala Ala Xaa
35 40

<210> 289
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<212> PRT
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<400> 289

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Glu Ala Lys
35 40

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<400> 290

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Glu Ala Xaa
35 40

<210> 291
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<223> Xaaen la posición 40 es Lys-palmitoilo

<400> 291

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Glu Ala Xaa
35 40

<210> 292
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<400> 292

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asp Asn Ile Ala Glu Ala Xaa
35 40

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<400> 293

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 294
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<400> 294

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

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<400> 295

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

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<400> 296

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

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<400> 297

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 298
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<223> Xaa es D-His

<400> 298

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
35

<210> 299
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<400> 299

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

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<222> (1)..(1)
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<400> 300

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 301
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<222> (1)..(1)
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<400> 301

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 302
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<220>
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<222> (1)..(1)
<223> Xaa es D-His

<400> 302

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
35

<210> 303
<211> 37
<212> PRT

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<223> Xaa es D-His

<400> 303

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 304
<211> 37
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<400> 304

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<210> 305
<211> 37
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<223> Xaa es D-His

<400> 305

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 306
<211> 37
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<400> 306

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
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<210> 307
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<223> Xaa es D-His

<400> 307

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

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<223> Xaa es D-His

<400> 308

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 309
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<223> Xaa es D-His

<400> 309

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 310
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<223> Xaa es D-His

<400> 310

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 311
<211> 38
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<400> 311

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 312
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<223> Xaa es D-His

<400> 312

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 313
<211> 38
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<222> (1)..(1)
<223> Xaa es D-His

<400> 313

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 314
<211> 38
<212> PRT
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<222> (1)..(1)
<223> Xaa es D-His

<400> 314

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
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<210> 315
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<222> (1)..(1)
<223> Xaa es D-His

<400> 315

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
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<210> 316
<211> 40
<212> PRT
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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-miristoilo

<400> 316

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Ala Ala Xaa
35 40

<210> 317
<211> 40
<212> PRT
<213> Artificial

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<220>
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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-palmitoilo

<400> 317

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Ala Ala Xaa
35 40

<210> 318
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<213> Artificial

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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-estearoilo

<400> 318

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Ala Ala Xaa
35 40

<210> 319
<211> 40
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<220>
<221> MOD_RES
<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-araquidoilo

<400> 319

Xaa Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Ala Ala Xaa
35 40

<210> 320
<211> 40
<212> PRT
<213> Artificial

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<222> (1)..(1)
<223> Xaa es D-His

<400> 320

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Lys
35 40

<210> 321
<211> 40
<212> PRT
<213> Artificial

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<223> Xaa es D-His

<220>
<221> MOD_RES
<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-miristoilo

<400> 321

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Xaa
35 40

<210> 322
<211> 40
<212> PRT
<213> Artificial

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<222> (1)..(1)
<223> Xaa es D-His

<220>
<221> MOD_RES
<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-palmitoilo

<400> 322

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu

1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Xaa
35 40

<210> 323
<211> 40
<212> PRT
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<221> MOD_RES
<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-araquidoilo

<400> 323

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Xaa
35 40

<210> 324
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 324

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 325
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 325

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 326
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 326

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 327
<211> 37
<212> PRT
<213> Artificial

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<223> Análogo oxm

<400> 327

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 328
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 328

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 329
<211> 37
<212> PRT
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<220>
<223> Análogo oxm

<400> 329

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
35

<210> 330
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 330

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 331
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 331

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 332
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 332

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 333
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 333

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
35

<210> 334
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 334

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 335
<211> 37

<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 335

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 336
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 336

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 337
<211> 37
<212> PRT
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<220>

<223> Análogo oxm

<400> 337

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 338
<211> 37
<212> PRT
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<400> 338

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 339
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 339

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 340
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 340

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 341
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 341

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala
35

<210> 342
<211> 38
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 342

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 343
<211> 38
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 343

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 344
<211> 38
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 344

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 345
<211> 38
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 345

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 346
<211> 38
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 346

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 347
<211> 40
<212> PRT
<213> Artificial

<220>
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<220>
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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-miristoilo

<400> 347

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Ala Ala Xaa
35 40

<210> 348
<211> 40
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<220>
<221> MOD_RES
<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-palmitoilo

<400> 348

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Ala Ala Xaa
35 40

<210> 349
<211> 40
<212> PRT
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<220>
<223> Análogo oxm

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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-estearoilo

<400> 349

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Ala Ala Xaa
35 40

<210> 350
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<213> Artificial

<220>
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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-araquidoilo

<400> 350

His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Ala Ala Xaa
35 40

<210> 351
<211> 40
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<400> 351

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Lys
35 40

<210> 352
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<212> PRT
<213> Artificial

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<220>
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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-miristoilo

<400> 352

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Xaa
35 40

<210> 353
<211> 40
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<220>
<221> MOD_RES
<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-palmitoilo

<400> 353

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Xaa
35 40

<210> 354
<211> 40
<212> PRT
<213> Artificial

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<222> (40)..(40)
<223> Xaaen la posición 40 es Lys-araquidoilo

<400> 354

His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Glu Ala Xaa
35 40

<210> 355
<211> 38
<212> PRT
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<222> (1)..(1)
<223> Xaa es D-His

<400> 355

Xaa Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu
1 5 10 15

Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Lys Asn Asn Ile Ala Lys
35

<210> 356
<211> 37
<212> PRT
<213> Artificial

<220>
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<222> (1)..(37)
<223> Xaa es tal como se ha definido en la reivindicación 1

<400> 356

Xaa Xaa Xaa Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Leu Xaa Xaa Xaa Xaa Xaa Xaa
20 25 30

Lys Asn Asn Ile Ala
35

<210> 357
<211> 37
<212> PRT
<213> Homo sapiens

<400> 357

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 358
<211> 37
<212> PRT
<213> Bos sp.

<400> 358

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Lys Asn Asn Ile Ala
35

<210> 359
<211> 37

<212> PRT
<213> Artificial

<220>
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<222> (1)..(37)
<223> Xaa es tal como se ha definido en la reivindicación 2

<400> 359

Xaa Xaa Xaa Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Leu Xaa Xaa Xaa Xaa Xaa Xaa
20 25 30

Lys Asn Asn Ile Ala
35

<210> 360
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<220>
<221> VARIANT
<222> (1)..(37)
<223> Xaa es tal como se ha definido en la reivindicación 3

<400> 360

Xaa Xaa Xaa Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Leu Xaa Xaa Xaa Xaa Xaa Xaa
20 25 30

Lys Asn Asn Ile Ala
35

<210> 361
<211> 37
<212> PRT
<213> Artificial

<220>
<223> Análogo oxm

<220>
<221> VARIANT
<222> (1)..(37)
<223> Xaa es tal como se ha definido en la reivindicación 4

<400> 361

Xaa Xaa Xaa Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Leu Xaa Xaa Xaa Xaa Xaa Xaa
20 25 30

Lys Asn Asn Ile Ala
35

REIVINDICACIONES

Habiendo así especialmente descrito y determinado la naturaleza de la presente invención y la forma cómo la misma ha de ser llevada a la práctica se declara reivindicar como de propiedad y derecho exclusivo:

1. Un péptido que comprende la secuencia de amino ácido:

Xaa1 Xaa2 Xaa3 Gly4 Thr5 Phe6 Thr7 Ser8 Asp9 Tyr10 Ser11 Lys12 Tyr13 Leu14

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Trp25 Leu26

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 Lys33 Asn34 Asn35 Ile36 Ala37;

donde:

Xaa1 es His1 o D-His1,

Xaa2 es Ser2 o Ala2,

Xaa3 es Gln3 o Asp3;

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

o Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24;

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 es:

Met27 Asn28 Thr29 Lys30 Arg31 Asn32,

Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,

o Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

o un péptido tal como se indicó anteriormente en el cual el residuo Asn34 es reemplazado con Asp34;

o un péptido tal como se indicó anteriormente en el cual Xaa3 es Glu3;

con la condición de que si
Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es
Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24,

entonces Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 no es
Met27 Asn28 Thr29 Lys30 Arg31 Asn32.

(SEC ID NO: 356).

2. Un péptido tal como se ha reivindicado en la reivindicación 1, donde

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
o Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24
(SEC ID NO: 359).

3. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 2, donde

Xaa1 Xaa2 Xaa3 es

His1 Ser2 Gln3, o.

D-His1 Ser2 Gln3, o

D-His1 Ala2 Gln3, o

D-His1 Ala2 Asp3

(SEC ID NO: 360).

4. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 3, donde

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 es:

Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,

o Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

(SEC ID NO: 361).

5. Un péptido tal como se ha reivindicado en la reivindicación 1 que tiene una secuencia de amino ácido seleccionada del grupo que consiste en:

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 1)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 2)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 3)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 4)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 5)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 6)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 7)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 8)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 9

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 10)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 11)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 12)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 13)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 14)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 15)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 16)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 17)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 18)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 19)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 20)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 21)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 22)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 23)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 24)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 25)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 26)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 27)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 28)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 29)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 30)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 31)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 32)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 33)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 34)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 35)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 36)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 37)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 38)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 39)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 40)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 41)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 42)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 43)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 44)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 45)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 46)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 47)

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 48)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 49)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 50)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 51)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 52)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 53)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 54)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 55)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 56)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 57)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 58)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 59

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 60

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 61

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 62)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 63)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 64)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 65)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 66)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 67)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 68)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 69)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 70)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 71)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 72)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 73)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 74)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 75)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 76)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 77)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 78)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 79)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 80)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 81)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 82)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 83)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 84)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 85)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 86)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 87)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 88)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 89)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 90)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 91)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 92)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 93)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 94)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 95)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 96)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 97)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 98)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 99)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 100)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 101)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 102)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 103)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 104)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 105)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 106)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 107)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 108)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 109)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 110)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 111)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 112)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 113)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 114)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 115)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 116)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 117)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 118)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 119)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 120)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 121)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 122)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 123)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 124)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 125)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 126)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 127)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 128)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 129)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 130)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 131)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 132)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 133)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 134)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 135)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 136)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 137)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 138)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 139)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 140)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 141)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 142)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 143)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 144)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 145)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 146)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 147)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 148)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 149)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 150)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 151)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 152)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 153)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 154)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 155)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 156)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 157)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 158)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 159)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 160)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 161)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 162)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 163)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 164)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 165)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 166)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 167)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 168)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 169)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 170)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 171)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 172)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 173)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 174)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 175)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 176)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 177)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 178)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 179)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 180)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 181)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 182)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 183)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 184)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 185)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 186)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 187)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 188)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 189)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 190)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 191)

D-HisAla Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 192)

6. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 5, donde el péptido tiene una fracción de extensión adicional de secuencia -A-B-C, donde:

A está ausente o 1, 2, 3 o 4 residuos Ala o 1, 2, 3 o 4 residuos Glu

B está ausente o 1, 2, 3 o 4 residuos Ala o 1, 2, 3 o 4 residuos Glu

con la condición de que A y B no comprendan ambos, residuos Ala, y que A y B no comprendan ambos, residuos Glu; y

C es Lys, o Lys con un ácido seleccionado de ácido cáprico, ácido láurico, ácido mirístico, ácido palmítico, ácido esteárico, y ácido araquídico, unido a través de su grupo –COOH al grupo $-NH_2$ de la cadena secundaria Lys por medio de un enlace peptídico.

7. Un péptido tal como se ha reivindicado en la reivindicación 6, donde A o B o ambos A y B están ausentes.

8. Un péptido tal como se ha reivindicado en la reivindicación 6, donde A es un residuo Glu, y B es un residuo Ala.

9. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 6 a 8, donde C es un residuo Lys.

10. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 6 a 8, donde:

- C es un residuo Lys con ácido láurico unido a través de su grupo –COOH al grupo -NH2 de la cadena secundaria Lys por medio de un enlace peptídico..
- C es un residuo Lys con ácido miristico unido a través de su grupo –COOH al grupo -NH2 de la cadena secundaria Lys por medio de un enlace peptídico.
- C es un residuo Lys con ácido palmítico unido a través de su grupo –COOH al grupo -NH2 de la cadena secundaria Lys por medio de un enlace peptídico.
- C es un residuo Lys con ácido esteárico unido a través de su grupo –COOH al grupo -NH2 de la cadena secundaria Lys por medio de un enlace peptídico.
- C es un residuo Lys con ácido unido a través de su grupo –COOH al grupo -NH2 de la cadena secundaria Lys por medio de un enlace peptídico.
- C es un residuo Lys con un ácido cáprico unido a través de su grupo –COOH al grupo -NH2 de la cadena secundaria Lys por medio de un enlace peptídico.

11. Un péptido de acuerdo con la reivindicación 6 que tiene la secuencia de estructura seleccionada del grupo que consiste en:

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 201)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 202)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala Lys (SEC ID NO: 203)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 204)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 205)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-miristoilo (SEC ID NO: 206)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-palmitoilo (SEC ID NO: 207)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-estearoilo (SEC ID NO: 208)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-arachidoilo (SEC ID NO: 209)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys (SEC ID NO: 210)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-miristoilo (SEC ID NO: 211)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-miristoilo (SEC ID NO: 212)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-palmitoilo (SEC ID NO: 213)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-araquídoilo (SEC ID NO: 214)

12. Un péptido de acuerdo con la reivindicación 1 que tiene la secuencia de estructura seleccionada del grupo que consiste en:

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 215)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 216)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 217)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 218)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 219)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 220)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 221)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEC ID NO: 222)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 223)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 224)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 225)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEC ID NO: 226)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 227)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 228)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 229)

D-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 230)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 231)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEC ID NO: 232)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 233)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 234)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 235)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 236)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 237)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 238)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 239)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 240)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEC ID NO: 241)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEC ID NO: 242)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala Lys (SEC ID NO: 243)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEC ID NO: 244)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEC ID NO: 245)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-miristoilo (SEC ID NO: 246)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-palmitoilo (SEC ID NO: 247)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-estearoilo (SEC ID NO: 248)

D-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-araquídoilo (SEC ID NO: 249)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys (SEC ID NO: 250)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-miristoilo (SEC ID NO: 251)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-palmitoilo (SEC ID NO: 252)

D-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-araquídoilo (SEC ID NO: 253)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 254)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 255)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 256)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 257)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 258)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 259)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 260)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEC ID NO: 261)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 262)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 263)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 264)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEC ID NO: 265)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 266)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 267)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 268)

L-His Ala Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 269)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 270)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala (SEC ID NO: 271)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 272)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 273)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 274)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 275)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 276)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 277)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 278)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala (SEC ID NO: 279)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEC ID NO: 280)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEC ID NO: 281)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asp Asn Ile Ala Lys (SEC ID NO: 282)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEC ID NO: 283)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Lys (SEC ID NO: 284)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-miristoilo (SEC ID NO: 285)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-palmitoilo (SEC ID NO: 286)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-estearoilo (SEC ID NO: 287)

L-His Ala Asp Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asp Asn Ile Ala Ala Ala Lys-araquidoilo (SEC ID NO: 288)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys (SEC ID NO: 289)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-miristoilo (SEC ID NO: 290)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-palmitoilo (SEC ID NO: 291)

L-His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asp Asn Ile Ala Glu Ala Lys-araquidoilo (SEC ID NO: 292).

13. Un péptido de acuerdo con la reivindicación 1 que tiene la secuencia de estructura seleccionada del grupo que comprende:

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 293)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 294)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 295)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 296)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 297)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 298)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 299)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 300)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 301)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 302)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 303)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 304)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 305)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 306)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 307)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 308)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 309)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 310)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 311)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 312)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala Lys (SEC ID NO: 313)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 314)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 315)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-miristoilo (SEC ID NO: 316)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-palmitoilo (SEC ID NO: 317)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-estearoilo (SEC ID NO: 318)

D-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-araquidoilo (SEC ID NO: 319)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys (SEC ID NO: 320)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-miristoilo (SEC ID NO: 321)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-palmitoilo (SEC ID NO: 322)

D-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-araquidoilo (SEC ID NO: 323)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 324)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 325)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 326)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 327)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 328)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 329)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 330)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 331)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 332)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala (SEC ID NO: 333)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 334)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 335)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 336)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 337)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 338)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 339)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 340)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala (SEC ID NO: 341)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 342)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 343)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Ile Val Lys Tyr Phe Ile Gln Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala Lys (SEC ID NO: 344)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 345)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Gln Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Lys (SEC ID NO: 346)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-miristoilo (SEC ID NO: 347)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-palmitoilo (SEC ID NO: 348)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-estearoilo (SEC ID NO: 349)

L-His Ala Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Ile Gln Trp Leu Lys Asn Gly Gly Pro Ser Lys Asn Asn Ile Ala Ala Ala Lys-araquidoilo (SEC ID NO: 350)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys (SEC ID NO: 351)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-miristoilo (SEC ID NO: 352)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-palmitoilo (SEC ID NO: 353)

L-His Ser Glu Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Gln Trp Leu Lys Asn Ala Gly Pro Ser Lys Asn Asn Ile Ala Glu Ala Lys-araquidoilo (SEC ID NO: 354)

14. Una composición farmacéutica que comprende un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 13 y uno o más portadores farmacéuticamente aceptables.

15. Una composición farmacéutica tal como se ha reivindicado en la reivindicación 14 la cual es para administración periférica.

16. Una composición farmacéutica tal como se ha reivindicado en las reivindicaciones 14 o 15 la cual es para administración subcutánea, intravenosa, intramuscular, intranasal, transdérmica, transmucosal, oral, bucal, sublingual o a través de los pulmones.

17. Uso de un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 13 para la manufactura de un medicamento para la prevención o tratamiento de la obesidad.

18. Uso de un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 13 para la manufactura de un medicamento para la prevención o tratamiento de diabetes o una co-morbilidad de la obesidad.

19. Uso de un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 13 para la manufactura de un medicamento para reducir el apetito en un sujeto, reducir la ingestión de comida en un sujeto o reducir la ingestión de calorías en un sujeto, reducir el peso corporal en un sujeto, reducir el aumento de peso corporal en un sujeto o aumentar el gasto de energía en un sujeto.

20. .El uso tal como se ha reivindicado en cualquiera de las reivindicaciones 17 a 19, donde el péptido es administrado periféricamente.

21. El uso tal como se ha reivindicado en cualquiera de las reivindicaciones 17 a 20, donde el péptido es administrado en forma subcutánea, intravenosa, intramuscular, intranasal, transdérmica, transmucosal, oral, bucal, sublingual o través de los pulmones.

22. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 13 para ser usado como medicamento.

23. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 13 para ser usado como medicamento para la prevención o tratamiento de la obesidad.

24. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 13 para ser usado como medicamento para la prevención o tratamiento de la diabetes o de una co-morbilidad de la obesidad.

25. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 1 a 13 para ser usado como medicamento para reducir el apetito en un sujeto, reducir la ingestión de comida en un sujeto o reducir la ingestión de calorías en un sujeto, reducir el peso corporal en un sujeto, reducir el aumento de peso corporal en un sujeto o aumentar el gasto de energía en un sujeto.

26. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 22 a 25, donde la composición peptídica es administrada periféricamente.

27. Un péptido tal como se ha reivindicado en cualquiera de las reivindicaciones 22 a 26, donde el péptido es administrado en forma subcutánea, intravenosa, intramuscular, intranasal, transdérmica, transmucosal, oral, bucal, sublingual o través de los pulmones.

28. Un método para el tratamiento o prevención de la obesidad en un sujeto que lo necesita, que comprende administrar a un sujeto un péptido de acuerdo con cualquiera de las reivindicaciones 1 a 13 o una composición farmacéutica de acuerdo con cualquiera de las reivindicaciones 14 a 16.

29. Un método para el tratamiento o prevención de la diabetes o una co-morbilidad de la obesidad en un sujeto que lo necesita que comprende administrar a un sujeto un péptido de acuerdo con cualquiera de las reivindicaciones 1 a 13 o una composición farmacéutica de acuerdo con cualquiera de las reivindicaciones 14 a 16.

30. Un método para reducir el apetito en un sujeto, reducir la ingestión de comida en un sujeto o reducir la ingestión de calorías en un sujeto, reducir el peso corporal en un sujeto, reducir el aumento de peso corporal en un sujeto o aumentar el gasto de energía en un sujeto que lo necesita, que comprende administrar al sujeto un péptido de acuerdo con cualquiera de las reivindicaciones

1 a 13 o una composición farmacéutica de acuerdo con cualquiera de las reivindicaciones 14 a 16.

31. Un método que produce pérdida de peso o previene el aumento de peso con propósitos cosméticos que comprende administrar a un sujeto un péptido de acuerdo con cualquiera de las reivindicaciones 1 a 13 o una composición farmacéutica de acuerdo con las reivindicaciones 14 a16.

32. Un método tal como se ha reivindicado en cualquiera de las reivindicaciones 28 a 31, donde el sujeto padece sobrepeso.

33. Un método tal como se ha reivindicado en cualquiera de las reivindicaciones 28 a 32, donde el sujeto es obeso.

34. Un método tal como se ha reivindicado en cualquiera de las reivindicaciones 28 a 33, donde el sujeto es diabético.

35. El método de cualquiera de las reivindicaciones 28 a 34, donde el péptido o la composición farmacéutica es administrado en forma periférica.

36. El método de cualquiera de las reivindicaciones 28 a 35, donde el péptido o la composición farmacéutica es administrado en forma subcutánea, intravenosa, intramuscular, intranasal, transdérmica, transmucosal, oral, bucal, sublingual o a través de los pulmones.

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RESUMEN

NUEVOS COMPUESTOS Y SUS EFECTOS SOBRE EL CONDUCTISMO DE LA ALIMENTACIÓN

La invención provee un péptido que comprende la secuencia de amino ácido que se da a continuación, conjuntamente con los usos del péptido y los métodos asociados con los mismos. El péptido es particularmente útil como supresor del apetito y para el tratamiento de la obesidad.

Xaa1 Xaa2 Xaa3 Gly4 Thr5 Phe6 Thr7 Ser8 Asp9 Tyr10 Ser11 Lys12 Tyr13 Leu14
Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 Trp25 Leu26
Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 Lys33 Asn34 Asn35 Ile36 Ala37;
donde:

Xaa1 es His1 o D-His1,

Xaa2 es Ser2 o Ala2,

Xaa3 es Gln3 o Asp3;

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es:

Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,
Glu15 Glu16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,
Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Glu16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Leu18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Leu23 Gln24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Glu24,

Glu15 Gln16 Glu17 Ile18 Val19 Lys20 Tyr21 Phe22 Ile23 Gln24,

o Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24;

Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 es:

Met27 Asn28 Thr29 Lys30 Arg31 Asn32,

Lys27 Asn28 Ala29 Gly30 Pro31 Ser32,

o Lys27 Asn28 Gly29 Gly30 Pro31 Ser32

o un péptido tal como se indicó anteriormente en el cual el residuo Asn34 es reemplazado con Asp34;

o un péptido tal como se indicó anteriormente en el cual Xaa3 es Glu3;

con la condición de que si

Xaa15 Xaa16 Xaa17 Xaa18 Xaa19 Xaa20 Xaa21 Xaa22 Xaa23 Xaa24 es

Asp15 Ser16 Arg17 Arg18 Ala19 Gln20 Asp21 Phe22 Val23 Gln24,

entonces Xaa27 Xaa28 Xaa29 Xaa30 Xaa31 Xaa32 no es

Met27 Asn28 Thr29 Lys30 Arg31 Asn32

Figure 1

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
PEPTIDE NO: 1	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 2	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 3	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 4	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 5	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 6	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 7	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 8	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 9	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 10	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 11	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 12	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 13	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 14	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 15	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 16	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 17	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 18	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 19	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 20	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 21	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 22	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 23	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 24	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 25	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 26	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 27	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 28	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 29	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 30	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 31	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 32	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 33	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 34	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 35	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 36	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 37	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 38	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 39	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 40	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 41	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 42	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 43	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 44	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 45	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 46	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 47	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 48	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 49	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 50	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
PEPTIDE NO: 51	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 52	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 53	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 54	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 55	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 56	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 57	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 58	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 59	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 60	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 61	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 62	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 63	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 64	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 65	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 66	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 67	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 68	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 69	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 70	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 71	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 72	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 73	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 74	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 75	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 76	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 77	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 78	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 79	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 80	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 81	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 82	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 83	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 84	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 85	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 86	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 87	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 88	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 89	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 90	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 91	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 92	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 93	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 94	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 95	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 96	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 97	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 98	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 99	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 100	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala

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PEPTIDE NO: 101	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 102	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 103	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 104	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 105	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 106	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 107	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 108	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 109	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 110	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 111	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 112	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 113	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 114	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 115	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 116	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 117	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 118	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 119	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 120	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 121	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 122	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 123	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 124	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 125	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 126	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 127	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 128	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 129	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 130	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 131	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 132	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 133	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 134	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 135	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 136	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 137	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 138	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 139	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 140	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 141	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 142	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 143	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 144	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 145	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 146	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 147	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 148	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 149	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 150	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Met	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala

SOLICITUD DE PATENTE DE INVENCION

09162877

TOMO 4/4

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
PEPTIDE NO: 151	D-His	Aib	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 152	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 153	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 154	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 155	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 156	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 157	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Ile	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 158	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 159	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 160	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 161	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 162	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 163	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 164	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 165	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 166	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 167	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 168	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 169	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 170	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 171	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 172	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 173	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 174	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 175	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 176	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 177	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 178	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 179	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 180	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 181	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 182	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 183	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 184	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 185	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 186	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 187	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 188	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 189	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Thr	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 190	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 191	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 192	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 193	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 194	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 195	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 196	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 197	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 198	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 199	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala
PEPTIDE NO: 200	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Ser	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
PEPTIDE NO: 201	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Ala	Lys-myristoyl
PEPTIDE NO: 202	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Ala	Lys-palmitoyl
PEPTIDE NO: 203	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Ala	Lys-stearoyl
PEPTIDE NO: 204	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Ala	Lys-arachidoyl
PEPTIDE NO: 205	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 206	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-myristoyl
PEPTIDE NO: 207	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-palmitoyl
PEPTIDE NO: 208	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-arachidoyl
PEPTIDE NO: 209	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Ala	Lys
PEPTIDE NO: 210	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Ala	Lys-myristoyl
PEPTIDE NO: 211	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-myristoyl
PEPTIDE NO: 212	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-palmitoyl
PEPTIDE NO: 213	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-arachidoyl
PEPTIDE NO: 214	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 215	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Ala	Lys
PEPTIDE NO: 216	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys	Ala	Lys
PEPTIDE NO: 217	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 218	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 219	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 220	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 221	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 222	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 223	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 224	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 225	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 226	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 227	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 228	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 229	D-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 230	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 231	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 232	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 233	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 234	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 235	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 236	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 237	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 238	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 239	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 240	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 241	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 242	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 243	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 244	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 245	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 246	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 247	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 248	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 249	D-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 250	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys

PEPTIDE NO: 251	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-myristoyl
PEPTIDE NO: 252	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-palmitoyl
PEPTIDE NO: 253	D-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-arachidoyl
PEPTIDE NO: 254	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 255	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 256	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 257	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 258	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 259	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 260	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 261	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 262	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 263	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 264	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 265	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 266	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 267	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 268	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 269	L-His	Ala	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 270	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 271	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 272	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 273	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 274	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 275	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 276	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 277	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 278	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 279	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala			
PEPTIDE NO: 280	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Lys		
PEPTIDE NO: 281	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Lys		
PEPTIDE NO: 282	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asp	Asn	Ile	Ala	Lys		
PEPTIDE NO: 283	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Lys		
PEPTIDE NO: 284	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Lys		
PEPTIDE NO: 285	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Ala	Ala	Lys-myristoyl
PEPTIDE NO: 286	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Ala	Ala	Lys-palmitoyl
PEPTIDE NO: 287	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Ala	Ala	Lys-stearoyl
PEPTIDE NO: 288	L-His	Ala	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Ala	Ala	Lys-arachidoyl
PEPTIDE NO: 289	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 290	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-myristoyl
PEPTIDE NO: 291	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-palmitoyl
PEPTIDE NO: 292	L-His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asp	Asn	Ile	Ala	Glu	Ala	Lys-arachidoyl
PEPTIDE NO: 293	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 294	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 295	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 296	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 297	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 298	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 299	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 300	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			

PEPTIDE NO: 301	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 302	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 303	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 304	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 305	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 306	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 307	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 308	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 309	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 310	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 311	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 312	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 313	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 314	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 315	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 316	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Ala	Ala	Lys-myristoyl
PEPTIDE NO: 317	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Ala	Ala	Lys-palmitoyl
PEPTIDE NO: 318	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Ala	Ala	Lys-stearoyl
PEPTIDE NO: 319	D-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Ala	Ala	Lys-arachidoyl
PEPTIDE NO: 320	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys
PEPTIDE NO: 321	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-myristoyl
PEPTIDE NO: 322	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-palmitoyl
PEPTIDE NO: 323	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-arachidoyl
PEPTIDE NO: 324	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 325	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 326	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 327	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 328	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 329	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 330	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 331	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 332	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 333	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 334	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 335	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 336	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 337	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 338	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 339	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 340	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 341	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser	Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala			
PEPTIDE NO: 342	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 343	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 344	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Met	Asn	Thr	Lys	Arg	Asn	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 345	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 346	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Gln	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		
PEPTIDE NO: 347	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Ala	Ala	Lys-myristoyl
PEPTIDE NO: 348	L-His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Ala	Ala	Lys-palmitoyl
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PEPTIDE NO: 354	L-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Leu	Val	Lys	Tyr	Phe	Leu	Gln	Trp	Leu	Lys	Asn	Ala	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Glu	Ala	Lys-arachidoyl
PEPTIDE NO: 355	D-His	Ser	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Glu	Glu	Glu	Ile	Val	Lys	Tyr	Phe	Ile	Gln	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Lys	Asn	Asn	Ile	Ala	Lys		

Figure 2

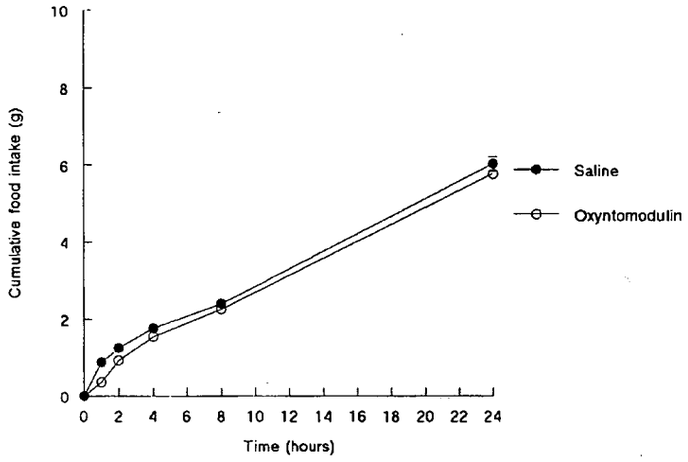


Figure 3.

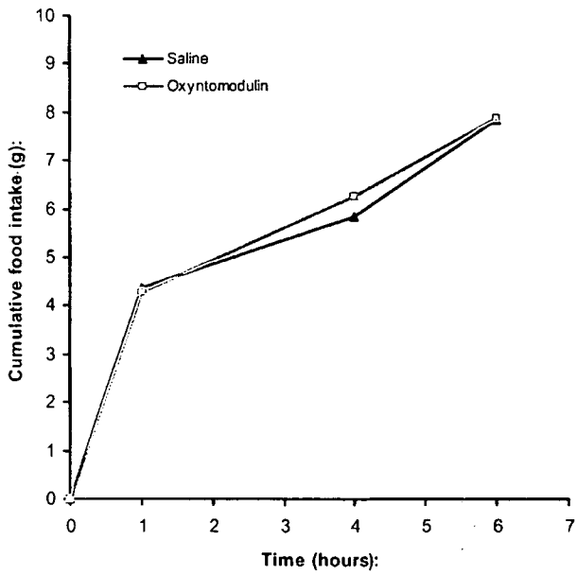


Figure 4

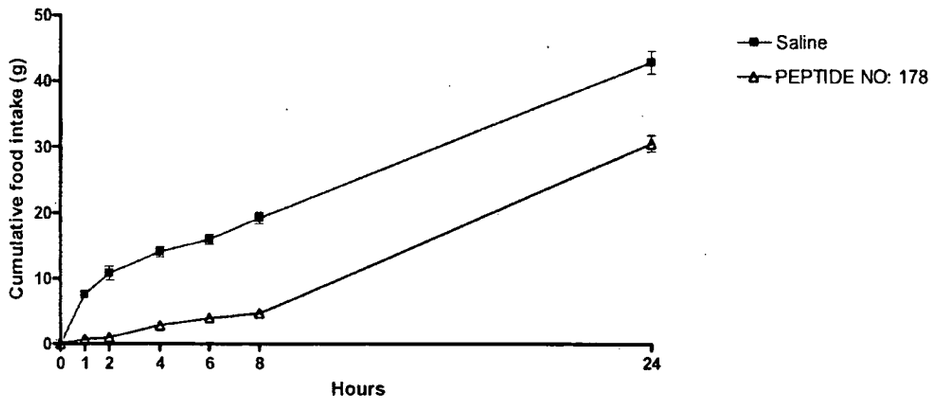


Figure 5

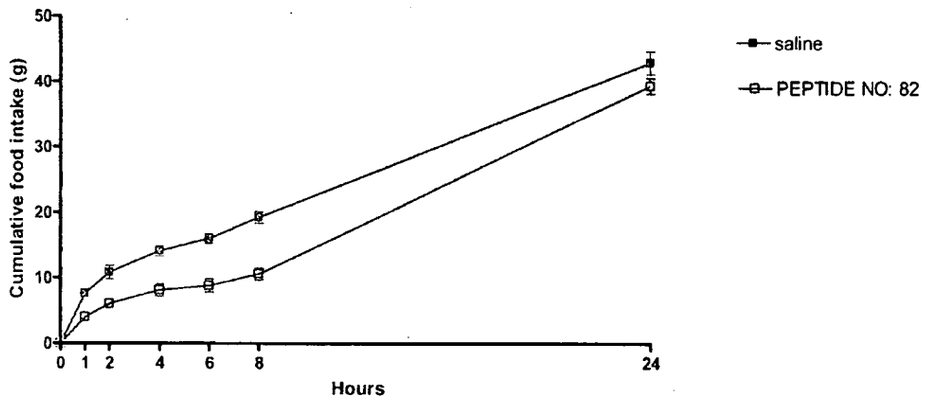


Figure 6

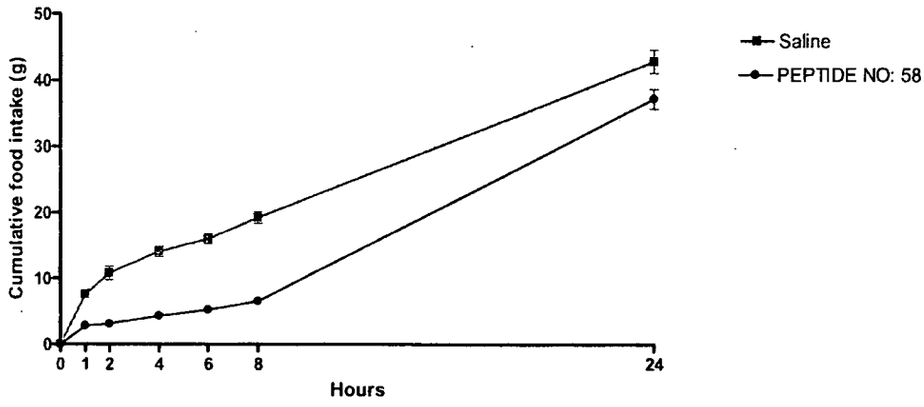


Figure 7

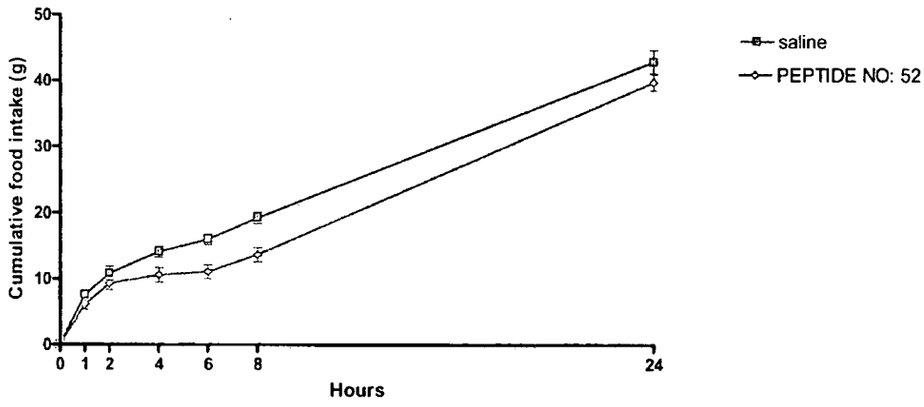


Figure 8

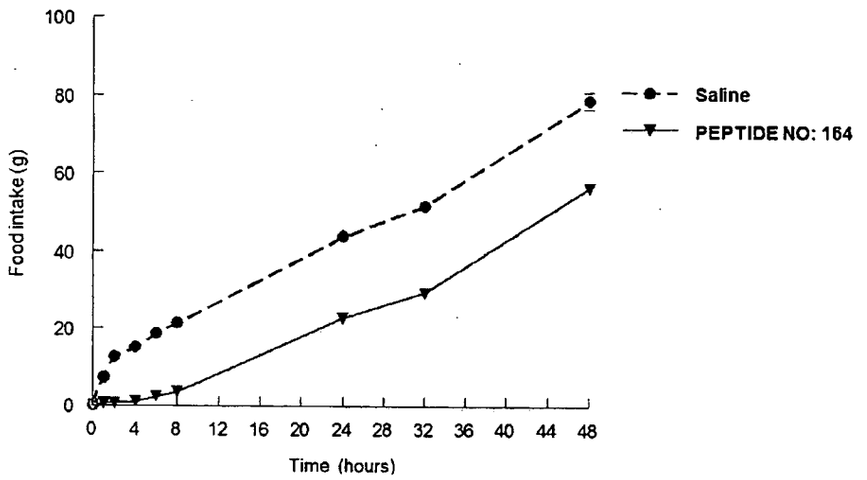


Figure 9

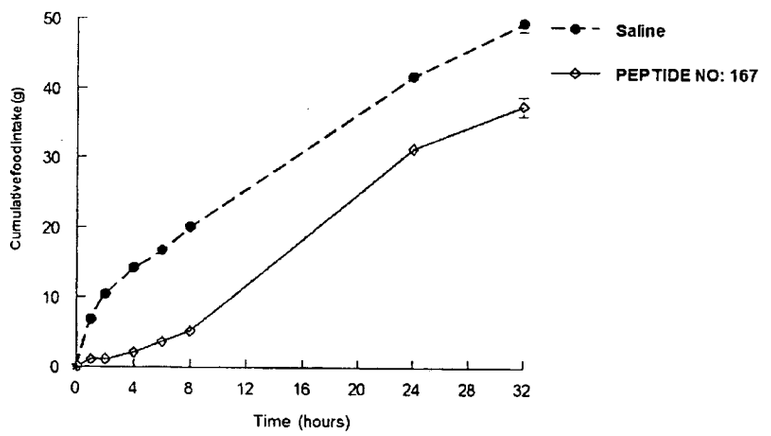


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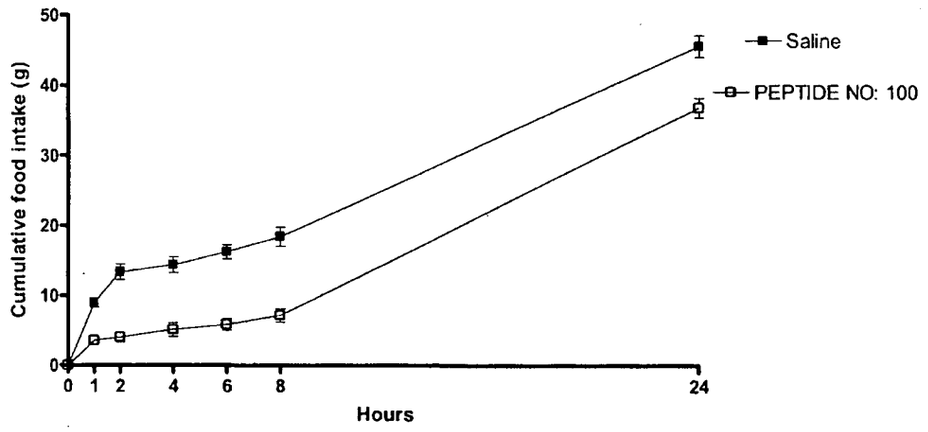


Figure 11

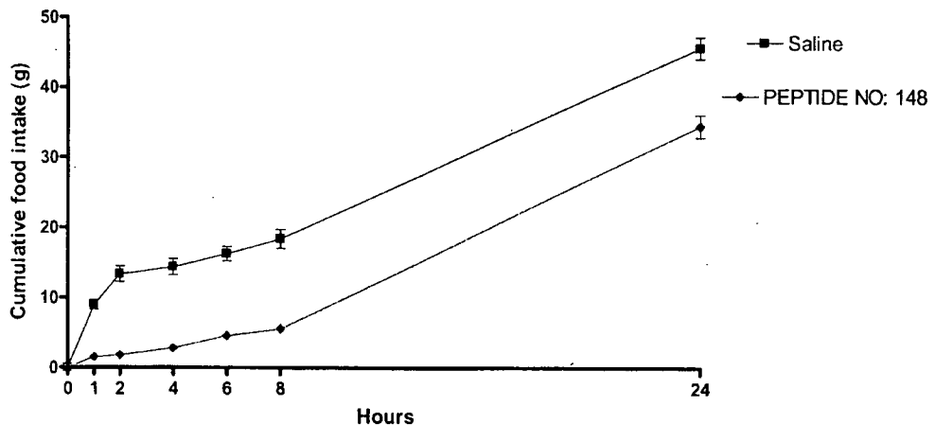


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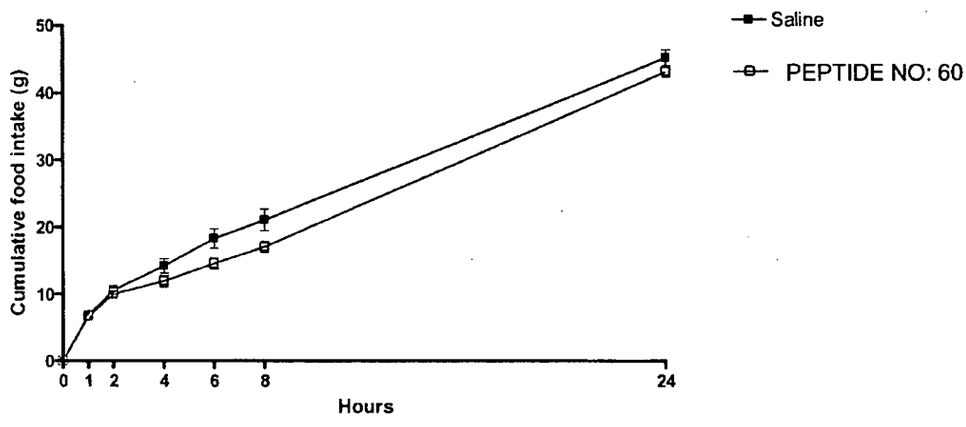


Figure 13

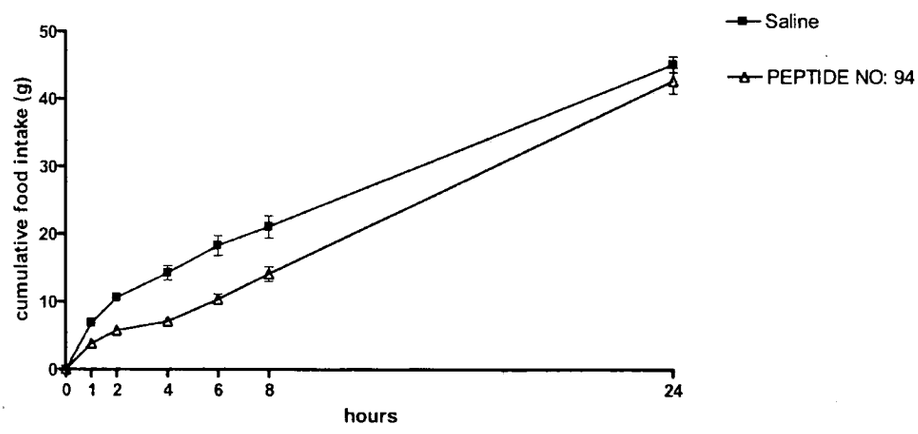


Figure 14

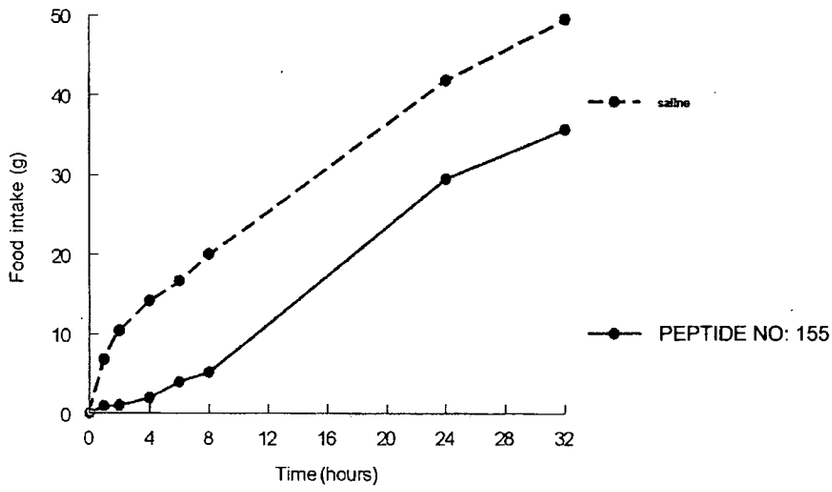


Figure 15

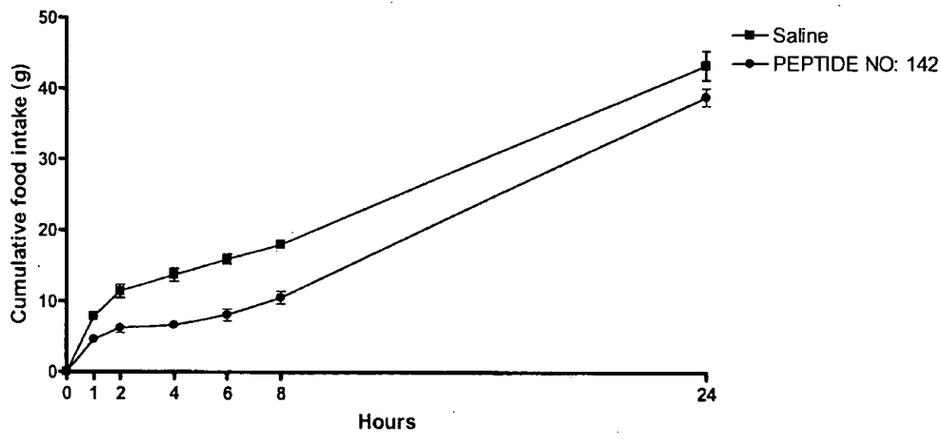


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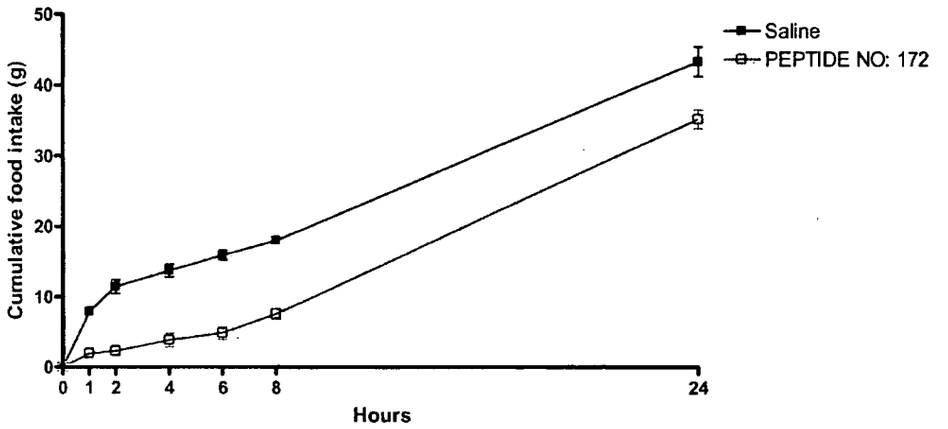


Figure 17

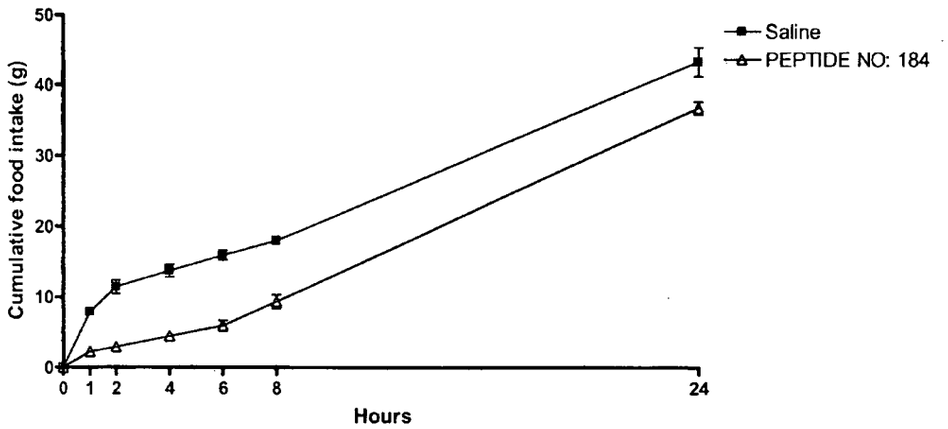


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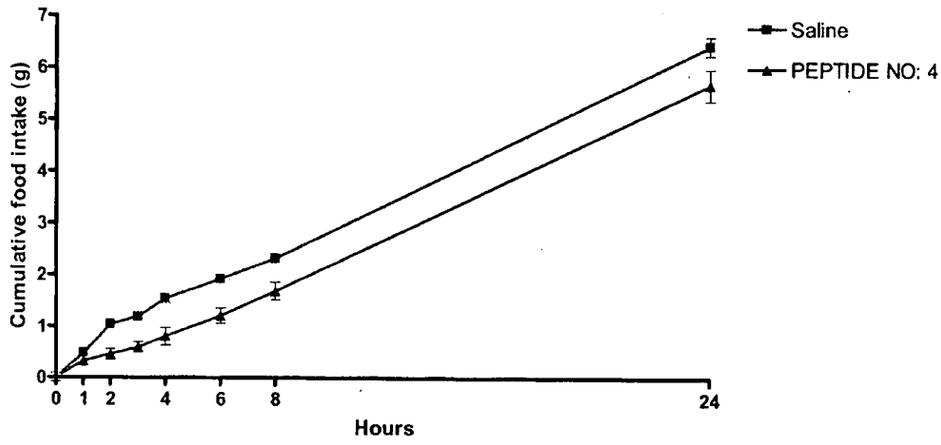


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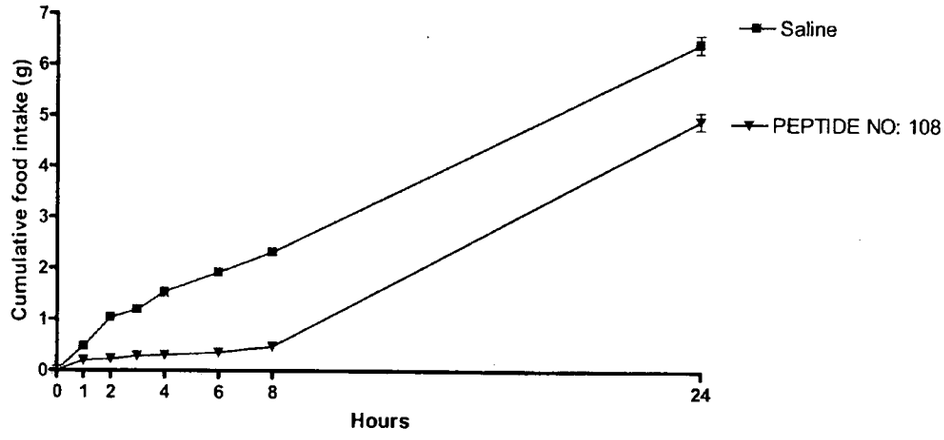


Figure 20

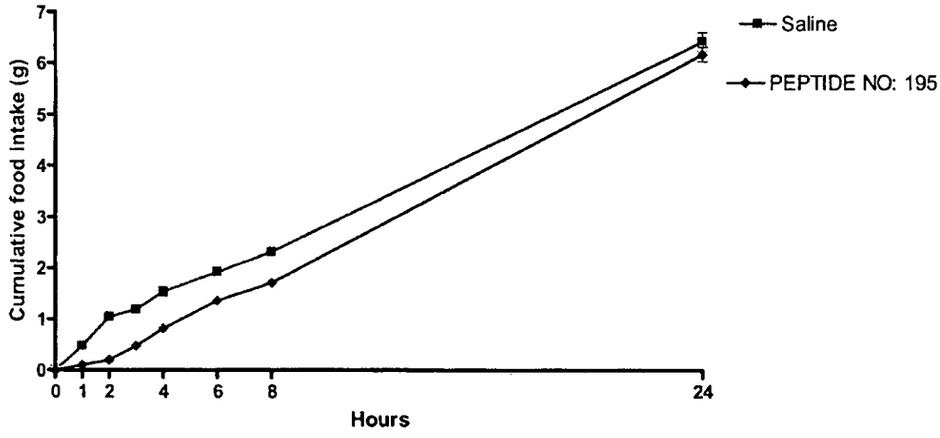


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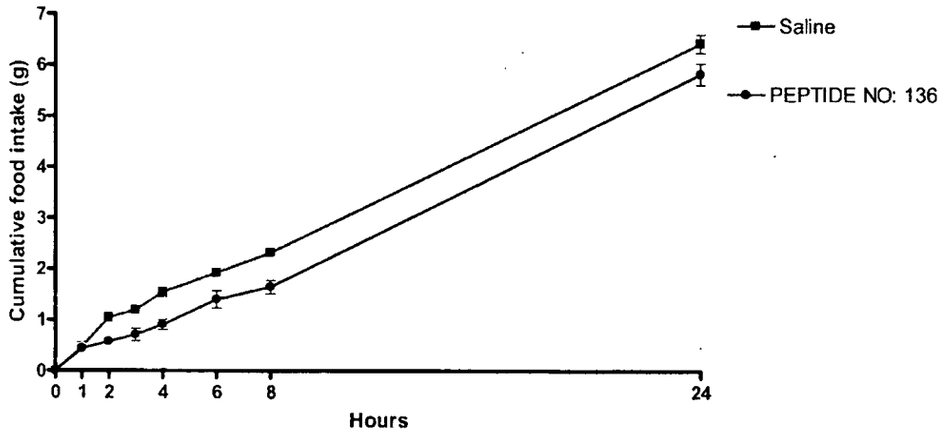


Figure 22

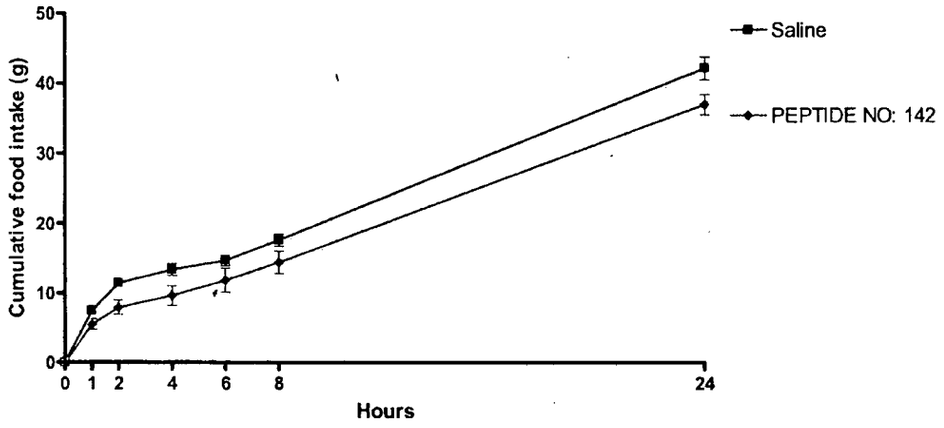


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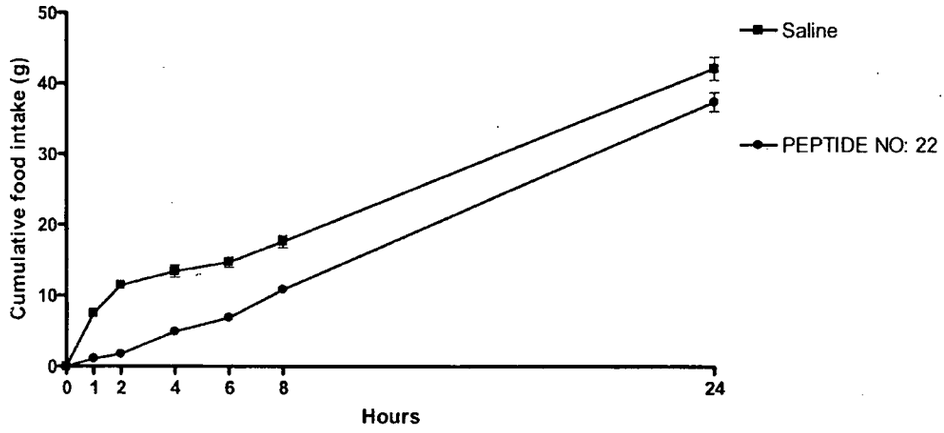


Figure 24

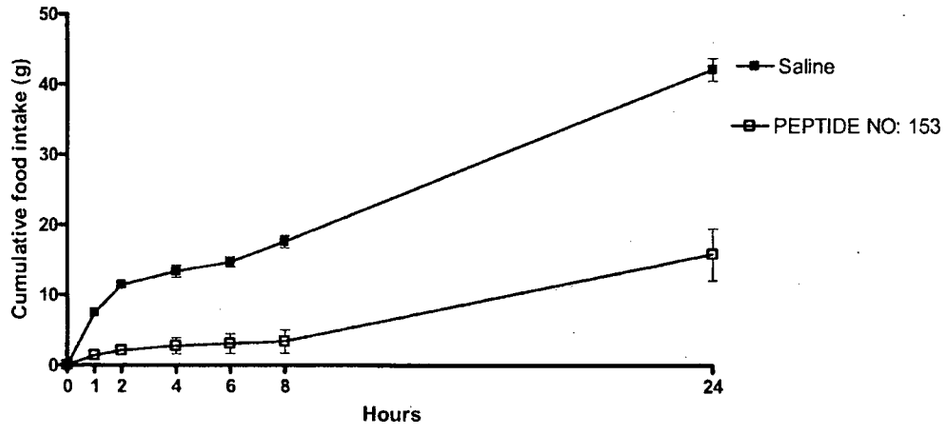


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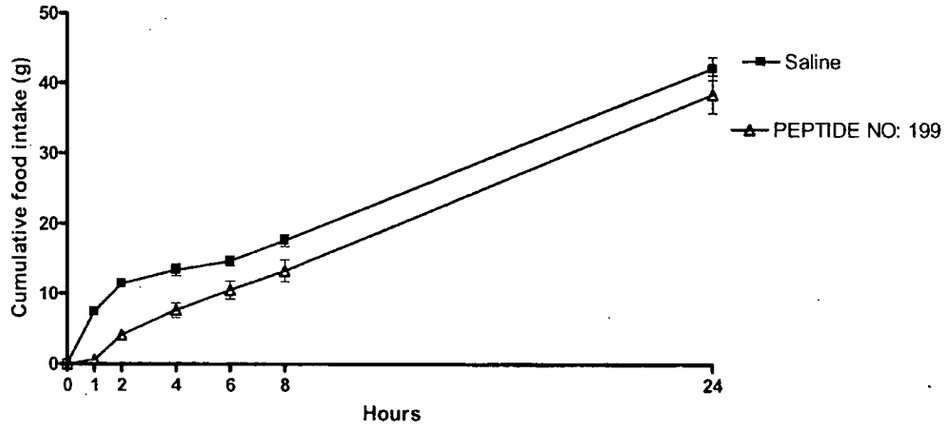


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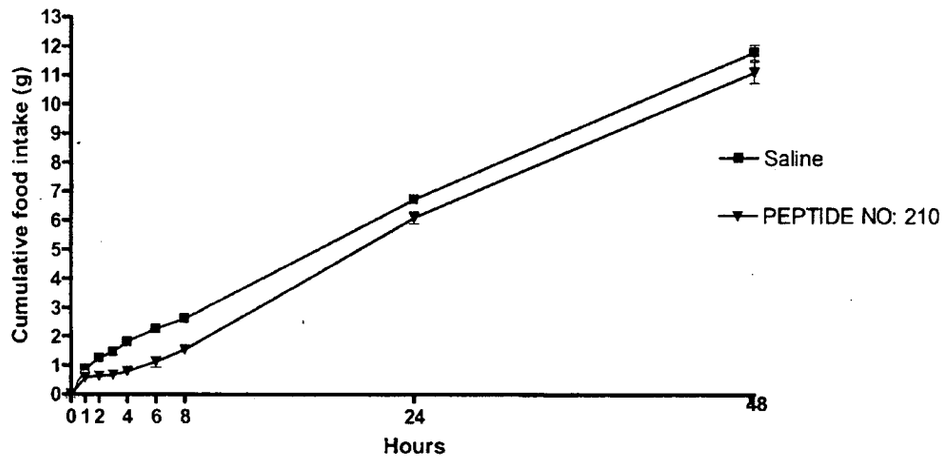


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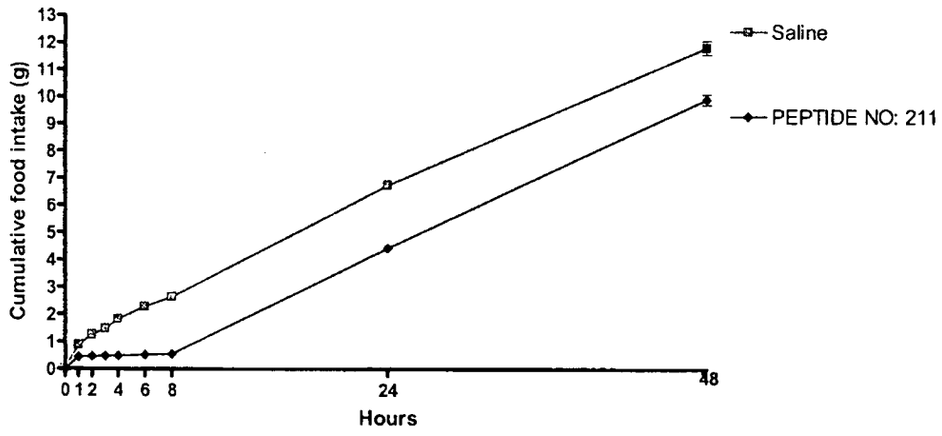


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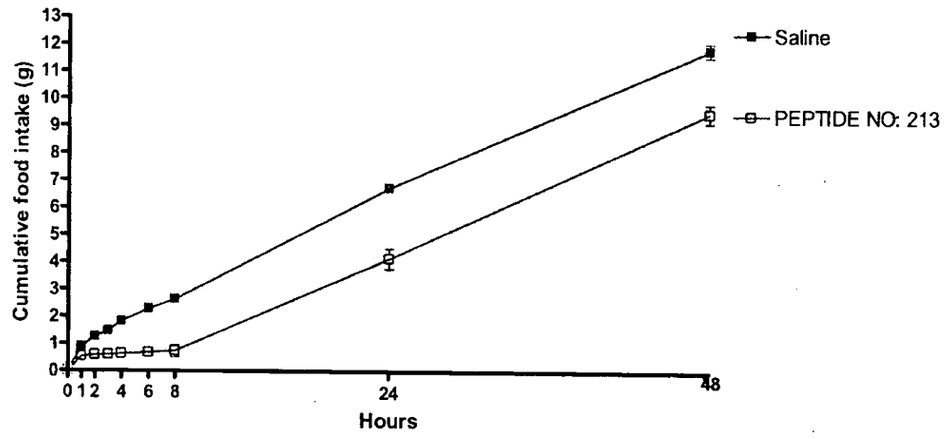


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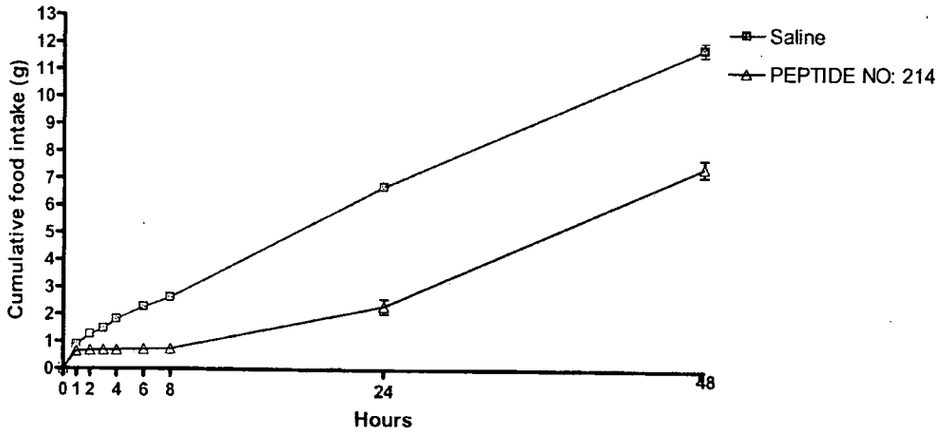


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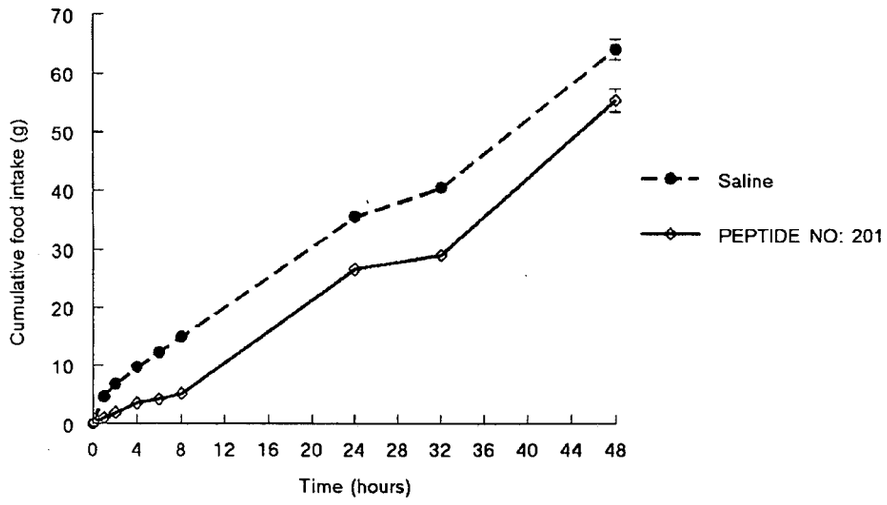


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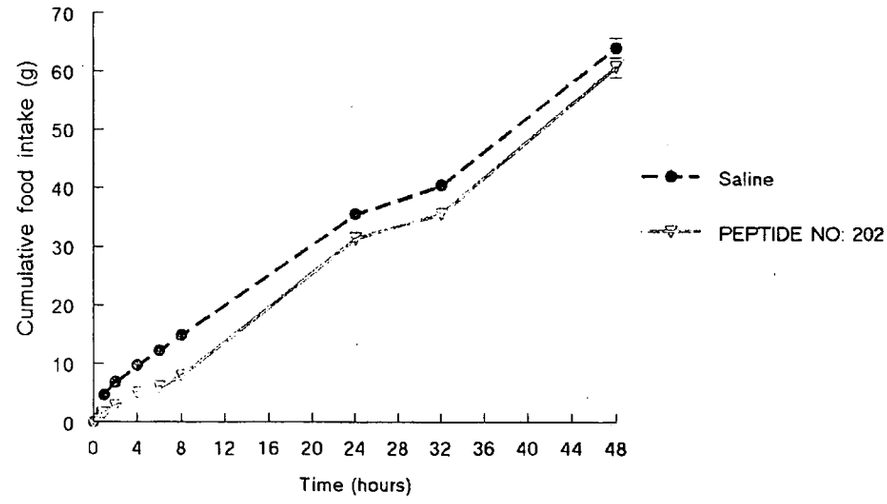


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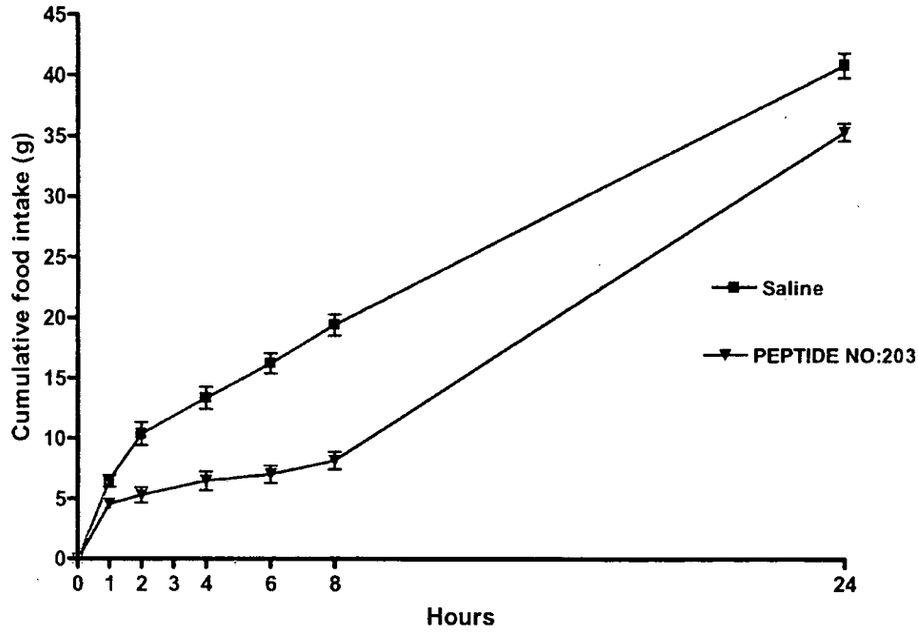


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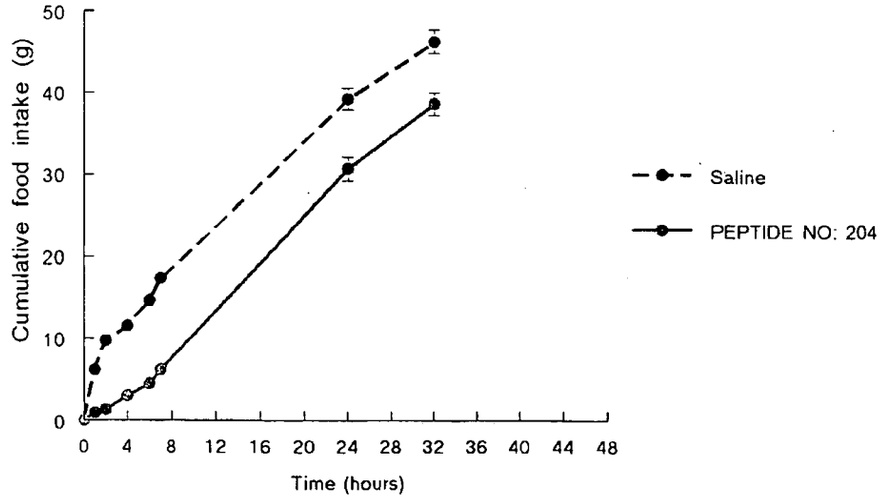


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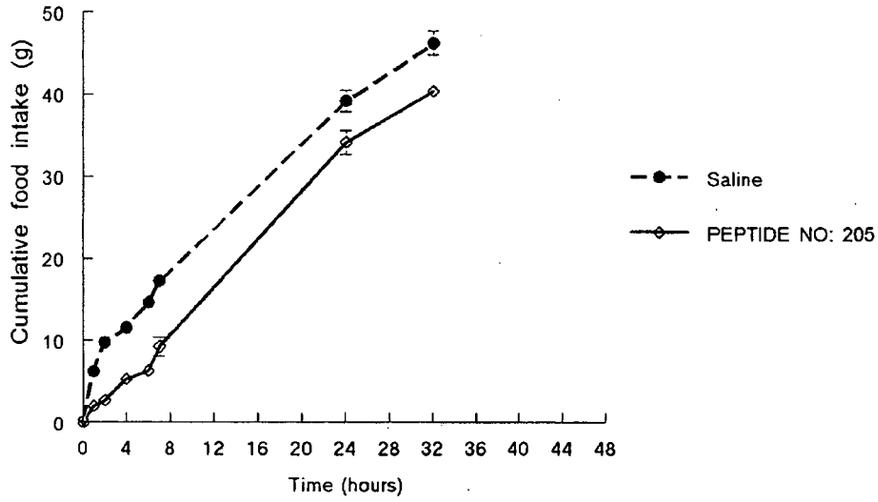


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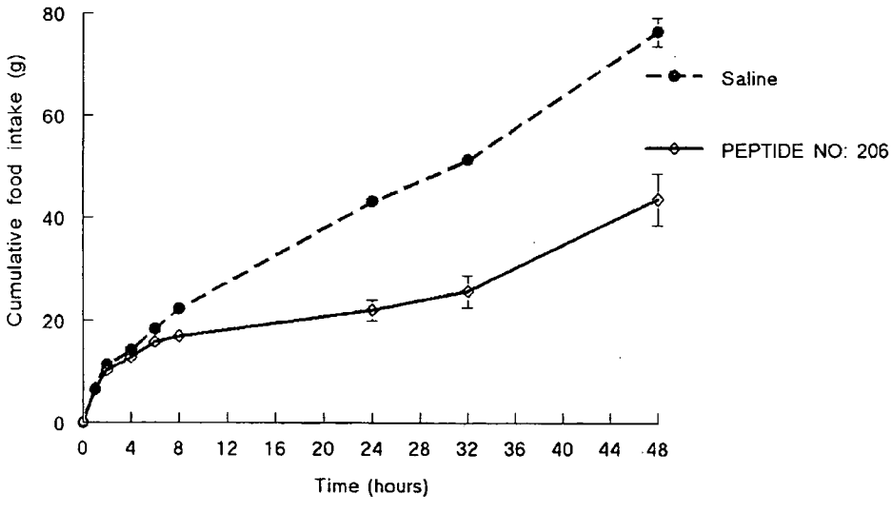


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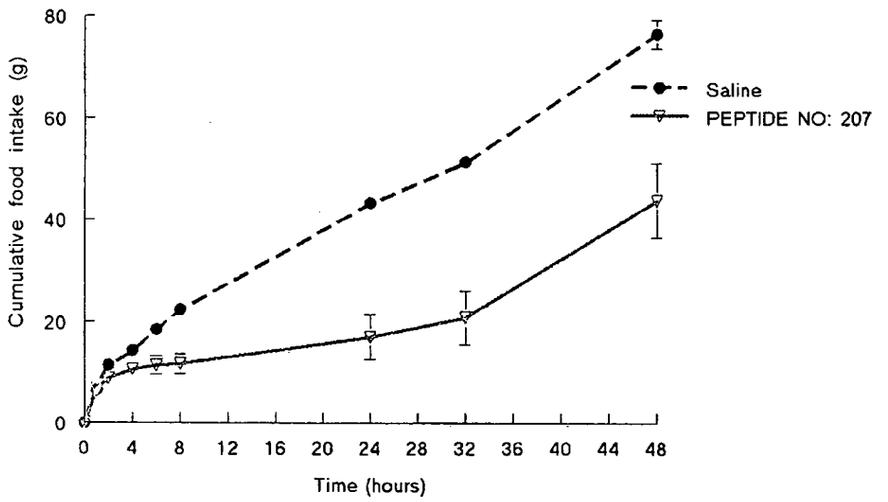


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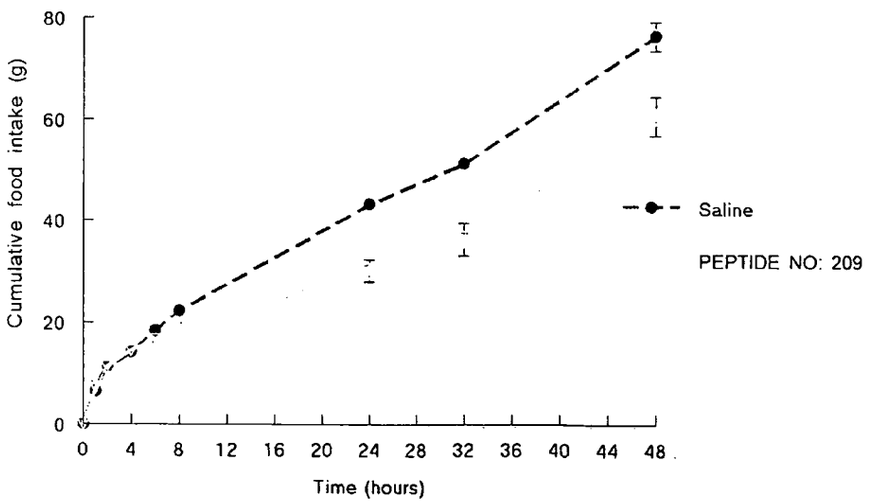


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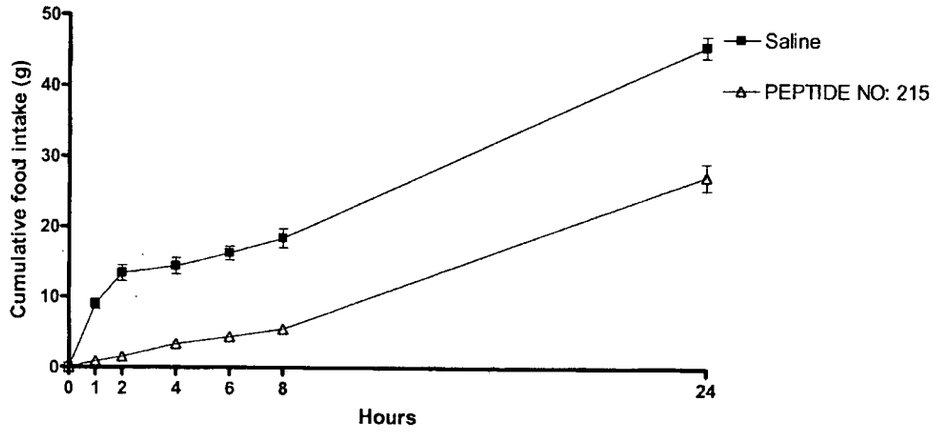


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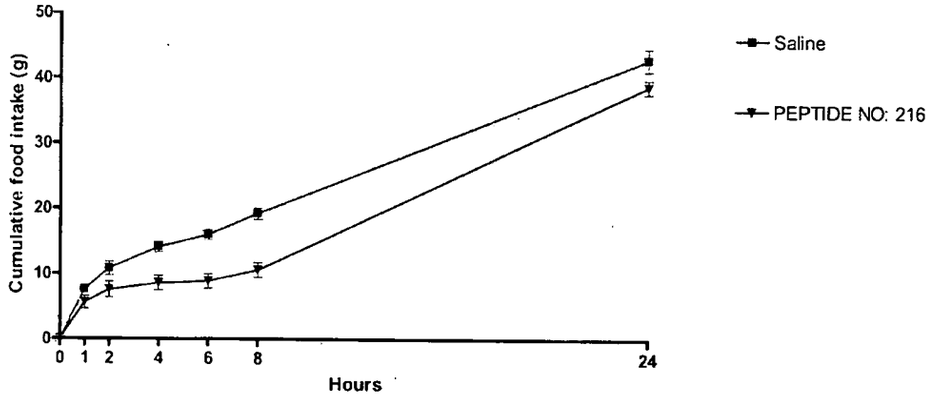


Figure 40

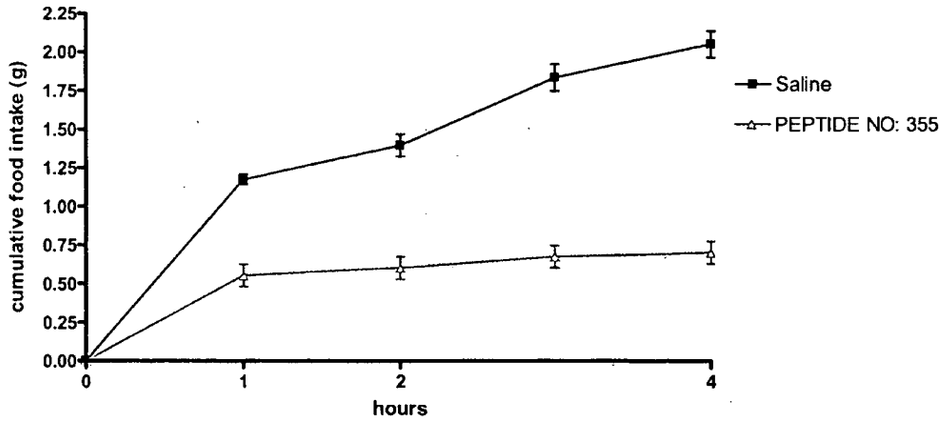
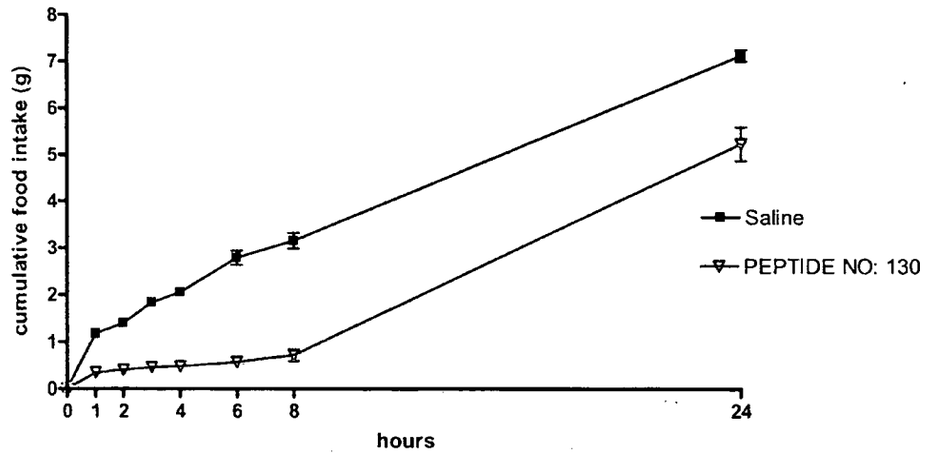


Figure 41



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 12599 WO PAB	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2007/004779	International filing date *(day/month/year)* 13.12.2007	Priority date *(day/month/year)* 13.12.2006
International Patent Classification (IPC) or national classification and IPC INV. A61K38/26		
Applicant Imperial Innovations Limited		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 10 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
2008-10-08	16.02.2009
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Obel, Nicolai Telephone No. +49 89 2399-8785

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

ABEL & IMRAY
20 Red Lion Street
London, WC1R 4PQ
GRANDE BRETAGNE

ABEL & IMRAY
CASE NO. 12599
G.O. MK
19 FEB 2009
A/C? Y N
CPA? Y N PAB

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	16.02.2009

Applicant's or agent's file reference 12599 WO PAB	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2007/004779	13.12.2007	13.12.2006

Applicant
Imperial Innovations Limited

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Yassine, Mahjouba Tel. +49 89 2399-5762

Form PCT/IPEA/416 (January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2007/004779

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-59	as originally filed
Sequence listings, Pages	
1-169	as originally filed
Claims, Numbers	
1-36	as originally filed
Drawings, Sheets	
1-27	as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

5. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 70.2 (e)).

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-36 (partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*.

☒ no international search report has been established for the said claims Nos. 1-36 (partially)

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has, within the applicable time limit:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest and, where applicable, the protest fee.

   ☐ paid additional fees under protest but the applicable protest fee was not paid.

   ☒ neither restricted the claims nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-36 (partially) .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-36(partially)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-36 (partially)
Industrial applicability (IA)	Yes:	Claims	1-36 (partially)
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ on paper

   ☒ in electronic form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in electronic form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

The present application is directed to protein variants of oxyntomodulin (oxm) for treating obesity and diseases related thereto such as diabetes.

1. Reference is made to the following documents:
   D1: DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; 9 September 2004 (2004-09-09), XP002471184 retrieved from CAA27627 Database accession no. CAA27627
   D2: WO 03/022304 A (IMP COLLEGE INNOVATIONS LTD [GB]; BLOOM STEPHEN ROBERT [GB]; GHATEI MO) 20 March 2003 (2003-03-20)
   D3: WO 2005/035761 A (COMPUGEN LTD [IL]; SHEMESH RONEN [IL]; KLIGER YOSSEF [IL]; NEVILLE LEW) 21 April 2005 (2005-04-21)
   D4: WO 2007/056362 A (INDIANA UNIVERSITY RES AND TEC [US]; DIMARCHI RICHARD D [US]; SMILEY D) 18 May 2007 (2007-05-18)
   D5: WO 2007/100535 A (MERCK & CO INC [US]; ANGELETTI P IST RICHERCHE BIO [IT]; ROY RANABIR S) 7 September 2007 (2007-09-07)
   D6: WO 2007/146038 A (HUMAN GENOME SCIENCES INC [US]; ROSEN CRAIG A [US]; BELL ADAM [US]; LA) 21 December 2007 (2007-12-21)

Re Item III.

2. The applicant has chosen not to pay any further search fees and only an opinion with regard to the first invention has thus been established.

Re Item IV.

3. This Authority considers that there are 1631 inventions covered by the claims indicated as follows:

   1: Claims 1-36 (partially)are directed to the protein variant: His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Glu Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys Arg Asn Lys Asn Asn Ile Ala. This represents the first inventions as the first possibility is selected for each of the indicated variable regions.

   2-1631: Claims 1-36 (partially) are directed to the remaining possible variants disclosed in claim 1

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The common technical concept is oxm variants suitable for treating obesity and the problem to be solved can be regarded as the provision of alternative oxm variants for the treatment of obesity.

The scope of claim 1 covers a wide range of polypeptides with the provision that if Xaa3 is Glu and Xaa15-Xaa24 is Asp Ser Arg Arg Ala Gln Asp Phe Val Gln then Xaa27-Xaa32 can not be the sequence set out in SEQ ID NO 356.

3.1 The prior art describes in D1 a protein sequence encoding oxm. The sequence in D1 comprises the human version of oxm with the modification that Lys30 and Lys33 have been replaced with Asn and Arg respectively. This sequence is annotated as a glucagon like hormone.

3.2 D2 (p. 2 l. 19-27, claim 2) discloses the human oxm sequence where Asn28 is replaced by Asp and specifies that the sequence can be used for treating obesity. It specifies further that any one or more (up to 22) amino acids can be replaced (p 3 l. 24 p. 4 l. 11). The reference to the replacement of 1 or more amino acids and since the replacement is a conservative substitution, it can be considered that the sequence is functionally identical to sequences disclosed in the present application. D2 species furthermore how the C-terminal can be modified by addition of further amino acids or chemically modified amino acids and the protein can be administered together with ethanol or polyethylene glycol. Such compositions can be administered to a patient by injections, gels or nasal administration (p. 4 l. 17 - p. 10 l. 19).

3.3 D3 (claims 2,20,84,85, p. 3 l. 10-18) discloses oxm variants ,SEQ ID NO 41-44, where Lys33 is replaced by Arg. These variants can be used for the treatment of obesity, metabolic disorders and diabetes.

It follows that neither the provision of oxm variants for the treatment of obesity and related diseases nor the problem to be solved is a new and inventive technical concept. No specific technical effect can be seen as arising from either

substitution of Asn28 or Lys33, see also 5, and the applicant should also note that Asn28 is not present in all embodiments falling within the scope of claim 1.

Hence, the application does not meet the requirements of unity of the invention as defined in Rules 13.1 and 13.2 PCT.

Re Item V.

4. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, i.e claims 28-36, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

5. The present application does meet the criteria of Article 33(2) PCT, because the subject-matter of claims 1-36 with regard to the first inventions is new. see 3.

6. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-36 with regard to the first invention does not involve an inventive step in the sense of Article 33(3) PCT.

The document D2 is regarded as being the closest prior art to the subject-matter of claims 1-36, see 3.2.

Claims 1-36 are directed to a polypeptide with the sequence indicated above, see 2, which can be modified at the C-terminal thus making it more stable under physiological conditions. The polypeptide can be used for the treatment of obesity, diabetes and metabolic diseases.

The subject-matter of the claims therefore differs from this known (D2) in that the polypeptide is 73% identical to the human version of oxm. 8 amino acids have been substituted in the region between amino acids 15 and 24.

The problem to be solved by the present invention may therefore be regarded as to provide an alternative version of oxm.

No technical effect has been documented in any experiments with regard to this sequence. The question to be asked is thus if it can be expected from the provided data that this specific sequence would indeed have an effect.

An effect is not unambiguously derivable from the provided data. The applicant has used a saline control as a benchmark in the experiments, but in order to establish a surprising effect a comparison with regard to oxm must be performed as oxm provided in the prior art already has the effect of reducing the food intake. This was demonstrated on Wistar rats, identical to those of the present application (D2, p. 16 l. 5). When administered oxm, a reduction in food intake in the ranger 10-80 % was observed using a dosage in the range 100-300 nmol/kg and an observation period of 1-24 h (D2, p. 19 l. 20 - p 34 l. 25).

An effect with regard to the prior art can not be established for some variants, for example:

SEQ ID NO 52 differs from SEQ ID NO 3 in positions 1 and 24 and has a maximum reduction of 20% using a dosage of 10 nmol/kg in rats.

SEQ ID NO 60 differs from SEQ ID NO 3 in positions 1,23 and 24 and has maximum reduction of 20% using a dosage of 100 nmol/kg in rats.

SEQ ID NO 94 differs from SEQ ID NO 3 in positions 1,18,23,24 and 27-31 and has maximum reduction of 50% using a dosage of 5 nmol/kg in rats.

SEQ ID NO 199 differs from SEQ ID NO 3 in positions 1-3,18,23,24 and 27-31 and has maximum reduction of 50% using a dosage of 500 nmol/kg in rats.

SEQ ID NO 206,207 and 209 differ from SEQ ID NO 3 in positions 1-3,18,23,24 and 29-31 and have maximum reductions of 50% using a dosage of 80 nmol/kg in rats. For these sequences, no reduction is observed until after 8 h. In the provided comparative example, fig 3, oxm is only measure until 8 h and the time span 8-24h can thus not be compared to any control experiment.

SEQ ID NO 216 differs from SEQ ID NO 3 in positions 1,27-31 and 34 and has maximum reduction of 50% using a dosage of 10 nmol/kg in rats.

It is thus not unambiguously derivable that SEQ ID NO 3 has an improved effect in the sense of a lower food intake or lower dosage than oxm provided in the prior art. The person skilled in the art would furthermore from D1 be aware that the amino acids 15-24 could be changed as the sequence of this document is annotated as glucagon like hormone.

The subject matter of claims 1-36 regarding the first inventions is thus not inventive in the sense of Article 56 EPC.

Re Item VIII.

7. The application does not meet the requirements of Article 6 PCT, because claims 2-4 are not clear.

Claims 2 - 4 define some of the amino acid fragments further, Xaa15-Xaa24, Xaa1-Xaa3 and Xaa27-Xaa32 and in each case a sequence is indicated, SEQ ID No 359 to 361. It is not clear which specific embodiments the indicated sequences represent as they are full proteins, i.e 37 amino acids, and the indicated claims are only with regard to fragments.

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2007/004779

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K38/26 C07K14/435

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; 9 September 2004 (2004-09-09), XP002471184 retrieved from CAA27627 Database accession no. CAA27627 Amino acids 53-89 abstract -----	1-36
Y	WO 03/022304 A (IMP COLLEGE INNOVATIONS LTD [GB]; BLOOM STEPHEN ROBERT [GB]; GHATEI MO) 20 March 2003 (2003-03-20) Claim 2 Page 21 lines 19-27 Page 3 line 24 - Page 4 line 11 Page 4 line 17 - Page 10 line 19 -----	1-36
	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 March 2008	21/05/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Obel, Nicolai

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2007/004779

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2005/035761 A (COMPUGEN LTD [IL]; SHEMESH RONEN [IL]; KLIGER YOSSEF [IL]; NEVILLE LEW) 21 April 2005 (2005-04-21) Claims 2,20,84,85 Page 3 lines 10-18	36
Y	WO 2004/062685 A (IMP COLLEGE INNOVATIONS LTD [GB]; BLOOM STEPHEN ROBERT [GB]; GHATEI MO) 29 July 2004 (2004-07-29) Claims 1-12	1-36
P,X	WO 2007/056362 A (INDIANA UNIVERSITY RES AND TEC [US]; DIMARCHI RICHARD D [US]; SMILEY D) 18 May 2007 (2007-05-18) Claims 1-46 SEQ ID NO 37	1-4, 6-10, 14-36
P,X	WO 2007/100535 A (MERCK & CO INC [US]; ANGELETTI P IST RICHERCHE BIO [IT]; ROY RANABIR S) 7 September 2007 (2007-09-07) Claims 1-12 SEQ ID NO 3	1-4, 6-10, 14-36
E	WO 2007/146038 A (HUMAN GENOME SCIENCES INC [US]; ROSEN CRAIG A [US]; BELL ADAM [US]; LA) 21 December 2007 (2007-12-21) SEQ ID NO 296 Paragraph 0032 Page 12	1-4, 6-10, 14-36

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2007/004779

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 28-36
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-36 partially

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-36 (partially)

The protein :
His Ser Gln Gly Thr Phe Thr Ser Asp Tyr ser Lys Tyr Leu Glu
Glu Glu Leu Val Lys Tyr Phe Leu Glu Trp Leu Met Asn Thr Lys
Arg Asn Lys Asn Asn Ile Ala
The use of said protein for the treatment of obesity

Inventions 2-1631: claims 1-36 (partially)

The further 1630 variants and the use of said variants for the treatment of obesity

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2007/004779

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03022304 A	20-03-2003	BR 0212374 A	17-08-2004
		CA 2459862 A1	20-03-2003
		CN 1551780 A	01-12-2004
		CN 101057968 A	24-10-2007
		EP 1427437 A1	16-06-2004
		JP 2005511503 T	28-04-2005
		KR 20050026685 A	15-03-2005
		MX PA04002142 A	31-05-2006
		NZ 531609 A	31-08-2006
		PL 367274 A1	21-02-2005
		US 2005070469 A1	31-03-2005
		ZA 200401804 A	12-07-2005
WO 2005035761 A	21-04-2005	NONE	
WO 2004062685 A	29-07-2004	AU 2004204369 A1	29-07-2004
		CA 2512939 A1	29-07-2004
		EP 1581248 A2	05-10-2005
		JP 2006515351 T	25-05-2006
		US 2006189522 A1	24-08-2006
		US 2008064636 A1	13-03-2008
WO 2007056362 A	18-05-2007	NONE	
WO 2007100535 A	07-09-2007	NONE	
WO 2007146038 A	21-12-2007	NONE	