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(54) Title: HAM15-52 ANALOGUES WITH IMPROVED AMYLIN RECEPTOR (HAMY3R) POTENCY

(57) Abstract: The present invention relates to hAM_{15-52} analogues with improved amylin receptor (hAMY3R) potency (hAMY3R-$EC_{50} \leq 250$ pM) and which are largely based on the sequence of the human adrenomedullin fragment hAM_{15-52}. The invention further relates to hAM_{15-52} analogues that are selective amylin receptor (hAMY3R) agonists (hAMY3R-$EC_{50} \leq 250$ pM and an hAM1R-$EC_{50} \geq 25$ nM) and which are largely based on the sequence of the human adrenomedullin fragment hAM_{15-52}. The hAM_{15-52} analogues according to the invention maintain the good physical stability of hAM_{15-52}. The invention further relates to pharmaceutical compositions comprising such polypeptides and their use in the treatment of a medical condition such as obesity, NASH and/or diabetes.

hAM_{15-52} analogues with improved amylin receptor (hAMY3R) potency

FIELD OF THE INVENTION

The present invention relates to hAM_{15-52} analogues with improved amylin receptor (hAMY3R) potency (hAMY3R-$EC_{50} \leq 250$ pM) and which are largely based on the sequence of the human adrenomedullin fragment hAM_{15-52}. The invention further relates to hAM_{15-52} analogues that are selective amylin receptor (hAMY3R) agonists (hAMY3R-$EC_{50} \leq 250$ pM and an hAM1R-$EC_{50} \geq 25$ nM). In particularly, the present invention is based on the realization that the human adrenomedullin fragment hAM_{15-52} may be converted into highly selective amylin receptor agonists (hAMY3R-$EC_{50} \leq 250$ pM and an hAM1R-$EC_{50} \geq 25$ nM) by replacing the amino acid in position X_{11} in hAM_{15-52} together with one or more of the amino acids in the positions X_4, X_{37} and/or X_{38} in hAM_{15-52}. Thus, replacing at least two amino acids on hAM_{15-52} resulted in hAM_{15-52} analogues with AMY3R and AM1R potencies comparable to $hAMY_{1-37}$ (amylin). The invention further relates to pharmaceutical compositions comprising such hAM_{15-52} analogues and their medical use in the treatment of a medical condition, such as obesity and/or diabetes.

BACKGROUND OF THE INVENTION

Obesity is a medical condition in which excess body fat has accumulated to the extent that it has a negative impact on health. It is affecting a huge number of individuals worldwide and increasing rapidly in certain parts of the world. The World Health Organisation (WHO) estimated that in 2016, approximately 650 million people were obese worldwide. Obesity is defined as a body mass index (BMI) above 30. Obesity is considered a major risk factor for developing a variety of medical conditions, such as cardiovascular diseases (e.g. hypertension, atherosclerosis, heart attacks or stroke), NASH musculoskeletal disorders, certain kinds of cancers, depression and diabetes type II, and hence is detrimental to human health. Cardiovascular diseases and diabetes are two main diseases associated with obesity. A large amount of research has been conducted in the obesity field in search for new treatments for obesity or obesity-related diseases and disorders.

Diabetes is a group of metabolic disorders characterized by a high blood sugar level. As of 2019, the International Diabetes Federation estimated that 463 million people are suffering from diabetes worldwide, approximately half of the individuals being diagnosed. Diabetes is divided into two types, namely type I and type II diabetes. Type I diabetes results from the pancreas's failure to produce enough insulin due to loss of beta cells caused by an autoimmune response. On the other hand, type II diabetes is a condition that begins with insulin resistance in which cells fail to respond to insulin properly and as the disease progresses may also result in a lack of insulin.

Human amylin ($hAMY_{1-37}$ or amylin) is a 37-residues peptide hormone that is co-secreted with insulin from the pancreatic β-cells with the amino acid sequence Lys-Cys-Asn-Thr-Ala-Thr-Cys-Ala-Thr-Gln-Arg-Leu-Ala-Asn-Phe-Leu-Val-His-Ser-Ser-Asn-Asn-Phe-Gly-Ala-Ile-Leu-Ser-Ser-Thr-Asn-Val-Gly-Ser-Asn-Thr-Tyr with a disulphide bridge between residues 2 and 7. Amylin supresses glucagon release and inhibits gastric

emptying and hence plays an important role in maintaining glucose homeostasis by decreasing the blood sugar concentration. Therefore, amylin is a potential candidate for treating diabetes. Furthermore, amylin has been shown to reduce food intake and plays an important role in satiety, also making it a potential candidate for treating obesity. However, amylin possesses some drawbacks such as a high tendency of fibrillation, a short *in vivo* half-life, and chemical instability at pH 7. Thus, native amylin is suboptimal for use as a pharmaceutically active ingredient.

A large number of amylin derivatives are known in the prior art, such as the ones disclosed in WO2016/146739. These amylin analogues attempt to solve some of the known drawbacks that human amylin possesses. One successful example is the amylin analogue Pramlintide, which has been approved by the FDA for use in type I and type II diabetes. However, Pramlintide is formulated at pH 4 as it fibrillates at pH 7. Thus, there is still a need for new amylin analogues with increased chemical stability, increased metabolic stability, and/or a reduced tendency for fibrillation. In particular, amylin analogues that are stable over a broader pH range are desirable. Furthermore, there is a need for new amylin analogues with increased effectiveness through e.g. increased potency, higher efficacy, and/or longer half-lives to allow less frequent dosing and increased patient compliance. The present invention sets out to solve one or more of the problems known from the prior art by applying a new chemical strategy.

SUMMARY OF THE INVENTION

In a first aspect, the present invention relates to hAM_{15-52} analogues with improved amylin receptor (hAMY3R) potency (hAMY3R-$EC_{50} \leq 250$ pM). Thus, in a first aspect the invention relates to hAM_{15-52} analogues or a pharmaceutically acceptable salt thereof comprising 38 amino acids (X_1-X_{38}), wherein the amino acid in position X_{11} is selected from R, W or Cit and wherein the hAM_{15-52} analogue has at least 50 % homology to hAM_{15-52} (SEQ ID NO: 1), such as at least 60 % homology to hAM_{15-52} (SEQ ID NO: 1). The inventors surprisingly found that the amino acid position X_{11} was highly important for increasing amylin receptor potency of hAM_{15-52}. Thus, a single substitution in X_{11} from K to R, W or Cit was enough to improve the amylin receptor potency (hAMY3R-$EC_{50} \leq 250$ pM) of hAM_{15-52} significantly while retaining adrenomedullin potency (hAM1R).

In a second aspect, the present invention provides selective hAM_{15-52} analogues (hAMY3R-$EC_{50} \leq 250$ pM and an hAM1R-$EC_{50} \geq 25$ nM), which act as agonists on the amylin receptor hAMY3R but which, unlike in the prior art (e.g. WO2016/146739), are derived from the backbone of the adrenomedullin fragment hAM_{15-52}. The inventors surprisingly found that each of the positions X_4, X_{37} and X_{38} were highly important for the hAM1R potency of hAM_{15-52} and that hAM1R potency of hAM_{15-52} could be abolished or reduced (hAM1R-$EC_{50} \geq 25$ nM) by certain amino acid substitutions in either of the positions X_4, X_{37} and/or X_{38}. Thus, in a second aspect, the invention relates to hAM_{15-52} analogues comprising 38 amino acids (X_1-X_{38}) or a pharmaceutically acceptable salt thereof, wherein the amino acid in position X_{11} is selected from R, W or Cit and wherein the hAM_{15-52} analogue has at least 50 % homology to hAM_{15-52} (SEQ ID NO: 1), such as at least 60 % homology to hAM_{15-52} (SEQ ID NO: 1) and further wherein X_4 is selected as F, Y, W, T,

M, I, A or C; X_{37} is selected as G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C or K; X_{38} is selected as Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K, with the proviso that at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position. The inventors surprisingly found that the human adrenomedullin fragment hAM_{15-52} may be converted into highly selective amylin receptor agonists (hAMY3R-EC_{50} value ≤ 250 pM and an hAM1R-EC_{50} ≥ 25 nM) by replacing the amino acid in position X_{11} in hAM_{15-52} together with one or more of the amino acids in the positions X_4, X_{37} and/or X_{38} in hAM_{15-52}. Thus, replacing at least two amino acids on hAM_{15-52} resulted in hAM_{15-52} analogues with hAMY3R and hAM1R potencies comparable to amylin rather than hAM_{15-52}. One benefit of this approach is that unlike human amylin, hAM_{15-52} is not prone to fibrillation, and by using this new chemical strategy, the inventors further envisaged that the good fibrillation properties of hAM_{15-52} could be maintained in the new hAM_{15-52} analogues. Therefore, the hAM_{15-52} analogues according to the invention comprise a significant part of the backbone present in hAM_{15-52} as an important part of the sequence (i.e. at least least 50 % homology to hAM_{15-52} (SEQ ID NO: 1)). Thus, in the second aspect of the invention, the first problem solved is the provision of new potent hAMY3R agonists with high selectivity over hAM1R, which are obtained by tweaking the polypharmacology of the hAM_{15-52} fragment into hAMY3R agonism. The second problem solved by the second aspect is the provision of new hAMY3R agonists which are less prone to fibrillation, thereby overcoming a problem inherent to human amylin. Unlike the amylin derivatives known from the prior art, the hAM_{15-52} analogues of the present invention possess a structurally distinct sequence belonging to the hAM_{15-52} fragment. Thus, the hAM_{15-52} analogues of the invention possess different physical-chemical properties compared to the amylin derivatives in the prior art, such as different solubility, chemical-, physical-, and/or metabolic stability.

In a third aspect, the invention relates to hAM_{15-52} analogues according to the first and/or second aspect for use as a medicament. More particularly, the third aspect of the invention relates to hAM_{15-52} analogues according to the first and/or second aspect for use in treating, preventing or ameliorating a variety of diseases, disorders or conditions, such as but not limited to excess food intake, excess body weight, obesity, Binge eating disorder, Prader-Willi syndrome, dyslipidemia, metabolic diseases/disorders, diabetes I or II, impaired glucose tolerance, insulin resistance syndrome and/or NASH.

In a fourth aspect, the invention relates to pharmaceutical compositions comprising one or more of the hAM_{15-52} analogues according to the first and/or second aspect and their medical use(s) in treating, preventing, or ameliorating a variety of diseases, disorders or conditions according to the third aspect. The pharmaceutical compositions may comprise a pharmaceutically acceptable carrier (vehicle) and/or one or more excipient(s).

In a fifth aspect, the invention relates to a method of treating a human or animal subject with one or more hAM_{15-52} analogue(s) according to the first and/or second aspect, wherein the human or animal subject is diagnosed with or suffering from one or more of the diseases, disorders or conditions, such as but not limited to excess food intake, excess body weight, obesity, Binge eating disorder, Prader-Willi

syndrome, dyslipidemia, metabolic diseases/disorders, diabetes I or II, impaired glucose tolerance, insulin resistance syndrome and/or NASH, preferably obesity, diabetes I or II and/or NASH.

The invention will now be explained in more detail from the alignment of the amylin ($hAMY_{1-37}$) and the adrenomedullin fragment (hAM_{15-52}) as shown in Table 1 below.

DEFINITIONS

In the present context, when the disclosure refers to positions of amino acids in the hAM_{15-52} analogues (i.e. X_1-X_{38}) that are derived/selected from $hAMY_{1-37}$ or retained/selected from the hAM_{15-52} fragment, the following alignment shown in Table 1 applies. Thus, position X_1 in the hAM_{15-52} analogues according to the invention corresponds to the first amino acid in human amylin ($hAMY_{1-37}$) and amino acid number 15 (hAM_{15}) in the hAM_{15-52} fragment.

Position X_{1-38}	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
hAM_{15-52}	G	C	R	F	G	T	C	T	V	Q	K	L	A	H	Q	I	Y	Q	F	T	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	G	Y
$hAMY_{1-37}$	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S	N	N	F	-	G	A	I	L	S	S	T	N	V	G	S	N	T	Y

Table 1

According to the present invention, the hAM_{15-52} analogues are generally amidated at the C-terminal (-$CONH_2$), like the native peptides; amylin and adrenomedullin. However, the hAM_{15-52} analogues of the present invention may also have either a free carboxylic acid (-COOH) or another post-translational modification such as a methyl ester (-COOMe). In a highly preferred embodiment of the invention, the hAM_{15-52} analogues are amidated at the C-terminal. The hAM_{15-52} analogues according to the present invention may have a free amine (-NH_2), be N-acylated (-NHCOR), N-methylated (-$NHCH_3$ or -$N(CH_3)_2$) or deaminated at the N-terminal. The hAM_{15-52} analogues may also be lipidated, e.g. at the N-terminal as exemplified herein, depending on the desired half-life of the polypeptides.

According to the present invention, lipidation has the usual meaning in the art. Thus, lipidation in the present context refers to the covalent attachment of a lipid optionally through a linker to hAM_{15-52} analogues of the invention. Lipidation is typically performed to improve the pharmacokinetic profile of a polypeptide by e.g. improving metabolic stability, reducing enzymatic degradation, lowering excretion and metabolism, all in all resulting in a prolonged *in vivo* half-life ($t_{1/2}$) of the hAM_{15-52} analogues. The hAM_{15-52} analogues according to the invention may be lipidated or non-lipidated. The lipidated hAM_{15-52} analogues exemplified herein are lipidated with a saturated C_{20}-diacid through various linkers as shown in table 2.
According to the present invention, the abbreviations Hyp, Cit, Aib, Aad, (NMe)G/Sar, (NMe)I have the usual meaning in the art. Thus, Hyp refers to L-hydroxyproline, Cit refers to L-citrulline, Aib refers to 2-aminoisobutyric acid, Aad refers to L-homoglutamic acid, (NMe)G refers to N-methylglycine also known as Sar or sarcosine and (NMe)I refer to N-methyl-L-isoleucine.

According to the present invention, EC_{50} values are used as a measure of agonist potency at a given receptor. An EC_{50} value is a measure of the concentration of a compound required to achieve half of that compound's maximal activity in a particular assay. Thus, an hAM_{15-52} analogue according to the invention having an hAMY3R-EC_{50} lower than the hAMY3R-EC_{50} of hAM_{15-52} in the given assay is considered to have higher potency or activity at the hAMY3R receptor than the adrenomedullin fragment hAM_{15-52}. Likewise, an hAM_{15-52} analogue according to the invention having an hAM1R-EC_{50} higher than the hAM1R-EC_{50} of hAM_{15-52}, in the given assay may be considered to have lower potency or activity at the hAM1R receptor than the adrenomedullin fragment hAM_{15-52}.

According to the present invention, an hAM_{15-52} analogue or derivative thereof may be in the form of a pharmaceutically acceptable salt. Thus, pharmaceutically acceptable salts are intended to include any salts that are commonly used in formulations of peptides. Such salts include both acid addition salts and basic salts, and examples may be found e.g. in Remington's Pharmaceutical Sciences, 17th edition. Likewise, various solvates of the hAM_{15-52} analogues or pharmaceutically acceptable salts thereof are also within the scope of the invention.

According to the present invention, hAM_{15-52} analogues are short chains of amino acids that have been linked by amide bonds. In the most preferred embodiment of the invention, the hAM_{15-52} analogues are 38 amino acids in length, not including any amino acids that function as spacers between an optional lipid and the hybrid polypeptides.

In the present context, unless otherwise stated, the amino acids are all L-amino acids (L-stereoisomer, natural amino acids). Thus, the absolute configuration of the amino acids is the (*S*)-configuration with the exception of L-cysteine and L-selenocysteine having the (*R*)-configuration.

In the present context, it should be understood that the amino acid Cys (X_2) and Cys (X_7) in the hAM_{15-52} analogues are covalently connected by a bridge, preferably a disulfide bridge (-S-S-) such as present in $hAMY_{1-37}$ and hAM_{15-52}. The cyclization of the disulfide bridge may be performed after purification of the hybrid polypeptides or prior to cleavage from the resin in the solid-phase peptide synthesis, optionally in the presence of suitable protecting groups. The disulfide bridge may be formed spontaneously by stirring the hybrid polypeptide in the presence of oxygen or may be formed by treating the hybrid polypeptides with another suitable oxidant such as iodine (I_2), optionally in the presence of a base.

In the present context, the hAM_{15-52} analogues or derivatives thereof according to the first or second aspect have an hAMY3R potency (EC_{50}) ≤ 250 pM, such as ≤ 200 pM, preferably an hAMY3R-EC_{50} ≤ 150 pM, such as ≤ 125 pM, more preferably an hAMY3R-EC_{50} ≤ 100 pM, such as ≤ 75 pM, yet more preferably an hAMY3R-EC_{50} ≤ 50 pM, such as ≤ 25 pM, most preferably an hAMY3R-EC_{50} ≤ 15 pM, such as ≤ 10 pM. Thus, the most hAMY3R potent hAM_{15-52} analogues may be more or less equipotent with native human amylin $hAMY_{1-37}$. For example, SEQ ID NOs: 3-44 have an hAMY3R-EC_{50} between 6.0-10 pM and are thus

more or equipotent compared to $hAMY_{1-37}$ (hAMY3R-EC_{50} = 10 pM) when measured under the same assay conditions.

In the present context, the hAM_{15-52} analogues or derivatives thereof according to the second aspect have an abolished or reduced EC_{50} when the EC_{50} value on hAM1R ≥ 25 nM, such as EC_{50} value on hAM1R ≥ 50 nM, such as an hAM1R-EC_{50} ≥ 100 nM, preferably an hAM1R-EC_{50} ≥ 150 nM, such as ≥ 200 nM, more preferably hAM1R-EC_{50} ≥ 250 nM, such as ≥ 300 nM, even more preferably an hAM1R-EC_{50} ≥ 350 nM, such as ≥ 400 nM, yet more preferably an hAM1R-EC_{50} ≥ 450 nM, such as ≥ 500 nM, yet more preferably an hAM1R-EC_{50} ≥ 600 nM, such as ≥ 700 nM, yet more preferably an hAM1R-EC_{50} ≥ 800 nM, such as ≥ 900 nM, yet more preferably an hAM1R-EC_{50} ≥ 1000 nM, most preferably an hAM1R-EC_{50} ≥ 5000 nM. Thus, in the present context, selectively in terms of potency towards the amylin receptor hAMY3R over the adrenomedullin receptor hAM1R (i.e. a selective amylin receptor agonist) should be understood as an hAM_{15-52} analogue or a derivative thereof according to the second aspect having an hAMY3R-EC_{50} value ≤ 250 pM and an hAM1R-EC_{50} ≥ 25 nM. Thus, a selective hAM_{15-52} analogue or a derivative thereof has a selectivity ratio (hAM1R EC_{50}/hAMY3R EC_{50}) of at least 100. Preferably, the hAM_{15-52} analogues or derivatives thereof have an hAMY3R-EC_{50} value ≤ 250 pM and an hAM1R-EC_{50} ≥ 50 nM and thus a selectivity ratio (hAM1R EC_{50}/hAMY3R EC_{50}) ≥ 200. More preferably, the hAM_{15-52} analogues or derivatives thereof have an hAMY3R-EC_{50} ≤ 200 pM, an hAM1R-EC_{50} ≥ 100 nM and thus a selectivity ratio (hAM1R EC_{50}/hAMY3R EC_{50}) ≥ 500. More preferably, an hAM_{15-52} analogue or a derivative thereof has an hAMY3R-EC_{50} ≤ 125 pM, an hAM1R-EC_{50} ≥ 200 nM and thus a selectivity ratio (hAM1R EC_{50}/hAMY3R EC_{50}) ≥ 1600. Even more preferably, the hAM_{15-52} analogue or a derivative thereof has an hAMY3R-EC_{50} ≤ 100 pM, an hAM1R-EC_{50} ≥ 500 nM and thus a selectivity ratio (hAM1R EC_{50}/hAMY3R EC_{50}) ≥ 5000. Most preferably, the hAM_{15-52} analogue or a derivative thereof has an hAMY3R-EC_{50} ≤ 50 pM, an hAM1R-EC_{50} ≥ 1000 nM and thus a selectivity ratio (hAM1R EC_{50}/hAMY3R EC_{50}) ≥ 20000. For example, any of SEQ ID NOs: 3-42 have a selectivity ratio of at least 6000 and most of them much higher.

A person skilled in the art is well aware that EC_{50} values depend on the assay type and assay conditions. Thus, in the present context when the disclosure refers to an EC_{50} value, it should be understood as an EC_{50} value obtained when measured according to the procedure described in the examples under general protocols for cAMP assays for measuring *in vitro* receptor activation. However, variation may also be present within the same assay under apparently identical assay conditions due to variation in e.g. receptor expression in the cells (i.e. receptor density). Thus, in order to compare EC_{50} values, $hAMY_{1-37}$ (SEQ ID NO: 2) and hAM_{15-52} (SEQ ID NO: 1) have been tested as internal standards for comparison between different assay runs or even different assays. The hAMY3R-EC_{50} and the hAM1R-EC_{50} of $hAMY_{1-37}$ (SEQ ID NO: 2) was determined to 10 pM and 5000 nM, respectively, using the same assay conditions and cell line as the hAM_{15-52} analogues (SEQ ID NO: 3-392). Likewise, the hAMY3R-EC_{50} and the hAM1R-EC_{50} of the hAM_{15-52} (SEQ ID NO: 1) was determined to 1.3 nM and 1.1 nM, respectively, using the same assay conditions and cell line as the hAM_{15-52} analogues (SEQ ID NO: 3-392). Thus, it follows that the hAM_{15-52} analogues or derivatives thereof according to the first or second aspect have a relative hAMY3R-EC_{50} ratio

(hAMY3R-EC_{50})/(hAMY_{1-37}-hAMY3R-EC_{50}) ≤ (250 pM)/(10 pM) ≤ 25. Preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAMY_{1-37}-hAMY3R-EC_{50}) ≤ 20. More preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAM_{1-37}-hAMY3R-EC_{50}) ≤ 12.5. Even more preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAMY_{1-37}-hAMY3R-EC_{50}) ≤ 10. Even more preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAMY_{1-37}-hAMY3R-EC_{50}) ≤ 5. Yet more preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAMY_{1-37}-hAMY3R-EC_{50}) ≤ 2. Most preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAMY_{1-37}-AMY3R-EC_{50}) ≤ 1 such that the hAM_{15-52} analogues or derivatives thereof an equipotent or more potent than hAMY_{1-37}. Likewise, the selective hAM_{15-52} analogues or derivatives thereof according to the second aspect have a relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAM_{15-52}-AMY3R-EC_{50}) ≤ (250 pM)/(1300 pM) ≤ 0.19 and a relative hAM1R-EC_{50} ratio (hAM1R-EC_{50})/(hAM_{15-52}-hAM1R-EC_{50}) ≥ (25 nM)/(1.1 nM) ≥ 22.7. Preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAM_{15-52}-hAMY3R-EC_{50}) ≤ (250 pM)/(1300 pM) ≤ 0.19 and a relative hAM1R-EC_{50} ratio (hAM1R-EC_{50})/(hAM_{15-52}-hAM1R-EC_{50}) ≥ (50 nM)/(1.1 nM) ≥ 45.5. More preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAM_{15-52}-hAMY3R-EC_{50}) ≤ 0.15 and a relative hAM1R-EC_{50} ratio (hAM1R-EC_{50})/(hAM_{15-52}-hAM1R-EC_{50}) ≥ 76.9. Yet more preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAM_{15-52}-hAMY3R-EC_{50}) ≤ 0.096 and a relative hAM1R-EC_{50} ratio (hAM1R-EC_{50})/(hAM_{15-52}-hAM1R-EC_{50}) ≥ 154. Even more preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAM_{15-52}-hAMY3R-EC_{50}) ≤ 0.077 and a relative hAM1R-EC_{50} ratio (hAM1R-EC_{50})/(hAM_{15-52}-hAM1R-EC_{50}) ≥ 384. Yet more preferably, the relative hAMY3R-EC_{50} ratio (hAMY3R-EC_{50})/(hAM_{15-52}-AMY3R-EC_{50}) ≤ 0.038 and a relative hAM1R-EC_{50} ratio (hAM1R-EC_{50})/(hAM_{15-52}-hAM1R-EC_{50}) ≥ 769. Most preferably, the relative hAM1R-EC_{50} ratio (hAM1R-EC_{50})/(hAM_{15-52}-hAM1R-EC_{50}) ≥ 2000.

According to the present invention, the term "treatment" should be understood in the broadest sense as prevention, amelioration, or treatment. Thus, treatment is also intended to include prophylactic treatment.

According to the present invention, from the aspect(s)/embodiment(s) which refer to "*wherein hAM_{15-52} analogue has (e.g.) at least 50 % homology to hAM_{15-52} (SEQ ID NO: 1)*" or "*a derivative thereof with (e.g.) at least 50 % homology to hAM_{15-52}*", it should be understood that the hAM_{15-52} analogue or derivative thereof has at least 50 % sequence identity with hAM_{15-52} (SEQ ID NO: 1) when aligned. As an example, SEQ ID NO: 169 illustrated below differs in two amino acids (X_{11} and X_{38}) from hAM_{15-52} (SEQ ID NO: 1) and thus has (38-2)/38 = 94.7 % sequence identity to hAM_{15-52} (SEQ ID NO: 1).

SEQ ID NO:1 G C R F G T C T V Q K L A H Q I Y Q F T D K D K D N V A P R S K I S P Q G Y
Derivative X: G C R F G T C T V Q R L A H Q I Y Q F T D K D K D N V A P R S K I S P Q G Hyp

DETAILED DESCRIPTION OF THE INVENTION

The calcitonin peptide family

The calcitonin family of peptides consists of the hormone peptides calcitonin (CT), calcitonin gene-related peptide (CGRP), islet amyloid polypeptide (IAPP, amylin or $hAMY_{1-37}$), and adrenomedullin (hAM) as well as their precursors. $hAMY_{1-37}$ is a 37-residues peptide hormone that is co-secreted with insulin from the pancreatic β-cells with the amino acid sequence Lys-Cys-Asn-Thr-Ala-Thr-Cys-Ala-Thr-Gln-Arg-Leu-Ala-Asn-Phe-Leu-Val-His-Ser-Ser-Asn-Asn-Phe-Gly-Ala-Ile-Leu-Ser-Ser-Thr-Asn-Val-Gly-Ser-Asn-Thr-Tyr. Amylin supresses glucagon release and inhibits gastric emptying and hence plays an important role in maintaining glucose homeostasis by decreasing the blood sugar concentration. Furthermore, amylin has shown to reduce food intake and plays an important role in satiety, making it a potential candidate for treating e.g. obesity and/or diabetes. hAM is a 52-residues peptide hormone expressed in all tissues with the amino acid sequence Tyr-Arg-Gln-Ser-Met-Asn-Asn-Phe-Gln-Gly-Leu-Arg-Ser-Phe-Gly-Cys-Arg-Phe-Gly-Thr-Cys-Thr-Val-Gln-Lys-Leu-Ala-His-Gln-Ile-Tyr-Gln-Phe-Thr-Asp-Lys-Asp-Lys-Asp-Asn-Val-Ala-Pro-Arg-Ser-Lys-Ile-Ser-Pro-Gln-Gly-Tyr. It is a potent vasodilator and has shown positive influence in cardiovascular diseases, such as myocardial infarction, limb ischemia and hypertension.

The biological activity of the calcitonin protein family is generally mediated via binding to the calcitonin receptor (CTR) and the calcitonin receptor like receptor (CRLR), both belonging to family 2 of the G-protein-coupled receptors (GPCR). These receptors may be co-expressed in combination with different receptor modifying proteins (RAMP1-3) generating functional receptors for the individual peptides in the calcitonin protein family. Co-expression of CTR with RAMP1 leads to formation of a receptor for amylin and CGRP (AMY1R), co-expression of CTR with RAMP2 leads to the amylin receptor 2 (AMY2R) and co-expression of CTR with RAMP3 leads to the amylin receptor (AMY3R). Co-expression of CRLR with RAMP1 leads to a formation of a receptor for CGRP (CGRP1R), co-expression of CRLR with RAMP2 leads to a formation of a receptor for adrenomedullin (AM1R) and co-expression of CRLR with RAMP3 leads to a formation of a receptor for adrenomedullin and CGRP (AM2R).

Several of the native peptides in the calcitonin protein family show considerable overlap in pharmacology between receptors. For example, adrenomedullin is approximately 100 times less potent on AMY3R compared to $hAMY_{1-37}$. The adrenomedullin fragment (hAM_{15-52}) is almost equipotent on AMY3R and AM1R with an EC_{50} of 1.3 nM on AMY3R and an EC_{50} value of 1.1 nM on AM1R (said EC_{50} value being measured according to the examples herein). $hAMY_{1-37}$ on the other hand has an EC_{50} value of 10 pM on AMY3R while being inactive on AM1R.

Determination of important amino acid positions in hAM_{15-52}

The inventors initially hypothesized that since hAM_{15-52} and $hAMY_{1-37}$ belong to the same family of hormones, the Calcitonin/CGRP/IAPP family, the AMY3R potency of hAM_{15-52} could be improved or even converted into selective AMY3R agonism over hAM1R agonism, by substituting certain amino acids in

hAM_{15-52} with amino acids derived from $hAMY_{1-37}$, thereby overcoming some of the drawbacks that are inherent to $hAMY_{1-37}$. All 37 $hAMY_{1-37}$ amino acids were systematically substituted into the hAM_{15-52}. Furthermore, X_{38} was selected as Hyp (Hydroxyproline), which is neither present in $hAMY_{1-37}$ nor in hAM_{15-52}. The inventors constructed random forest models (Breiman, L. (2001), Random Forests, Machine Learning 45(1), 5-32.) describing the relationship between peptides sequence and hAMY3R and the hAM1R potency, respectively, and systematically synthesised and screened peptide sequences. For each hAM_{15-52} analogue, the amino acid in each sequence position were used as features, and receptor EC_{50} values were used as response to construct the models. The "randomForest" package implemented in the statistical programming language R was used to calculate the importance of each position and the most important positions were identified to be critical for hAMY3R and/or hAM1R activity (A. Liaw and M. Wiener (2002). Classification and Regression by randomForest. R News 2(3), 18-22.). Based on this systematic analysis the inventors identified X_4, X_{37} and X_{38} to be important for hAM1R activity, while of less importance for hAMY3R activity. The inventors identified X_{11} to be critical for hAMY3R activity, while of less importance for hAM1R activity. Finally, the inventors identified X_{17} to be of some importance for hAMY3R activity, while of less importance for hAM1R activity. Thus, the inventors identified X_{11} as a key position for improving hAMY3R potency in hAM_{15-52} and X_4, X_{37} and X_{38} as key positions for eliminating hAM1R potency in hAM_{15-52}. Since X_{17} was only of some importance for hAMY3R activity, this position was not considered a key position but only a preferred position to further improve the AMY3R potency of the hAM_{15-52} analogues.

The systematic investigation showed that the hAMY3R potency of hAM_{15-52} could be improved by substituting the amino acid K present in hAM_{15-52} in position X_{11} with the amino acid R present in $hAMY_{1-37}$. Furthermore, the systematic investigation showed that the hAM1R potency of hAM_{15-52} could be decreased by substituting the amino acids present in position X_4, X_{37} and X_{38} in hAM_{15-52} with the corresponding amino acids found in present in $hAMY_{1-37}$.

Deeper investigation of amino acids in the position X_4, X_{11}, X_{17}, X_{37} and X_{38}.

The inventors systematically substituted representative amino acids covering representative amino acids for all the known amino acids into the 5 identified positions, at one position at the time (Table 6). As shown in example 1, all (SEQ ID: 1-360 had lost their activity on the hAM1R, with varying degree of potency on AMY3R. In order to score the individual amino acids on the 5 positions, the average EC_{50} value for peptides containing a given amino acid in a given position was compared to the average EC_{50} value hAM_{15-52} analogues containing the reference amino acid in that position. Given a cut-off of 4-fold changes in potency, each amino acid in each position was scored as giving increased (I), decreased (D) or unchanged (U) potency, relative to the reference amino acid, on hAMY3R. The results are summarized in Table 6. From this data, it was shown that any of the amino acids R, W or Cit were capable of maintaining the AMY3R potency when present in position X_{11} when compared to the reference whereas other representative amino acids decreased the potency. It was further shown that any of the amino acids Y, W, T, M, I, F, A, or C in X_4, any of the amino acids Y, W, T, Q, P, M, I, H, F, E, A, R, C or K in X_{37} and any

of the amino acids Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K in X_{38} were able to maintain or improve AMY3R potency while remaining inactive on hAM1R.

Aspect 1: hAM_{15-52} analogues with improved amylin potency

Thus, in a first aspect, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising 38 amino acids (X_1-X_{38}) with an hAMY3R-$EC_{50} \leq 250$ pM, wherein the amino acid in position X_{11} is selected from R, W or Cit and wherein the hAM_{15-52} analogue has at least 50% homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, (SEQ ID NO: 1). From example 1 (Table 2), it can be seen that almost all of the synthesized hAM_{15-52} analogues have at least 50 % homology to hAM_{15-52}, that a vast majority of the synthesized hAM_{15-52} analogues have at least 60 % of homology to hAM_{15-52}, and that a large portion of the synthesized hAM_{15-52} analogues have at least 80 % homology to hAM_{15-52} (SEQ ID NO: 1). All of these hAM_{15-52} analogues maintain the good fibrillation properties of hAM_{15-52} (SEQ ID NO: 1) compared to $hAMY_{1-37}$ (SEQ ID NO: 2) (see example 2, Table 3). E.g., SEQ ID NO: 32 shows that the good physical stability (i.e. low fibrillation) of hAM_{15-52} can be maintained as long as the hAM_{15-52} analogues have at least 50 % homology to hAM_{15-52}.

Thus, in a first aspect, the invention relates to a way to highly improve the hAMY3R potency of the hAM_{15-52} fragment by a single substitution to R, W or Cit in position X_{11}, while maintaining the good physical stability (i.e. good fibrillation properties of hAM_{15-52}). These hAM_{15-52} analogues will therefore be highly potent agonists on both hAMY3R and hAM1R (see SEQ ID NO: 361-392).

In the most preferred embodiment of the invention, X_{11} is selected as R. In another embodiment, X_{11} is selected as W. In yet an embodiment, X_{11} is selected as Cit. The inventors found that this single amino acid substitution in X_{11} provided increased hAMY3R potency to the hAM_{15-52} analogue(s) while retaining hAM1R potency. The inventors further found that the hAMY3R potency could be maintained when X_{17} was Y, T, Q, M, I, F, A, R or K, or even further improved by selecting X_{17} as W or H. Thus, in an embodiment X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R or K. In a preferred embodiment, X_{17} is selected as Y, W or H, more preferably W or H.

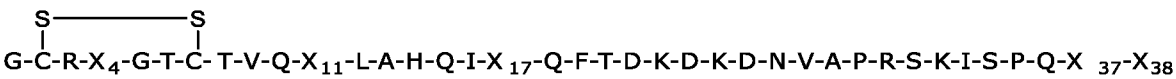
In an embodiment, the invention relates to an hAM_{15-52} analogue comprising 38 amino acids (X_1-X_{38}) or a pharmaceutically acceptable salt thereof, wherein the amino acid in position X_{11} is selected from R, W or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R or K, preferably X_{17} is selected as W or H and wherein the hAM_{15-52} analogue has at least 50 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52} (SEQ ID NO: 1).

In yet an embodiment, the invention relates to an hAM_{15-52} analogue comprising 38 amino acids (X_1-X_{38}) or a pharmaceutically acceptable salt thereof, wherein the amino acid in position X_{11} is R; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R or K, preferably X_{17} is selected as W or H and wherein the hAM_{15-52} analogue has at least 50% homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, (SEQ ID NO: 1).

In yet an embodiment, the invention relates to an hAM_{15-52} analogue comprising 38 amino acids (X_1-X_{38}) or a pharmaceutically acceptable salt thereof, wherein the amino acid in position X_{11} is W; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R or K, preferably X_{17} is selected as W or H and wherein the hAM_{15-52} analogue has at least 50% homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, (SEQ ID NO: 1).

In yet an embodiment, the invention relates to an hAM_{15-52} analogue comprising 38 amino acids (X_1-X_{38}) or a pharmaceutically acceptable salt thereof, wherein the amino acid in position X_{11} is Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R or K, preferably X_{17} is selected as W or H and wherein the hAM_{15-52} analogue has at least 50% homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, (SEQ ID NO: 1).

In a preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, Y, W, T, M, I, A, or C;

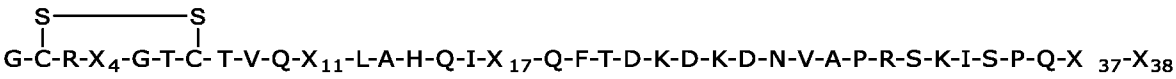
X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R, W, or Cit; X_{17} is

selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K.

In another preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, Y, W, T, M, I, A, or C;

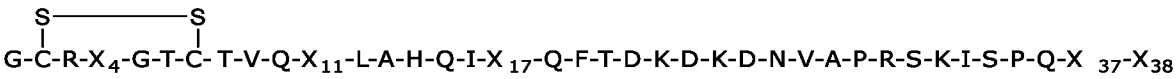
X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K.

In a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, or H;

X_4 is selected from F, Y, W, T, M, I, A, or C;

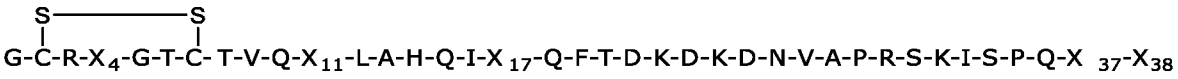
X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52} , wherein X_{11} is selected from R; X_{17} is selected as Y,

W, or H; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, or H;

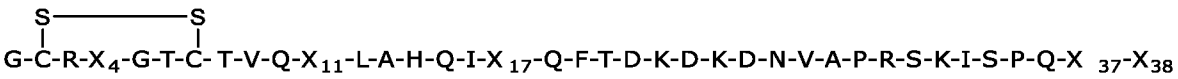
X_4 is selected from F, W, M, I, or C;

X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R; X_{17} is selected as Y, W, or H; X_4 is selected from F, W, M, I, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, or H;

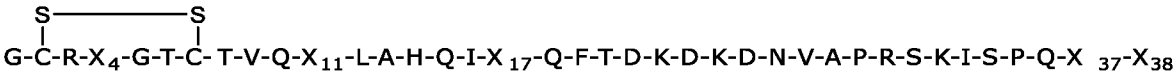
X_4 is selected from F, Y, W, T, M, I, A, or C;

X_{37} is selected from G, Y, W, P, H, or F;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, X_{11} is selected from R; X_{17} is selected as Y, W or H; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, W, P, H, or F; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, or H;

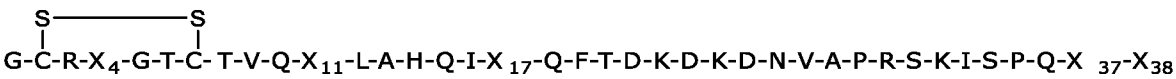
X_4 is selected from F, Y, W, T, M, I, A, or C;

X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

X_{38} is selected from Hyp, Y, W, M, or F;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R; X_{17} is selected as Y, W, or H; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, M, or F.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, or H;

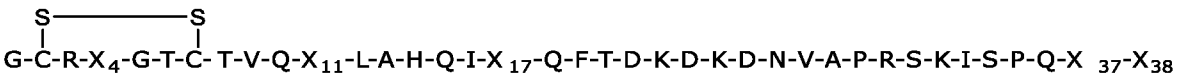
X_4 is selected from F, W, M, I, or C;

X_{37} is selected from G, Y, W, P, H, or F;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R; X_{17} is selected as Y, W or H; X_4 is selected from F, W, M, I, or C; X_{37} is selected from G, Y, W, P, H, or F; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, or H;

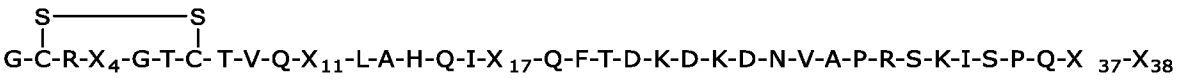
X_4 is selected from F, W, M, I, or C;

X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

X_{38} is selected from Hyp, Y, W, M, or F;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R; X_{17} is selected as Y, W, or H; X_4 is selected from F, W, M, I, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, M, or F.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, or H;

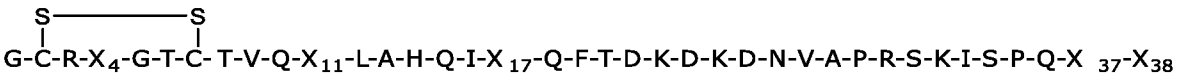
X_4 is selected from F, Y, W, T, M, I, A, or C;

X_{37} is selected from G, Y, W, P, H, or F;

X_{38} is selected from Hyp, Y, W, M, or F;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R; X_{17} is selected as Y, W, or H; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, W, P, H, or F; X_{38} is selected from Hyp, Y, W, M, or F.

In yet an even more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R;

X_{17} is selected as Y, W, or H;

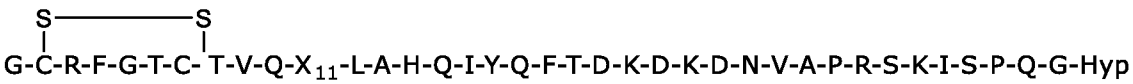
X_4 is selected from F, W, M, I, or C;

X_{37} is selected from G, Y, W, P, H, or F;

X_{38} is selected from Hyp, Y, W, M, or F;

or a derivative thereof with at least 50% homology to hAM_{15-52}, preferably at least 60% homology to hAM_{15-52}, such as at least 70% homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, even more preferably at least 85 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R; X_{17} is selected as Y, W or H; X_4 is selected from F, W, M, I, or C; X_{37} is selected from G, Y, W, P, H, or F; X_{38} is selected from Hyp, Y, W, M, or F.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue comprising the amino acid sequence of formula (I):



(I)

wherein, X_{11} is selected from R, W, or Cit

or a derivative thereof with at least 50% homology to hAM_{15-52}, least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, most preferably at least 90 % homology to hAM_{15-52} to hAM_{15-52}, such as at least 95 % homology to hAM_{15-52}, wherein, X_{11} is selected from R, W, or Cit.

In a most preferred embodiment, the invention relates to an hAM_{15-52} analogue of SEQ ID NO: 3-392 or a derivative thereof with at least 90 % homology to any one of SEQ ID NO: 3-392, preferably at least 95 % homology any one of SEQ ID NO: 3-392, more preferably at least 96 % homology any one of SEQ ID NO: 3-392 most preferably at least 97 % homology any one of SEQ ID NO: 3-392 with the proviso that a derivative thereof has R, W, or Cit in position X_{11}, preferably R in position X_{11}.

In yet a most preferred embodiment, the invention relates to an hAM_{15-52} analogue of SEQ ID NO: 3-392 or a derivative thereof with at least 90 % homology to any one of SEQ ID NO: 3-392, preferably at least 95 % homology to any one of SEQ ID NO: 3-392, more preferably at least 96 % homology any one of SEQ ID NO: 3-392, most preferably at least 97 % homology any one of SEQ ID NO: 3-278, with the proviso that a derivative thereof has the same amino acid in position X_{11}, as the respective SEQ ID NO: 3-392 from it is derived.

Aspect 2: Selective hAM_{15-52} analogues with improved amylin potency

Number of positions needed to abolish or reduce AM1R potency in hAM_{15-52}.

The inventors found that hAM1R potency could be abolished or reduced in hAM_{15-52} by changing at least one amino acid in any of the positions X_4, X_{37} or X_{38} since all of them were critical for hAM1R potency.

Decreasing hAM1R potency with amino acids in position X_4, X_{37} or X_{38}.

X_4: The inventors found that the amino acids Y, W, T, M, I, A or C in position X_4 were capable of decreasing the hAM1R potency. Thus, in an embodiment, X_4 is selected from Y, W, T, M, I, A or C. Furthermore, the amino acids W, M, I or C in position X_4 were most effective at improving hAMY3R potency (see example 5, table 6). Thus, in a highly preferred embodiment of the invention, X_4 is selected as W, M, I or C. Since the inventors found that a single position chosen among *X_4, X_{37} or X_{38}* was enough to abolish or reduce AM1R potency it follows that in some embodiments X_4 is F (i.e. the native amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position) and the AM1R potency is abolished or reduced using position *X_{37} and/or X_{38}*. Thus, in any of the above embodiments for X_4, F may be included and the AM1R potency abolished or reduced using position X_7 and/or X_{38}.

X_{37}: Likewise, the inventors found that the amino acids Y, S, W, T, Q, P, M, I, H, F, E, A, R, C in position X_{37} were capable of decreasing the hAM1R potency. Thus, in an embodiment, X_{37} is selected from Y, S, W, T, Q, P, M, I, H, F, E, A, R, C. Furthermore, the amino acids Y, W, P, H or F in position X_{37} were most effective at improving hAMY3R potency (see example 5, table 6). Thus, in a highly preferred embodiment of the invention, X_{37} is selected as Y, W, P, H or F. Since the inventors found that a single position chosen among *X_4, X_{37} or X_{38}* was enough to abolish or reduce AM1R potency it follows that in some embodiments X_{37} is G (i.e. the native amino present in hAM_{15-52} (SEQ ID NO: 1) in said position), and the AM1R potency is abolished or reduced using position *X_4 and/or X_{38}*. Thus, in any of the above embodiments for X_{37}, G may be included and the AM1R potency abolished or reduced using position X_4 and/or X_{38}.

X_{38}: Likewise, the inventors found that the amino acids Hyp, W, T, Q, P, M, I, H, F, E, A, R, or K in position X_{38} were capable of decreasing the hAM1R potency. Thus, in an embodiment, X_{38} is selected from Hyp, W, T, Q, P, M, I, H, F, E, A, R, or K. Furthermore, the amino acids Hyp, W, M or F were most effective at improving hAMY3R potency (see example 5, table 6). Thus, in a highly preferred embodiment of the invention, X_{38} is selected as Hyp, W, M or F. In the most preferred embodiment of the invention, X_{38} is selected as Hyp. Since the inventors found that a single position chosen among *X_4, X_{37} or X_{38}* was enough to abolish or reduce AM1R potency it follows that in some embodiments X_{38} is Y (i.e. the native amino present in hAM_{15-52} (SEQ ID NO: 1) in said position), and the AM1R potency is abolished or reduced using position *X_4 and/or X_{37}*. Thus, in any of the above embodiments for X_{38}, Y may be included and the AM1R potency abolished or reduced using position X_4 and/or X_{37}.

A simple illustration of aspect 2 of the invention can be seen by comparing the alignment of hAM_{15-52} (SEQ ID NO: 1) and SEQ ID NO: 169 shown below.

SEQ ID NO:1 G C R F G T C T V Q K L A H Q I Y Q F T D K D K D N V A P R S K I S P Q G Y
SEQ ID NO:169 G C R F G T C T V Q R L A H Q I Y Q F T D K D K D N V A P R S K I S P Q G Hyp
SEQ ID NO:1 hAMY3R EC_{50} 1.274 nM and hAM1R EC_{50} 1.113 nM
SEQ ID NO:169 hAMY3R EC_{50} 0.063 nM and hAM1R EC_{50} 2981.0 nM

As can be seen, the R in position X_{11} has improved the potency on AMY3R approximately 20-fold, and the Hyp in position X_{38} has decreased the potency on AM1R approximately 2500-fold. Therefore, only two substitutions have converted hAM_{15-52} into an amylin agonist with same pharmacological profile as $hAMY_{1-37}$. At the same time, SEQ ID NO: 169 has maintained the physical stability (ThT signal: 2.700 %) of hAM_{15-52} (ThT signal: 2.600 %) compared to $hAMY_{1-37}$ (ThT signal: 100.0 %) (see example 2, Table 3).
Thus, in a second aspect, the invention relates to a way to more or less completely abolish hAM1R potency of the hAM_{15-52} fragment by one or more substitutions in position X_4, X_{37} and/or X_{38} and at the same time improve or maintain sufficient AMY3R potency. These hAM_{15-52} analogues will therefore be highly potent and selective hAMY3R analogues. At the same time these hAM_{15-52} analogues maintain the physical stability of hAM_{15-52} due to the sequence homology (identity) with hAM_{15-52}. As shown in example 2, Table 3, the good physical stability of hAM_{15-52} may be maintained or even improved in the peptides (due to at least 50 % homology to hAM_{15-52}), while providing new hAMY3R agonists that are as potent and selective as natural human amylin. In other words, the second aspect of the present invention has created a functional human amylin analogue disguised in an adrenomedullin backbone.

Increasing hAMY3R potency with amino acids in position X_{17}.
The inventors further found that the hAMY3R potency could be maintained when X_{17} as Y, T, Q, M, I, F, A, R, or K, or even further improved when X_{17} was W or H. Thus, in an embodiment, X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K. In a preferred embodiment, X_{17} is selected as W, or H.

Thus, in a second aspect, the invention relates to hAM_{15-52} analogues comprising 38 amino acids (X_1-X_{38}) or a pharmaceutically acceptable salt thereof, wherein the amino acid in position X_{11} is selected from R, W or Cit and wherein the hAM_{15-52} analogue has at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52}, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, most preferably at least 90 % homology to hAM_{15-52}, such as at least 95 % homology to hAM_{15-52} (SEQ ID NO: 1) and further wherein X_4 is selected as F, Y, W, T, M, I, A or C; X_{37} is selected as G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C or K; X_{38} is selected as Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K, with the proviso that at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position, more preferably, at least two of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position. In the second aspect, the hAM_{15-52} analogues have an hAMY3R-$EC_{50} \leq 250$ pM and an hAM1R-$EC_{50} \geq 25$ nM.

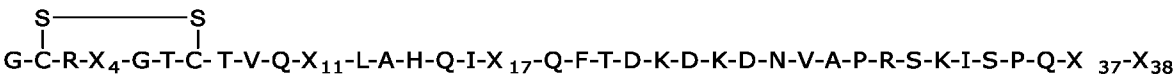
In an embodiment, X_4 is selected as F, W, M, I or C; X_{37} is selected as G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected as Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K, with the proviso that at least one of the positions X_4, $X_{37,}$ or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position, more preferably, at least two of the positions X_4, $X_{37,}$ or X_{38} are not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In an embodiment, X_4 is selected as F, Y, W, T, M, I, A or C; X_{37} is selected as G, Y, W, P, H or F; X_{38} is selected as Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K, with the proviso that at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position, more preferably, at least two of the positions X_4, X_{37} or X_{38} are not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In an embodiment, X_4 is selected as F, Y, W, T, M, I, A or C; X_{37} is selected as G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C or K; X_{38} is selected as Hyp, Y, W, M or F, with the proviso that at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position, more preferably, at least two of the positions X_4, $X_{37,}$ or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In an embodiment, X_4 is selected as F, W, M, I, or C; X_{37} is selected as G, Y, W, P, H, or F; X_{38} is selected as Hyp, Y, W, M or F, with the proviso that at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position, more preferably, at least two of the positions X_4, $X_{37,}$ or X_{38} are not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In a preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, K;

X_4 is selected from F, Y, W, T, M, I, A, or C;

X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

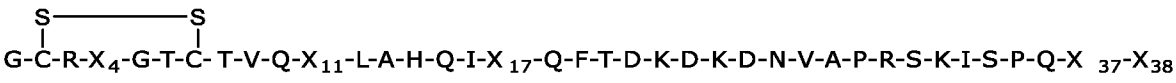
X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;

or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to $hAM_{15-52,}$ preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to $hAM_{15-52,}$, more

preferably at least 80 % homology, even more preferably at least 85 % homology, such as at least 90 % homology, most preferably at least 95 % homology, wherein X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, K; X_4 is selected from F, Y, W, T, M, I, A or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R or K;

X_4 is selected from F, W, M, I or C;

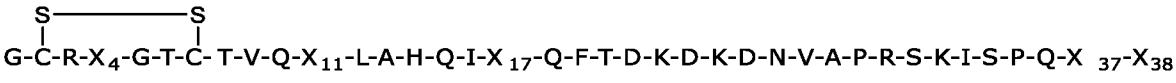
X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C or K;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;

or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology, such as at least 85 % homology, more preferably at least 90 % homology, most preferably at least 95 % homology, wherein X_{11} is selected from R, W or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R or K; X_4 is selected from F, W, M, I or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In another more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, Y, W, T, M, I, A, or C;

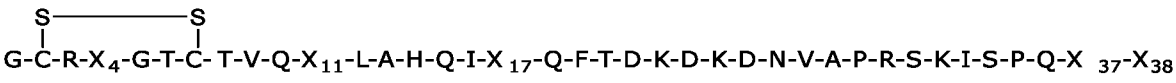
X_{37} is selected from G, Y, W, P, H, or F;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;

or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology, such as at least 85 % homology, more preferably at least 90 % homology, most preferably at least 95 % homology, wherein X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, W, P, H, or F; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37}, or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, Y, W, T, M, I, A, or C;

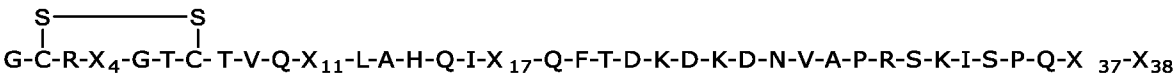
X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

X_{38} is selected from Hyp, Y, W, M, or F;

and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;

or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology, such as at least 85 % homology, more preferably at least 90 % homology, most preferably at least 95 % homology, wherein X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, M, or F; and further wherein at least one of the positions X_4, X_{37}, or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In yet a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, W, M, I, or C;

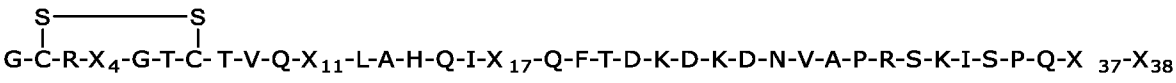
X_{37} is selected from G, Y, W, P, H, or F;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;

or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, more preferably at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, W, M, I, or C; X_{37} is selected from G, Y, W, P, H, or F; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In a preferred embodiment of the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, W, M, I, or C;

X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

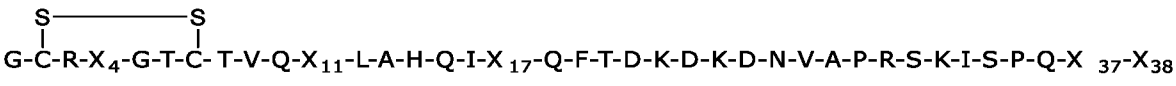
X_{38} is selected from Hyp, Y, W, M, or F;

and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;

or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, more preferably at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52},

wherein X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, W, M, I, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, M, or F; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In a preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, Y, W, T, M, I, A, or C;

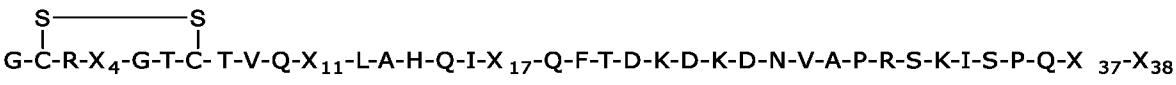
X_{37} is selected from G, Y, W, P, H, or F;

X_{38} is selected from Hyp, Y, W, M, or F;

and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;

or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology, such as at least 85 % homology to hAM_{15-52}, more preferably at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A or C; X_{37} is selected from G, Y, W, P, H or F; X_{38} is selected from Hyp, Y, W, M, or F; and further wherein at least one of the positions X_4, X_{37}, or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In a more preferred embodiment, the invention relates to an hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, W, M, I, or C;

X_{37} is selected from G, Y, W, P, H, or F;

X_{38} is selected from Hyp, Y, W, M, or F;
and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;
or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology to hAM_{15-52}, such as at least 85 % homology to hAM_{15-52}, more preferably at least 90 % homology to hAM_{15-52}, most preferably at least 95 % homology to hAM_{15-52}, wherein X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, W, M, I, or C; X_{37} is selected from G, Y, W, P, H, or F; X_{38} is selected from Hyp, Y, W, M, or F; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In any of the above-mentioned embodiments, X_{11} is most preferably R, and/or X_{17} is most preferably Y, W, or H. Furthermore, in any of the above-mentioned embodiments, most preferably at least two of the positions X_4, X_{37} or X_{38} are not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In a more highly preferred embodiment, the invention relates to an hAM_{15-52} analogue with the sequence SEQ ID NOs: 3-360 or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52} (SEQ ID NO: 1), wherein, in the derivative, X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, S, W, T, Q, P, Mv, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In yet a more highly preferred embodiment, the invention relates to an hAM_{15-52} analogue with the sequence SEQ ID NOs: 3-360 or a derivative thereof with at least 90 % homology (identity) to any one of SEQ ID NO: 3-360, preferably at least 95 % homology to any one of SEQ ID NO: 3-360, most preferably at least 97 % homology to anyone of SEQ ID NOs: 3-360, with the proviso that in the derivative, X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In any of the above-mentioned embodiments, X_4 is preferably selected as F, W, M, I, or C; X_{11} is preferably selected as R; X_{37} is preferably selected as G, Y, W, P, H, or F; X_{38} is preferably selected as Hyp, Y, W, M,

or F; X_{17} is preferably selected as W or H. Furthermore, in any of the above-mentioned embodiments, most preferably at least two of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

In the most preferred embodiment, the invention relates to an hAM_{15-52} analogue with the sequence SEQ ID NOs: 3-360 or a derivative thereof with at least 90 % homology (identity) to anyone of SEQ ID NOs: 3-360, preferably at least 95 % homology to anyone of SEQ ID NOs: 3-360, most preferably at least 97 % homology to anyone of SEQ ID NOs: 3-360, with the proviso that a derivative thereof has the same amino acids in positions X_4, X_{11}, X_{37}, and X_{38}, preferably the same amino acids in position X_4, X_{11}, X_{17}, X_{37}, and X_{38}, as the respective hAM_{15-52} analogue of SEQ ID NO: 3-360 from which it is derived.

Medical use

In a third aspect, the invention relates to hAM_{15-52} analogues according to the first and/or second aspect for use as a medicament. More particularly, the third aspect of the invention relates to hAM_{15-52} analogues according to the first and/or second aspect for use in treating, preventing or ameliorating a variety of diseases, disorders or conditions, such as but not limited to excess food intake, excess body weight, obesity, Binge eating disorder, Prader-Willi syndrome, dyslipidemia, metabolic diseases/disorders, diabetes I or II, impaired glucose tolerance, insulin resistance syndrome and/or NASH. A preferred embodiment relates to one or more hAM_{15-52} analogue(s) for use in the treatment of obesity, diabetes, NASH or combinations thereof.

Pharmaceutical compositions

In a fourth aspect, the invention relates to pharmaceutical compositions comprising one or more of the hAM_{15-52} analogues according to the first and/or second aspect and their medical use(s) in treating, preventing, or ameliorating a variety of diseases, disorders or conditions according to the third aspect. The pharmaceutical compositions may comprise a pharmaceutically acceptable carrier (vehicle) and/or one or more excipient(s) in accordance with conventional techniques in the art, such as those disclosed in 'Remington: Essentials of Pharmaceutics', Ed. by Linda A. Felton, Pharmaceutical press 2012.

Suitable formulations include but are not limited to tablets, pills, capsules, emulsions, suspensions, sustained release, or solutions. It should be appreciated that different routes of administration may be used depending on the choice of formulation and chemical and/or metabolic stability of the polypeptides. Such administration routes may include but are not limited to oral administration, parenteral administration (intravenous (IV), subcutaneous (SC), intradermal (ID) and intramuscular (IM)), or inhalation. In a preferred embodiment of the invention, the administration route is parental administration. In an even more preferred embodiment, the administration route is subcutaneous.

Method of treatment

In a fifth aspect, the invention relates to a method of treating a human or animal subject with one or more hAM_{15-52} analogue(s) according to the first and/or second aspect, wherein the human or animal subject is diagnosed with or suffering from one or more of the diseases, disorders according to the third aspect. The method involves administering one or more compounds according to a first and/or second aspect in an effective therapeutic amount to treat diseases, disorders or conditions mentioned in the third aspect. In some instances, a human or animal subject may benefit more from an hAM_{15-52} analogue having potency on both hAMY3R/hAM1R, e.g. when the patient is in high risk of cardiovascular disease and cardioprotective effects are desired. Thus, in an embodiment, the human or animal subject is treated with one or more hAM_{15-52} analogue(s) having mixed hAMY3R/hAM1R potency, such as those exemplified in SEQ ID: 361-392. Likewise, in some instances a human or animal subject may benefit most from a selective hAMY3R hAM_{15-52} analogue. Thus, in an embodiment, the human or animal subject is treated with one or more selective hAMY3R hAM_{15-52} analogue(s), such as those exemplified in SEQ ID: 3-360.

EXAMPLES

General protocols for synthesis of the hybrid polypeptides

The peptides were synthesized using a SyroII fully automated parallel peptide synthesizer (MultiSynTech GmbH, Germany), equipped with heating block, on Tentagel S RAM with a loading of 0.23-0.25 mmol/g (Rapp polymer GmbH, Germany). N^{α}-Fmoc deprotection was performed in two stages by treating the resin with 40 % piperidine/DMF (0.2 M HOBt (1-hydroxybenzotriazole)) for 3 min at 45°C followed by 20 % piperidine/DMF (0.1 M HOBt) for 7-12 min at 75°C. Except Asp, Cys and His residues which were N^{α}-Fmoc deprotections at room temperature; i.e. 40 % piperidine/DMF (0.2 M HOBt) for 3 min followed by 20 % piperidine/DMF (0.1 M HOBt) for 15 min. The coupling chemistry was DIC (N,N'-diisopropyl-carbodiimide)/Oxyma (ethyl cyano(hydroxyimino)acetate) in DMF using amino acid solutions of 0.5 M in DMF and a molar excess of 6-fold. Standard Fmoc protected amino acids were used. Coupling conditions was single or double couplings for 15 min at 75°C. Except His and Cys residues, which were double coupled for 15 min at 50°C. The Fmoc-amino acids were dissolved at 0.5 M in DMF containing 0.5 M Oxyma, except His which was dissolved in NMP. The resin was washed 4x with NMP after N^{α}-Fmoc deprotection and 3x after couplings.

The disulfide bridge was formed on the resin by using Trityl (Trt) as the protecting group for cysteine and treating with 1 % iodine in 75 % HFIP (Hexafluoroisopropanol) in DCM for 1 min. The resin was washed 3x with 75 % HFIP in DCM followed by 4x DCM.

After synthesis, the resin was washed with DCM and dried, and the polypeptide was cleaved from the resin by a 35 min treatment with TFA (trifluoroacetic acid)/TES (triethylsilane)/water (95/2.5/2.5) at 42°C, followed by precipitation with 4 volumes of cold diethyl ether, further washing with diethyl ether and left to dry.

The peptides were characterized by LC-MS (Waters, Denmark) and quantified by LC-CAD (ThermoFisher scientific, Denmark). Finally, the peptides were freeze dried to give a white powder using a Telstar benchtop freeze drier.

General protocols for cAMP assays for measuring in vitro receptor activation

hAMY3-R:

Cells stably overexpressing the hAMY3 receptor were obtained from Ogeda (now Astellas Pharma), sub-cloned and a monoclonal cell-line with an appropriate assay-window was expanded, aliquoted and frozen. An aliquot was thawed and plated in DPBS with 0.05 % casein and 0.5 mM IBMX as 2000 cells/well in a 384-well format. The cells were then immediately stimulated for 30 min at room temperature with graded doses of test compound using human amylin (Bachem, cat no. H-7905) as a positive control. cAMP accumulation was measured using a Cisbio assay for Gs coupled receptors (cat. no. 62AM4PEC), where the assay reagents were added as per the manufacturer's instructions and time-resolved fluorescence energy transfer recorded after one hour.

hAM1-R:

Cells stably overexpressing the hAM1 receptor were obtained from Ogeda (now Astellas Pharma), sub-cloned and a monoclonal cell-line with an appropriate assay-window was expanded, aliquoted and frozen. An aliquot was thawed and plated in DPBS with 0.05 % casein and 0.5 mM IBMX as 8000 cells/well in a 384-well format. The cells were then immediately stimulated for 30 min at room temperature with graded doses of test compound using human adrenomedullin 1-52 (Bachem, cat no. H-2932) as a positive control. cAMP accumulation was measured using a Cisbio assay for Gs coupled receptors (cat. no. 62AM4PEC), where the assay reagents were added as per the manufacturer's instructions and time-resolved fluorescence energy transfer recorded after one hour.

General protocols for determination of physical stability of peptide analogues

Peptides were dissolved in buffers (50 mM sodium acetate at pH 4 or 50 mM sodium phosphate at pH 7) and incubated for one hour. The samples were then divided into two replicates of 80 µl in a black 384 well plate (µ-clear, Greiner Bio-One) and mixed with Thioflavin T (ThT) to a final concentration of 4 µM. The plate was sealed and placed in a plate reader (CLARIOstar, BMG) where the temperature was set at 40°C during the course of the experiment. The samples were further stressed by shaking the plate at 700 rpm (linear) for five minutes before every measurement. The fluorescence was measured every 10 min for four days by exciting the ThT at 450 nm and measuring the emission at 480 nm. For each peptide, the ThT signal over time was smoothened using Local Polynomial Regression fitting (LOESS) as implemented in the statistical programming environment R. For the smoothened data, the maximum ThT signal was normalized in percent between the maximum ThT signal for hAMY and the buffer background. Thus, high values indicate fibrillation properties similar to hAMY while low values indicate no fibrillation.

General protocols for acute food intake study

The effect on cumulative food intake was measured in in male Sprague Dawley rats (6 weeks of age, Taconic, Denmark) following a single dose using a fully automated food intake monitoring system (HM-2; MBRose ApS, Faaborg, Denmark), allowing for advanced synchronous real-time monitoring of food intake behaviour of individual animals. The animals were housed in groups of 4 in a light-, temperature-, and humidity-controlled room (a 12/12 LD cycle, lights on at 02:00 AM; 22 ± 2 ◦C; 50 % relative humidity). The mice had ad libitum access to regular chow diet (Altromin 1324, Brogaarden A/S, Lynge, Denmark) and domestic quality tap water. Mice arrived at day 7, and a minimum of 5 days of habituation to the system was allowed prior to beginning of the study. During these days, the animals were handled daily to accustom them to the experimental paradigm. On the day of dosing, the animals were randomized into groups according to body weight. Animals were fasted for four hours prior to dosing. Animals were dosed SC 30 or 180 min prior to lights out, and food intake data were collected automatically for a total of 48 h post-dosing with automatic food recordings every 5 min.

General protocols for chronic diet-induced obesity (DIO) study

Sprague-Dawley rats (Taconic, Denmark) arrived at the age of 5 weeks. After one week of acclimation, they were evenly grouped based on their baseline body weight and offered ad libitum access a two-choice diet consisting of chow pellet (Altromin #1324, Brogaarden, Lynge, Denmark) and a high palatable high sugar/fat diet (1:1:1 mixture of Nutella (Ferrero, Alba, Italy), peanut butter (PCD, Rotterdam, Netherlands) and powdered standard chow (Altromin #1324, Brogaarden, Lynge, Denmark); 29.3 % fat, 33.2 % carbohydrate, and 18 % protein) for up to 36 weeks. The rats were pair-housed throughout the study under controlled environmental conditions (12-hour light/dark cycle, lights off at 15:00; 22 ± 1 °C; 50 ± 10% relative humidity). Body weight, food and water intake were monitored daily during the entire period of the study. One day before the experiment, the rats were randomized according to body weight into experimental groups (n = 9-10), which received compound or vehicle SC. QD (once daily) for 28 days.

Example 1

EC_{50} values at hAMY3R and hAM1R were measured according to the general protocol above. Percent homology (identity) for the hAM_{15-52} analogues were calculated in comparison to hAM_{15-52}. The results are summarized in Table 2 below.

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
1	1.274	1.113	100.0	None	NA
2	0.01	>5000.000	18.4	None	NA
3	0.006	123.548	73.7	None	NA
4	0.006	>5000.000	63.2	C20DA-yGlu	1

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
5	0.006	>5000.000	63.2	C20DA-yGlu	1
6	0.006	>5000.000	63.2	C20DA-yGlu-OEG-OEG	36
7	0.006	>5000.000	63.2	None	NA
8	0.006	>5000.000	44.7	None	NA
9	0.006	>5000.000	44.7	None	NA
10	0.007	551.970	68.4	None	NA
11	0.007	>5000.000	63.2	C20DA-yGlu	1
12	0.007	>5000.000	60.5	C20DA-yGlu-OEG-OEG	27
13	0.007	>5000.000	63.2	None	NA
14	0.007	>5000.000	63.2	None	NA
15	0.007	>5000.000	50.0	None	NA
16	0.008	125.467	78.9	None	NA
17	0.008	294.942	71.1	None	NA
18	0.008	817.242	68.4	None	NA
19	0.008	>5000.000	28.9	None	NA
20	0.008	>5000.000	71.1	None	NA
21	0.008	>5000.000	63.2	C20DA-yGlu	1
22	0.008	>5000.000	63.2	C20DA-yGlu	1
23	0.008	>5000.000	63.2	None	NA
24	0.008	>5000.000	63.2	None	NA
25	0.008	>5000.000	63.2	None	NA
26	0.008	>5000.000	63.2	None	NA
27	0.008	>5000.000	63.2	None	NA
28	0.008	>5000.000	65.8	None	NA
29	0.008	>5000.000	55.3	None	NA
30	0.008	>5000.000	63.2	None	NA
31	0.008	>5000.000	60.5	None	NA
32	0.008	>5000.000	50.0	None	NA
33	0.008	>5000.000	52.6	None	NA
34	0.009	54.627	73.7	None	NA
35	0.009	>5000.000	63.2	C20DA-yGlu	1
36	0.009	>5000.000	63.2	C20DA-yGlu-OEG-OEG	3
37	0.010	>5000.000	63.2	C20DA-yGlu	1
38	0.010	>5000.000	63.2	C20DA-yGlu	1

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
39	0.010	>5000.000	65.8	C20DA-yGlu	1
40	0.010	>5000.000	60.5	C20DA-yGlu-OEG-OEG	25
41	0.010	>5000.000	60.5	C20DA-yGlu-OEG-OEG	26
42	0.010	>5000.000	63.2	None	NA
43	0.010	>5000.000	63.2	None	NA
44	0.010	>5000.000	63.2	None	NA
45	0.011	50.470	86.8	None	NA
46	0.011	78.480	86.8	None	NA
47	0.011	500.000	63.2	C20DA-yGlu	1
48	0.011	760.539	63.2	C20DA-yGlu	1
49	0.011	2981.000	81.6	None	NA
50	0.011	>5000.000	65.8	C20DA-yGlu	1
51	0.011	>5000.000	63.2	C20DA-yGlu	1
52	0.011	>5000.000	63.2	None	NA
53	0.011	>5000.000	63.2	None	NA
54	0.012	46.194	81.6	None	NA
55	0.012	63.776	63.2	C20DA-yGlu	1
56	0.012	103.250	73.7	None	NA
57	0.012	590.397	63.2	C20DA-yGlu	1
58	0.012	>5000.000	21.1	None	NA
59	0.012	>5000.000	26.3	None	NA
60	0.012	>5000.000	68.4	C20DA-yGlu	1
61	0.012	>5000.000	63.2	C20DA-yGlu	1
62	0.012	>5000.000	63.2	C20DA-yGlu	1
63	0.012	>5000.000	63.2	C20DA-yGlu	1
64	0.012	>5000.000	63.2	None	NA
65	0.012	>5000.000	57.9	None	NA
66	0.012	>5000.000	60.5	None	NA
67	0.013	116.497	71.1	C20DA-yGlu	1
68	0.013	254.722	68.4	C20DA-yGlu	1
69	0.013	680.331	60.5	C20DA-yGlu	1
70	0.013	2981.000	84.2	None	NA

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
71	0.013	>5000.000	60.5	C20DA-yGlu	1
72	0.013	>5000.000	63.2	C20DA-yGlu	1
73	0.013	>5000.000	63.2	C20DA-yGlu	1
74	0.013	>5000.000	63.2	C20DA-yGlu-OEG-OEG	14
75	0.013	>5000.000	65.8	None	NA
76	0.014	>5000.000	13.2	C20DA-yGlu	1
77	0.014	>5000.000	65.8	C20DA-yGlu	1
78	0.014	>5000.000	60.5	C20DA-yGlu	1
79	0.014	>5000.000	60.5	C20DA-yGlu	1
80	0.015	44.303	15.8	C20DA-yGlu	1
81	0.015	138.500	84.2	None	NA
82	0.015	612.158	63.2	C20DA-yGlu	1
83	0.015	815.473	63.2	C20DA-yGlu	1
84	0.015	2981.000	81.6	None	NA
85	0.015	>5000.000	63.2	C20DA-yGlu	1
86	0.015	>5000.000	60.5	C20DA-yGlu	1
87	0.015	>5000.000	60.5	C20DA-yGlu	1
88	0.015	>5000.000	60.5	C20DA-yGlu	1
89	0.015	>5000.000	60.5	C20DA-yGlu-OEG-OEG	20
90	0.016	58.530	81.6	None	NA
91	0.016	839.591	63.2	C20DA-yGlu	1
92	0.016	932.795	60.5	C20DA-yGlu	1
93	0.016	>5000.000	28.9	None	NA
94	0.016	>5000.000	60.5	C20DA-yGlu	1
95	0.016	>5000.000	60.5	C20DA-yGlu	1
96	0.016	>5000.000	60.5	C20DA-yGlu	1
97	0.016	>5000.000	63.2	C20DA-yGlu	1
98	0.017	66.880	86.8	None	NA

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
99	0.017	364.198	71.1	C20DA-yGlu	1
100	0.017	>5000.000	60.5	C20DA-yGlu	1
101	0.017	>5000.000	63.2	None	NA
102	0.018	>5000.000	71.1	None	NA
103	0.018	>5000.000	63.2	C20DA-yGlu	1
104	0.018	>5000.000	63.2	C20DA-yGlu	1
105	0.018	>5000.000	60.5	C20DA-yGlu	1
106	0.018	>5000.000	60.5	C20DA-yGlu	1
107	0.019	646.950	60.5	C20DA-yGlu	1
108	0.019	>5000.000	60.5	C20DA-yGlu	1
109	0.020	2981.000	84.2	None	NA
110	0.020	>5000.000	63.2	C20DA-yGlu	1
111	0.021	2981.000	89.5	None	NA
112	0.021	>5000.000	60.5	C20DA-yGlu	1
113	0.022	2981.000	89.5	None	NA
114	0.022	>5000.000	63.2	None	NA
115	0.023	129.800	84.2	None	NA
116	0.024	48.170	89.5	None	NA
117	0.024	51.555	78.9	None	NA
118	0.024	2981.000	84.2	None	NA
119	0.024	>5000.000	65.8	C20DA-yGlu	1
120	0.025	>5000.000	57.9	C20DA-yGlu	1
121	0.026	2981.000	84.2	None	NA
122	0.026	>5000.000	60.5	C20DA-yGlu	1
123	0.027	31.653	73.7	None	NA
124	0.027	34.840	86.8	None	NA
125	0.027	2981.000	86.8	None	NA
126	0.027	>5000.000	63.2	C20DA-AMCHC-yGlu-OEG-OEG	1
127	0.028	107.400	92.1	None	NA
128	0.028	130.300	34.2	None	NA
129	0.029	366.900	89.5	None	NA
130	0.030	>5000.000	57.9	C20DA-yGlu	1

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
131	0.031	33.760	92.1	None	NA
132	0.031	2981.000	89.5	None	NA
133	0.031	>5000.000	57.9	C20DA-yGlu	1
134	0.032	2981.000	86.8	None	NA
135	0.033	68.400	86.8	None	NA
136	0.033	>5000.000	60.5	C20DA-yGlu-OEG-OEG	17
137	0.034	>5000.000	57.9	C20DA-yGlu	1
138	0.035	2981.000	86.8	None	NA
139	0.035	2981.000	84.2	None	NA
140	0.036	31.400	92.1	None	NA
141	0.036	258.400	89.5	None	NA
142	0.036	2981.000	84.2	None	NA
143	0.038	2981.000	84.2	None	NA
144	0.038	>5000.000	57.9	C20DA-yGlu	1
145	0.039	2981.000	89.5	None	NA
146	0.040	2981.000	92.1	None	NA
147	0.040	3108.878	86.8	None	NA
148	0.040	>5000.000	26.3	None	NA
149	0.040	>5000.000	28.9	None	NA
150	0.040	>5000.000	89.5	None	NA
151	0.041	44.920	84.2	None	NA
152	0.041	212.700	89.5	None	NA
153	0.041	>5000.000	60.5	C20DA-yGlu	1
154	0.042	2981.000	97.4	None	NA
155	0.045	116.500	92.1	None	NA
156	0.047	2981.000	86.8	None	NA
157	0.047	2981.000	86.8	None	NA
158	0.048	2981.000	92.1	None	NA
159	0.048	>5000.000	63.2	C20DA-yGlu	1
160	0.050	2981.000	86.8	None	NA
161	0.051	2981.000	86.8	None	NA
162	0.051	>5000.000	31.6	None	NA
163	0.053	2981.000	81.6	None	NA
164	0.054	106.200	94.7	None	NA
165	0.054	2981.000	86.8	None	NA
166	0.056	2981.000	84.2	None	NA
167	0.056	2981.000	92.1	None	NA

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
168	0.062	>5000.000	92.1	None	NA
169	0.063	2981.000	94.7	None	NA
170	0.064	2981.000	84.2	None	NA
171	0.064	>5000.000	86.8	None	NA
172	0.066	2981.000	86.8	None	NA
173	0.069	>5000.000	86.8	None	NA
174	0.071	133.300	94.7	None	NA
175	0.074	2981.000	89.5	None	NA
176	0.076	2981.000	86.8	None	NA
177	0.077	2981.000	84.2	None	NA
178	0.080	2981.000	84.2	None	NA
179	0.082	2981.000	89.5	None	NA
180	0.082	>5000.000	26.3	None	NA
181	0.082	>5000.000	63.2	None	NA
182	0.085	100.100	94.7	None	NA
183	0.088	2981.000	89.5	None	NA
184	0.090	4495.564	86.8	None	NA
185	0.090	>5000.000	86.8	None	NA
186	0.091	>5000.000	86.8	None	NA
187	0.093	2981.000	86.8	None	NA
188	0.094	47.640	86.8	None	NA
189	0.096	2981.000	89.5	None	NA
190	0.097	2981.000	89.5	None	NA
191	0.098	2981.000	89.5	None	NA
192	0.098	>5000.000	86.8	None	NA
193	0.099	>5000.000	84.2	None	NA
194	0.112	3526.547	86.8	None	NA
195	0.112	>5000.000	60.5	None	NA
196	0.114	>5000.000	84.2	None	NA
197	0.120	2981.000	86.8	None	NA
198	0.122	3962.089	86.8	None	NA
199	0.124	2981.000	89.5	None	NA
200	0.126	38.156	81.6	C20DA-yGlu	1
201	0.126	4881.061	86.8	None	NA
202	0.126	>5000.000	86.8	None	NA
203	0.127	>5000.000	86.8	None	NA
204	0.129	2981.000	86.8	None	NA
205	0.130	3228.702	89.5	None	NA
206	0.130	>5000.000	86.8	None	NA
207	0.131	>5000.000	28.9	None	NA

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
208	0.133	242.450	73.7	C20DA-yGlu	1
209	0.136	1020.000	89.5	None	NA
210	0.137	>5000.000	63.2	None	NA
211	0.151	2756.647	86.8	None	NA
212	0.153	>5000.000	89.5	None	NA
213	0.153	>5000.000	84.2	None	NA
214	0.157	2981.000	86.8	None	NA
215	0.161	>5000.000	86.8	None	NA
216	0.164	2981.000	86.8	None	NA
217	0.167	>5000.000	89.5	None	NA
218	0.169	>5000.000	86.8	None	NA
219	0.171	4246.488	86.8	None	NA
220	0.182	>5000.000	86.8	None	NA
221	0.184	>5000.000	63.2	C20DA-AMCHC-gGlu-OEG-OEG-K(C20DA-AMCHC-gGlu-OEG-OEG)	1
222	0.184	>5000.000	86.8	None	NA
223	0.186	47.652	78.9	C20DA-yGlu	1
224	0.186	2981.000	86.8	None	NA
225	0.186	>5000.000	65.8	C20DA-yGlu	1
226	0.186	>5000.000	86.8	None	NA
227	0.187	4570.819	84.2	None	NA
228	0.205	>5000.000	86.8	None	NA
229	0.207	2981.000	89.5	None	NA
230	0.208	>5000.000	89.5	None	NA
231	0.209	>5000.000	65.8	C20DA-yGlu	1
232	0.213	>5000.000	86.8	None	NA
233	0.220	>5000.000	63.2	$(C20DA-OEG-yGlu-OEG)_2$-K-	1
234	0.227	>5000.000	71.1	None	NA
235	0.233	1416.600	86.8	None	NA
236	0.234	2239.417	86.8	None	NA
237	0.235	4245.930	86.8	None	NA
238	0.235	>5000.000	86.8	None	NA
239	0.236	>5000.000	86.8	None	NA
240	0.240	>5000.000	89.5	None	NA

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
241	0.242	2291.534	86.8	None	NA
242	0.248	>5000.000	86.8	None	NA
243	0,018	3336.098	63,2	None	NA
244	0,006	>5000.000	44,7	None	NA
245	0,017	>5000.000	44,7	None	NA
246	0,010	>5000.000	63,2	None	NA
247	0,004	>5000.000	50.0	None	NA
248	0,027	3587,646	71,1	None	NA
249	0,006	>5000.000	63,2	None	NA
250	0,011	>5000.000	63,2	None	NA
251	0,006	>5000.000	63,2	None	NA
252	0,006	>5000.000	65,8	None	NA
253	0,004	>5000.000	60,5	None	NA
254	0,006	>5000.000	63,2	None	NA
255	0,007	>5000.000	65,8	None	NA
256	0,007	>5000.000	50.0	None	NA
257	0,016	2037,788	73,7	None	NA
258	0,010	>5000.000	63,2	None	NA
259	0,013	4324,040	86,8	None	NA
260	0,011	4163,023	86,8	None	NA
261	0,018	>5000.000	81,6	None	NA
262	0,014	>5000.000	63,2	None	NA
263	0,005	1283,849	81,6	None	NA
264	0,006	3469,936	73,7	None	NA
265	0,030	>5000.000	63,2	None	NA
266	0,053	>5000.000	60,5	None	NA
267	0,007	2490,994	84,2	None	NA
268	0,014	>5000.000	65,8	None	NA
269	0,005	>5000.000	81,6	None	NA
270	0,003	1877,713	81,6	None	NA
271	0,010	96,618	86,8	None	NA
272	0,009	>5000.000	71,1	None	NA
273	0,021	>5000.000	84,2	None	NA
274	0,019	877,430	89,5	None	NA
275	0,020	>5000.000	89,5	None	NA
276	0,056	>5000.000	63,2	None	NA
277	0,058	>5000.000	84,2	None	NA
278	0,011	154,831	89,5	None	NA
279	0,013	241,240	78,9	None	NA
280	0,024	>5000.000	84,2	None	NA
281	0,034	>5000.000	84,2	None	NA

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
282	0,143	3880,504	73,7	None	NA
283	0,035	>5000.000	86,8	None	NA
284	0,028	590,750	92,1	None	NA
285	0,157	>5000.000	89,5	None	NA
286	0,025	138,873	92,1	None	NA
287	0,055	>5000.000	89,5	None	NA
288	0,030	>5000.000	86,8	None	NA
289	0,005	3502,991	86,8	None	NA
290	0,047	>5000.000	84,2	None	NA
291	0,064	>5000.000	89,5	None	NA
292	0,070	>5000.000	84,2	None	NA
293	0,063	>5000.000	89,5	None	NA
294	0,045	>5000.000	92,1	None	NA
295	0,194	>5000.000	86,8	None	NA
296	0,392	>5000.000	89,5	None	NA
297	0,026	>5000.000	84,2	None	NA
298	0,057	>5000.000	86,8	None	NA
299	0,110	>5000.000	86,8	None	NA
300	0,076	>5000.000	92,1	None	NA
301	0,138	>5000.000	86,8	None	NA
302	0,071	4332,084	81,6	None	NA
303	0,103	>5000.000	86,8	None	NA
304	0,139	>5000.000	84,2	None	NA
305	0,085	>5000.000	92,1	None	NA
306	0,003	>5000.000	44,7	None	NA
307	0,010	>5000.000	44,7	None	NA
308	0,014	>5000.000	63,2	None	NA
309	0,025	>5000.000	63,2	None	NA
310	0,003	>5000.000	50.0	None	NA
311	0,060	>5000.000	78,9	None	NA
312	0,012	>5000.000	71,1	None	NA
313	0,004	>5000.000	63,2	None	NA
314	0,008	>5000.000	63,2	None	NA
315	0,012	>5000.000	63,2	None	NA
316	0,012	>5000.000	65,8	None	NA
317	0,004	>5000.000	60,5	None	NA
318	0,009	>5000.000	63,2	None	NA
319	0,018	>5000.000	65,8	None	NA
320	0,009	>5000.000	63,2	None	NA
321	0,317	>5000.000	63,2	None	NA
322	0,014	1390,178	86,8	None	NA

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
323	0,014	>5000.000	81,6	None	NA
324	0,028	>5000.000	63,2	None	NA
325	0,025	>5000.000	63,2	None	NA
326	0,053	>5000.000	81,6	None	NA
327	0,090	>5000.000	73,7	None	NA
328	0,010	>5000.000	63,2	None	NA
329	0,032	>5000.000	63,2	None	NA
330	0,008	>5000.000	65,8	None	NA
331	0,006	3566,754	84,2	None	NA
332	0,007	>5000.000	81,6	None	NA
333	0,236	107,471	63,2	None	NA
334	0,013	>5000.000	71,1	None	NA
335	0,015	>5000.000	84,2	None	NA
336	0,029	738,478	89,5	None	NA
337	0,019	1583,677	89,5	None	NA
338	0,089	>5000.000	63,2	None	NA
339	0,047	>5000.000	84,2	None	NA
340	0,022	671,058	89,5	None	NA
341	0,029	>5000.000	84,2	None	NA
342	0,054	>5000.000	84,2	None	NA
343	0,017	117,363	86,8	None	NA
344	0,121	>5000.000	89,5	None	NA
345	0,051	113,116	92,1	None	NA
346	0,085	>5000.000	86,8	None	NA
347	0,068	>5000.000	84,2	None	NA
348	0,041	>5000.000	84,2	None	NA
349	0,046	>5000.000	84,2	None	NA
350	0,044	1180,470	92,1	None	NA
351	0,943	>5000.000	86,8	None	NA
352	0,040	1116,541	84,2	None	NA
353	0,027	2918,791	89,5	None	NA
354	0,091	>5000.000	86,8	None	NA
355	0,140	>5000.000	86,8	None	NA
356	0,079	>5000.000	86,8	None	NA
357	0,115	>5000.000	86,8	None	NA
358	0,071	>5000.000	81,6	None	NA
359	0,145	>5000.000	86,8	None	NA
360	0,165	>5000.000	84,2	None	NA
361	0.006	0.913	76.3	None	NA
362	0.007	18.150	86.8	None	NA
363	0.010	1.771	71.1	None	NA

ID	hAMY3R EC_{50} (nM)	hAM1R EC_{50} (nM)	identity (% ADM)*	Lipidation	Lipidation position
364	0.010	13.585	84.2	None	NA
365	0.012	1.211	86.8	None	NA
366	0.013	12.090	89.5	None	NA
367	0.014	0.563	89.5	None	NA
368	0.015	0.997	89.5	None	NA
369	0.017	2.477	84.2	None	NA
370	0.017	10.304	73.7	C20DA-yGlu	1
371	0.019	3.029	92.1	None	NA
372	0.020	3.941	84.2	C20DA-yGlu	1
373	0.020	7.712	86.8	None	NA
374	0.021	12.000	89.5	None	NA
375	0.022	0.403	92.1	None	NA
376	0.022	12.022	81.6	None	NA
377	0.024	0.243	81.6	None	NA
378	0.027	0.893	76.3	C20DA-yGlu	1
379	0.029	0.458	89.5	None	NA
380	0.031	0.162	86.8	C20DA-yGlu	1
381	0.032	7.608	86.8	None	NA
382	0.034	5.124	92.1	None	NA
383	0.034	5.935	92.1	None	NA
384	0.036	1.090	92.1	None	NA
385	0.036	7.003	89.5	None	NA
386	0.039	7.354	78.9	C20DA-yGlu	1
387	0.040	0.992	94.7	None	NA
388	0.043	4.006	84.2	C20DA-yGlu	1
389	0.045	1.039	71.1	C20DA-yGlu	1
390	0.048	0.889	86.8	C20DA-yGlu	1
391	0.068	0.665	92.1	None	NA
392	0.113	5.034	84.2	C20DA-yGlu	1

Table 2. Table 2 shows that hAM_{15-52} analogues (SEQ ID NO: 3-392) with improved hAMY3R potency compared to hAM_{15-52} may be obtained by changing the amino acid K present in hAM_{15-52} in position X_{11} into R, W or Cit. Table 2 further shows that highly selective (hAMY3R-EC_{50} ≤ 250 pM and an hAM1R-EC_{50} ≥ 25 nM) hAMY3R hAM_{15-52} analogues (SEQ ID NO: 3-360) may be obtained by abolishing or reducing the hAM1R potency using the positions X_4, X_{37} and/or X_{38}. All lipidations at position 1 were performed at the N-terminal and the lipidation in the other positions were performed at an epsilon N in Lys. AMCHC refers to trans-4-(aminomethyl)cyclohexanecarboxylic acid. OEG refers to 8-amino-3,6-dioxaoctanoic acid or 8Ado.

Example 2

Fibrillation was determined according to the general protocol for determination of physical stability of peptide analogues. The data for selected hAM_{15-52} analogues are summarized in Table 3 below.

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ID	Max ThT signal (%)	identity (% ADM)*
1	2.600	100.0
2	100	18.4
7	2.800	63.2
13	5.000	63.2
14	3.100	63.2
20	9.100	71.1
23	4.200	63.2
24	6.800	63.2
25	33.400	63.2
26	0.000	63.2
27	21.80	63.2
28	8.200	65.8
29	9.300	55.3
32	5.300	50.0
42	6.300	63.2
43	1.200	63.2
45	3.000	86.8
46	5.800	86.8
49	3.200	81.6
52	7.600	63.2
64	2.700	63.2
65	1.000	57.9
70	8.800	84.2
81	4.000	84.2
84	14.200	81.6
90	2.000	81.6
98	12.600	86.8
109	9.300	84.2
113	14.700	89.5
114	2.200	63.2
115	2.500	84.2
116	11.700	89.5
118	7.400	84.2
121	1.800	84.2
124	4.800	86.8
125	7.200	86.8

ID	Max ThT signal (%)	identity (% ADM)*
129	1.400	89.5
131	6.800	92.1
132	5.200	89.5
134	17.400	86.8
135	3.300	86.8
138	6.800	86.8
139	4.800	84.2
140	3.100	92.1
141	3.200	89.5
143	2.200	84.2
145	2.000	89.5
146	3.600	92.1
147	5.100	89.2
150	18.200	91.9
152	1.900	89.5
156	15.300	86.8
158	6.300	92.1
160	21.500	86.8
161	14.300	86.8
163	2.000	81.6
164	24.300	94.7
165	4.800	86.8
166	2.000	84.2
167	6.600	92.1
168	12.500	94.6
169	2.700	94.7
170	1.800	84.2
171	5.000	89.2
172	13.900	86.8
173	4.400	89.2
175	3.200	89.5
176	6.800	86.8
181	8.800	63.2
182	15.600	94.7
184	0.800	89.2
185	2.800	89.2
186	0.600	89.2
187	1.600	86.8
189	6.000	89.5
190	12.900	89.5
191	6.300	89.5
192	4.100	89.2

ID	Max ThT signal (%)	identity (% ADM)*
193	2.700	86.5
194	6.000	89.2
195	6.100	60.5
196	0.500	86.5
197	5.600	86.8
198	4.200	89.2
199	8.900	89.5
201	1.000	89.2
202	12.600	89.2
203	1.200	89.2
204	2.200	86.8
205	7.800	91.9
206	1.500	89.2
210	1.400	63.2
211	5.200	89.2
212	1.900	91.9
213	6.500	86.5
214	2.700	86.8
215	0.600	89.2
217	13.800	91.9
218	4.500	89.2
219	0.700	89.2
220	1.100	89.2
222	11.700	89.2
224	2.000	86.8
226	27.000	89.2
227	8.500	86.5
228	19.600	89.2
230	0.600	91.9
232	1.200	89.2
235	0.800	89.2
236	0.600	89.2
237	0.300	89.2
238	0.600	89.2
239	0.200	89.2
240	3.700	91.9
241	0.900	89.2
242	0.800	89.2
243	8.550	63.2
244	4.100	44.7
245	3.350	44.7
246	4.200	63.2

ID	Max ThT signal (%)	identity (% ADM)*
247	1.350	50.0
248	13.600	71.1
249	15.600	63.2
250	6.400	63.2
251	10.600	63.2
252	27.550	63.2
253	9.600	60.5
254	12.050	63.2
255	25.000	65.8
256	18.650	50.0
257	20.950	73.7
258	32.700	63.2
259	13.450	86.8
260	34.100	86.8
261	22.650	81.6
262	9.550	63.2
263	1.050	81.6
264	1.350	73.7
265	26.550	63.2
266	20.900	60.5
267	30.900	84.2
268	8.850	65.8
269	34.500	81.6
270	25.450	81.6
271	10.850	86.8
272	16.750	71.1
273	29.000	84.2
274	26.800	89.5
275	19.850	89.5
276	8.950	63.2
277	21.600	84.2
278	13.350	89.5
279	13.450	78.9
280	26.450	84.2
281	22.650	84.2
282	4.700	73.7
283	17.100	86.8
284	21.300	92.1
285	31.200	89.5
286	2.900	92.1
287	10.650	89.5
288	17.450	86.8

ID	Max ThT signal (%)	identity (% ADM)*
289	21.150	86.8
290	17.300	84.2
291	19.200	89.5
292	19.700	84.2
293	24.200	89.5
294	16.850	92.1
295	19.450	86.8
296	26.050	89.5
297	27.500	84.2
298	31.250	86.8
299	26.550	86.8
300	17.850	92.1
301	16.950	86.8
302	24.250	81.6
303	18.150	86.8
304	22.350	84.2
305	24.600	92.1
306	3.000	44.7
307	11.200	44.7
308	14.500	63.2
309	4.250	63.2
310	3.500	50.0
311	6.450	78.9
312	17.000	71.1
313	15.050	63.2
314	11.900	63.2
315	17.150	86.8
316	20.450	89.5
317	5.550	86.8
318	14.900	89.5
319	3.900	92.1
320	11.100	89.5
321	21.700	94.7
322	18.400	92.1
323	27.500	81.6
324	11.850	63.2
325	10.100	63.2
326	2.350	81.6
327	3.600	73.7
328	33.250	63.2
329	6.350	63.2
330	14.600	65.8

ID	Max ThT signal (%)	identity (% ADM)*
331	21.150	84.2
332	2.100	81.6
333	25.700	63.2
334	10.150	71.1
335	1.600	84.2
336	18.700	89.5
337	16.800	89.5
338	2.950	63.2
339	20.050	84.2
340	1.700	89.5
341	20.500	84.2
342	19.800	84.2
343	24.850	86.8
344	13.350	89.5
345	3.250	92.1
346	1.200	86.8
347	15.500	84.2
348	2.750	84.2
349	15.250	84.2
350	15.700	92.1
351	7.200	86.8
352	25.800	84.2
353	30.300	89.5
354	17.400	86.8
355	25.350	86.8
356	1.250	86.8
357	19.750	86.8
358	24.350	81.6
359	20.350	86.8
360	26.350	84.2
362	8.900	86.8
366	3.300	89.5
373	18.000	86.8
374	4.800	89.5
383	9.600	92.1
385	8.800	89.5
387	14.300	94.7
391	3.700	92.1

Table 3. Table 3 shows that the hAM_{15-52} analogues according to the invention maintain the good fibrillation properties from hAM_{15-52}. Most of the fibrillation data are comparable to and some even better than hAM_{15-52} (SEQ ID NO: 1) at pH 7 (ThT signal of 2.6 %). All of the fibrillation data are far superior compared to the reference $hAMY_{1-37}$ (SEQ ID NO: 2) (ThT signal on 100 %).

Example 3

The effect of selected hAM_{15-52} analogues on acute food intake in lean rats were determined. The results are summarized in Table 4 below.

ID	Dose	Average cumulative food intake (g)	% to vehicle	Significance level to Veh
NA	Vehicle	44.4	100	NA
4	10 nmol/kg	26.3	59.23	***
4	30 nmol/kg	13.7	30.86	***
46	10 nmol/kg	23.3	52.48	***
46	30 nmol/kg	10.7	24.10	***
60	10 nmol/kg	30.9	69.59	***
60	30 nmol/kg	20.3	45.72	***
NA	Vehicle	40.7	100	NA
78	10 nmol/kg	13.7	33.66	***
69	10 nmol/kg	7.13	17.52	***
70	10 nmol/kg	24.9	61.18	***
85	10 nmol/kg	18.6	45.70	***
124	10 nmol/kg	24.2	59.46	***
93	10 nmol/kg	19.1	46.93	***
NA	Vehicle	41.9	100	NA
36	10 nmol/kg	23.3	55.61	***
6	10 nmol/kg	27.5	65.63	***

Table 4. Table 4 shows that hAM_{15-52} analogues have potent anorectic effects for up to 48 hours following a single SC injection in lean healthy rats (n=7-8), thereby providing proof-of-principle. Dunnett's test one-factor linear model***: $P < 0.001$ compared to Vehicle (three independent runs were conducted).

Example 4

The Effect of chronic treatment of selected hAM_{15-52} analogues according to the invention in diet-induced obese (DIO) rats were determined. The results are summarized in Table 5 below.

ID	Dose	Average body weight day 28 (gram)	% to vehicle	Significance level to Veh
NA	Vehicle	716	100	NA
46	1 nmol/kg	674	94.13	***
46	3 nmol/kg	620	86.59	***
46	10 nmol/kg	618	86.31	***
NA	Vehicle	776	100	NA
78	10 nmol/kg	687	88.53	***

Table 5. Table 5 shows that daily SC injections of SEQ ID NO: 46 or 78 cause a significant reduction in body weight in diet-induced obese rats (n=10) following a 28-day treatment period, thereby providing proof-of-concept. Dunnett's test one-factor linear model***: $P < 0.001$ compared to Vehicle (two independent runs were conducted).

Example 5

Deeper investigation of representative amino acids in the position X_4, X_{11}, X_{17}, X_{37} and X_{38} and the corresponding change in potency. The results are summarized in Table 6 below.

Amino acid	Position 4	Position 11	Position 17	Position 37	Position 38
Y	U	D	R	I	I
W	I	U	I	I	I
T	R	D	U	R	U
Q	D	D	U	U	U
P	D	D	D	I	U
M	I	D	U	U	I
I	I	D	U	U	U
H	D	D	I	I	U
F	I	D	U	I	I
E	D	D	D	U	U
A	U	D	U	U	U
R	D	R	U	U	U
C	I	D	D	U	N/A
K	D	D	U	U	U
Hyp	N/A	N/A	N/A	N/A	R
Cit	N/A	U	N/A	N/A	N/A

Table 6. Table 6 shows whether the amino acid change causes increase (I) in hAMY3R potency, unchanged potency (U), or decreased potency (D) compared to the reference (R) amino acid. N/A Not available.

Table 7. SEQUENCE LISTING

ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	G	C	R	F	G	T	C	T	V	Q	K	L	A	H	Q	I	Y	Q	F	T
2	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
3	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
4	K	C	N	T	A	T	C	T	V	D	R	L	A	H	Q	I	Y	Q	F	T
5	K	C	N	T	A	T	C	T	V	Q	R	L	A	D	Q	I	Y	Q	F	T
6	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
7	K	C	N	T	A	T	C	T	V	Q	R	L	A	A	Q	I	Y	Q	F	T
8	K	C	N	T	S	T	C	T	V	A	R	L	A	D	Q	I	T	Q	F	S
9	R	C	N	A	S	T	C	T	V	N	R	L	A	D	Q	I	T	Q	F	S
10	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
11	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	N	Q	F	T
12	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
13	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	A	I	Y	Q	F	T
14	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
15	K	C	N	T	S	T	C	T	V	A	R	L	A	D	Q	I	T	Q	F	S
16	G	C	R	F	G	T	C	T	V	Q	R	L	A	N	F	L	Y	Q	F	T
17	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
18	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
19	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
20	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
21	K	C	N	T	A	T	C	T	V	Q	R	L	A	N	Q	I	Y	Q	F	T
22	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	T	Q	F	T
23	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	A
24	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
25	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
26	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
27	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
28	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
29	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	-	Q	F
30	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
31	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
32	R	C	Q	T	S	T	C	T	V	A	R	L	A	E	Q	I	A	Q	Y	T
33	R	C	Q	A	S	T	C	T	V	A	Cit	L	A	E	Q	I	A	Q	Y	T
34	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
35	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Q	Q	F	T
36	K	C	K	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
37	K	C	N	T	A	T	C	T	V	A	R	L	A	H	Q	I	Y	Q	F	T
38	K	C	N	T	A	T	C	T	V	N	R	L	A	H	Q	I	Y	Q	F	T
39	R	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
40	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T

41	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
42	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	A	F	T
43	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
44	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
45	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
46	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
47	K	C	N	T	A	T	C	T	V	Q	R	L	A	Y	Q	I	Y	Q	F	T
48	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	Y	T
49	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
50	K	C	N	T	S	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
51	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
52	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
53	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
54	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
55	K	C	N	T	A	T	C	T	V	E	R	L	A	H	Q	I	Y	Q	F	T
56	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
57	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	S
58	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
59	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
60	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
61	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
62	K	C	N	T	S	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
63	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
64	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
65	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	-	Q	F
66	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
67	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
68	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
69	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
70	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
71	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	Y	T
72	K	C	Q	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
73	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
74	K	C	N	T	A	T	C	T	V	Q	R	L	A	K	Q	I	Y	Q	F	T
75	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
76	R	C	G	T	A	T	C	A	T	E	R	L	A	AAD	F	L	Q	R	S	-
77	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
78	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	A	Q	F	T
79	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	S
80	R	C	Q	T	A	T	C	A	T	E	R	L	A	H	F	L	Q	R	S	-
81	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
82	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T

83	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	A
84	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
85	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	V	Q	F	T
86	K	C	N	T	A	T	C	T	V	A	R	L	A	H	Q	I	N	Q	F	T
87	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
88	K	C	N	T	S	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
89	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	K
90	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
91	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
92	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
93	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
94	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	Y
95	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
96	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
97	K	C	A	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
98	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
99	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
100	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
101	K	C	N	A	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
102	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
103	K	C	N	T	A	T	C	T	V	V	R	L	A	H	Q	I	Y	Q	F	T
104	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	Y
105	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	A
106	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
107	K	C	N	T	A	T	C	T	V	A	R	L	A	H	Q	I	A	Q	F	T
108	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
109	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
110	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	E	Q	F	T
111	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
112	K	C	N	T	A	T	C	T	V	D	R	L	A	H	Q	I	A	Q	F	T
113	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
114	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	A	T
115	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
116	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
117	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
118	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
119	K	C	N	T	Aib	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
120	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
121	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
122	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
123	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
124	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T

125	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
126	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
127	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
128	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
129	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
130	K	C	N	T	A	T	C	T	V	D	R	L	A	H	Q	I	A	Q	F	T
131	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
132	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
133	K	C	N	T	A	T	C	T	V	A	R	L	A	E	Q	I	Y	Q	F	T
134	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
135	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
136	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	K	Q	F	T
137	K	C	N	T	A	T	C	T	V	A	R	L	A	H	Q	I	N	Q	F	T
138	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
139	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
140	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
141	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
142	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
143	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
144	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	A	Q	F	T
145	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
146	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
147	G	C	R	I	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
148	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
149	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
150	G	C	R	W	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
151	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
152	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
153	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	E	Q	I	A	Q	F	T
154	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
155	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
156	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
157	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
158	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
159	K	C	N	T	A	T	C	T	V	I	R	L	A	H	Q	I	Y	Q	F	T
160	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
161	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
162	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
163	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
164	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
165	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
166	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
167	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T

168	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
169	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
170	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
171	G	C	R	W	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
172	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
173	G	C	R	M	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
174	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
175	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
176	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
177	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
178	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
179	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
180	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
181	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	-	F	T
182	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
183	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
184	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
185	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
186	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
187	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
188	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
189	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
190	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
191	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
192	G	C	R	M	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
193	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	H	Q	F	T
194	K	C	R	M	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
195	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	-	Q	T
196	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	A	Q	F	T
197	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
198	G	C	R	I	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
199	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
200	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
201	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
202	G	C	R	W	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
203	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
204	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
205	K	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
206	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
207	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	H	S	S
208	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
209	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
210	K	C	N	T	A	T	C	T	V	Q	R	L	A	H	Q	A	Y	Q	F	T

211	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
212	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
213	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	W	Q	F	T
214	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
215	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
216	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
217	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	L	Y	Q	F	T
218	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
219	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
220	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
221	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
222	G	C	R	M	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
223	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
224	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
225	K	C	N	T	L	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
226	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
227	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	H	Q	F	T
228	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	H	Q	F	T
229	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
230	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
231	K	C	N	T	Y	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
232	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
233	K	C	N	T	A	T	C	T	V	Q	R	L	A	E	Q	I	Y	Q	F	T
234	K	C	N	T	A	T	C	A	T	Q	R	L	A	N	F	L	V	Q	F	T
235	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
236	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
237	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
238	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
239	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
240	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
241	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
242	G	C	R	T	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
243	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	A	Q	I	Y	Q	F	T
244	K	C	N	T	S	T	C	T	V	A	Cit	L	A	D	Q	I	T	Q	F	S
245	R	C	N	A	S	T	C	T	V	N	Cit	L	A	D	Q	I	T	Q	F	S
246	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	A	Q	F	T
247	K	C	N	T	S	T	C	T	V	A	Cit	L	A	D	Q	I	T	Q	F	S
248	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
249	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	A
250	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
251	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
252	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
253	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	-

254	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
255	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
256	R	C	Q	T	S	T	C	T	V	A	Cit	L	A	E	Q	I	A	Q	Y	T
257	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
258	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
259	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
260	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
261	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
262	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
263	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	F	L	Y	Q	F	T
264	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	F	L	Y	Q	F	T
265	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	-
266	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	E	Q	I	Y	Q	F	T
267	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
268	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
269	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
270	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
271	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
272	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
273	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
274	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
275	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
276	K	C	N	T	A	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	A	T
277	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
278	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
279	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	F	L	Y	Q	F	T
280	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
281	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
282	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	F	L	Y	Q	F	T
283	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
284	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
285	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
286	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
287	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
288	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
289	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
290	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
291	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
292	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
293	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
294	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
295	G	C	R	I	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
296	G	C	R	W	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T

297	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
298	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
299	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
300	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
301	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
302	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
303	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
304	G	C	R	T	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
305	G	C	R	F	G	T	C	T	V	Q	Cit	L	A	H	Q	I	Y	Q	F	T
306	K	C	N	T	S	T	C	T	V	A	W	L	A	D	Q	I	T	Q	F	S
307	R	C	N	A	S	T	C	T	V	N	W	L	A	D	Q	I	T	Q	F	S
308	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	A	I	Y	Q	F	T
309	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	A	Q	F	T
310	K	C	N	T	S	T	C	T	V	A	W	L	A	D	Q	I	T	Q	F	S
311	G	C	R	F	G	T	C	T	V	Q	W	L	A	N	F	L	Y	Q	F	T
312	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
313	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	A
314	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
315	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
316	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
317	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	-
318	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
319	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
320	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
321	K	C	N	T	A	T	C	T	V	Q	W	L	A	E	Q	I	Y	Q	F	T
322	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
323	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
324	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
325	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
326	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	F	L	Y	Q	F	T
327	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	F	L	Y	Q	F	T
328	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
329	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	-
330	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
331	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
332	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
333	K	C	N	A	A	T	C	T	V	Q	W	L	A	E	Q	I	Y	Q	F	T
334	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
335	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
336	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
337	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
338	K	C	N	T	A	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	A	T
339	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T

340	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
341	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
342	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
343	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
344	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
345	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
346	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
347	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
348	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
349	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
350	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
351	G	C	R	I	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
352	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
353	G	C	R	F	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
354	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
355	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
356	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
357	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
358	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
359	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
360	G	C	R	T	G	T	C	T	V	Q	W	L	A	H	Q	I	Y	Q	F	T
361	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
362	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
363	K	C	N	F	A	T	C	A	T	Q	R	L	A	N	F	L	V	Q	F	T
364	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
365	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
366	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
367	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
368	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
369	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
370	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
371	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
372	G	C	R	F	G	T	C	T	V	Q	R	L	A	N	Q	I	Y	Q	F	T
373	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
374	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
375	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
376	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
377	G	C	R	F	A	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
378	K	C	N	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
379	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
380	G	C	R	F	A	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
381	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
382	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T

383	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
384	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
385	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
386	G	C	R	F	G	T	C	T	V	Q	R	L	A	N	F	L	Y	Q	F	T
387	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
388	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
389	K	C	N	F	A	T	C	A	T	Q	R	L	A	N	F	L	V	Q	F	T
390	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T
391	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	Q	I	Y	Q	F	T
392	G	C	R	F	G	T	C	T	V	Q	R	L	A	H	F	L	Y	Q	F	T

Table 7 continued.

ID	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**
1	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	G	Y
2	N	N	F	-	G	A	I	L	S	S	T	N	V	G	S	N	T	Y
3	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Hyp
4	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
5	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
6	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	K	G	Hyp
7	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
8	N	K	D	K	A	Q	V	S	P	P	T	E	V	G	P	N	S	Hyp
9	N	K	D	K	A	Q	V	S	P	P	T	E	V	G	P	N	S	Hyp
10	D	K	D	K	D	N	V	A	P	P	T	E	V	G	S	N	G	Hyp
11	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
12	D	K	D	K	D	N	K	A	P	P	T	N	V	G	S	N	G	Hyp
13	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
14	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
15	D	K	D	K	A	N	V	S	P	P	T	E	V	G	P	N	S	Hyp
16	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Y
17	D	K	D	K	D	N	V	A	P	R	T	E	V	G	S	N	G	Hyp
18	D	K	D	K	D	N	V	A	P	P	T	E	V	G	S	N	G	P
19	N	N	F	G	A	-	I	L	P	R	T	K	V	G	S	N	G	Y
20	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Hyp
21	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
22	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
23	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
24	A	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
25	D	K	D	A	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
26	D	K	D	K	A	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
27	D	K	D	K	D	N	A	A	P	P	T	N	V	G	S	N	G	Hyp
28	D	K	D	K	D	N	V	A	P	A	T	N	V	G	S	N	G	Hyp
29	T	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
30	D	K	D	K	D	N	V	-	P	P	T	N	V	G	S	N	G	Hyp

31	D	K	D	K	D	N	V	-	A	P	T	N	V	G	S	N	G	Hyp
32	D	K	D	K	D	Q	V	A	P	P	T	N	V	G	S	N	S	Hyp
33	D	K	D	K	D	Q	V	A	P	P	T	E	V	G	P	N	S	Hyp
34	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Y
35	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
36	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
37	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
38	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
39	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
40	D	K	D	K	K	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
41	D	K	D	K	D	K	V	A	P	P	T	N	V	G	S	N	G	Hyp
42	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
43	D	K	A	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
44	D	K	D	K	D	N	V	A	P	P	Y	N	E	G	S	N	G	Hyp
45	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Hyp
46	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Hyp
47	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
48	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
49	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Hyp
50	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
51	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
52	D	K	D	K	D	A	V	A	P	P	T	N	V	G	S	N	G	Hyp
53	D	K	D	K	D	N	V	A	A	P	T	N	V	G	S	N	G	Hyp
54	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Y
55	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
56	D	K	D	K	D	N	V	A	P	R	T	N	V	G	S	N	T	Y
57	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
58	N	N	F	G	A	-	I	L	S	S	T	K	V	G	S	N	T	Y
59	N	N	F	G	A	-	I	L	P	S	T	K	V	G	S	N	G	Y
60	D	K	D	K	D	N	V	A	P	P	T	K	V	G	S	N	G	Hyp
61	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
62	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
63	D	K	D	K	D	N	V	A	P	P	T	A	V	G	S	N	G	Hyp
64	D	A	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
65	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
66	D	K	D	K	D	N	V	S	P	P	T	N	V	G	S	N	G	Hyp
67	D	K	D	K	D	N	V	A	P	R	T	E	V	G	S	N	G	Hyp
68	D	K	D	K	D	N	V	A	P	P	T	E	V	G	S	N	G	Hyp
69	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	S	Hyp
70	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Hyp
71	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
72	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
73	D	K	D	K	D	N	V	A	P	P	T	Q	V	G	S	N	G	Hyp

74	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
75	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
76	-	S	F	(NMe)G	A	-	(NMe)I	L	S	S	T	E	V	G	S	N	T	Hyp
77	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
78	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
79	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
80	-	S	F	(NMe)G	A	-	(NMe)I	L	S	S	T	E	V	G	S	N	T	Hyp
81	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	N	G	Hyp
82	N	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
83	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
84	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	N	G	Y
85	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
86	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
87	D	K	N	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
88	D	K	D	K	D	P	V	A	P	P	T	N	V	G	S	N	G	Hyp
89	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
90	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	N	G	Hyp
91	D	K	N	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
92	D	K	D	K	D	P	V	A	P	P	T	N	V	G	S	N	G	Hyp
93	N	N	F	G	A	-	I	A	P	S	T	K	V	G	S	N	G	Y
94	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
95	N	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
96	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	T	Hyp
97	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
98	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	N	G	Y
99	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Hyp
100	D	K	D	K	D	Q	V	A	P	P	T	N	V	G	S	N	G	Hyp
101	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
102	D	K	D	K	D	N	V	A	P	R	T	E	V	G	S	N	G	Y
103	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
104	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
105	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
106	A	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
107	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
108	D	K	D	K	A	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
109	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Y
110	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
111	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	Q	G	Hyp
112	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
113	D	K	D	K	D	N	V	A	P	R	T	K	I	S	P	N	G	Hyp
114	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp

115	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	N	G	Hyp
116	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	Q	G	Y
117	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Y
118	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Hyp
119	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
120	D	K	D	K	D	P	V	A	P	P	T	N	V	G	S	N	S	Hyp
121	D	K	D	K	D	N	V	A	P	R	S	N	V	G	P	Q	G	Hyp
122	D	K	A	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
123	D	K	D	G	A	-	I	A	P	R	T	K	I	G	S	Q	G	Y
124	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	N	G	Hyp
125	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	Q	G	Hyp
126	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
127	D	K	D	K	D	N	V	A	P	R	S	K	I	G	P	Q	G	Hyp
128	N	N	F	G	A	-	I	A	P	S	T	K	I	G	P	N	G	Y
129	D	K	D	K	D	N	V	A	P	R	S	K	V	G	P	Q	G	Y
130	D	K	D	K	D	P	V	A	P	P	T	N	V	G	S	N	G	Hyp
131	D	K	D	K	D	N	V	A	P	R	S	N	V	S	P	Q	G	Y
132	D	K	D	K	D	N	V	A	P	R	T	K	V	S	P	Q	G	Hyp
133	D	K	D	K	D	P	V	A	P	P	T	N	V	G	S	N	G	Hyp
134	D	K	D	K	D	N	V	A	P	R	T	K	V	S	P	N	G	Hyp
135	D	K	D	K	D	N	V	A	P	R	S	N	V	G	P	Q	G	Hyp
136	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
137	D	K	D	K	D	P	V	A	P	P	T	N	V	G	S	N	G	Hyp
138	D	K	D	K	D	N	V	A	P	R	S	N	V	G	P	Q	G	Y
139	D	K	D	K	D	N	V	A	P	R	S	K	V	G	P	N	G	Hyp
140	D	K	D	K	D	N	V	A	P	R	T	N	I	S	P	Q	G	Y
141	D	K	D	K	D	N	V	A	P	R	T	N	I	S	P	Q	G	Hyp
142	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	N	G	Y
143	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Hyp
144	D	K	D	K	D	P	V	A	P	P	T	N	V	G	S	N	G	Hyp
145	D	K	D	K	D	N	V	A	P	R	S	N	V	S	P	Q	G	Hyp
146	D	K	D	K	D	N	V	A	P	R	T	K	I	S	P	Q	G	Hyp
147	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
148	N	N	F	G	A	-	I	L	S	S	T	K	I	G	S	N	G	Y
149	N	N	F	G	A	-	I	L	P	S	T	K	V	G	P	N	G	Y
150	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
151	D	K	D	K	D	N	V	A	P	R	S	N	I	G	P	N	G	Hyp
152	D	K	D	K	D	N	V	A	P	R	S	K	V	G	P	Q	G	Hyp
153	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
154	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	G	Y
155	D	K	D	K	D	N	V	A	P	R	T	K	V	S	P	Q	G	Y
156	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Y
157	D	K	D	K	D	N	V	A	P	R	S	K	I	G	P	N	G	Hyp

158	D	K	D	K	D	N	V	A	P	R	S	N	I	S	P	Q	G	Hyp
159	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
160	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Y
161	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	Q	G	Hyp
162	N	N	F	G	A	-	I	L	P	S	T	K	I	G	P	N	G	Y
163	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	N	G	Hyp
164	D	K	D	K	D	N	V	A	P	R	T	K	I	S	P	Q	G	Y
165	D	K	D	K	D	N	V	A	P	R	S	N	I	G	P	Q	G	Hyp
166	D	K	D	K	D	N	V	A	P	R	S	N	V	S	P	N	G	Hyp
167	D	K	D	K	D	N	V	A	P	R	S	K	V	S	P	Q	G	Hyp
168	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
169	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	G	Hyp
170	D	K	D	K	D	N	V	A	P	R	T	N	I	S	P	N	G	Hyp
171	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
172	D	K	D	K	D	N	V	A	P	R	S	N	V	S	P	N	G	Y
173	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
174	D	K	D	K	D	N	V	A	P	R	S	K	V	S	P	Q	G	Y
175	D	K	D	K	D	N	V	A	P	R	S	K	V	S	P	N	G	Hyp
176	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	Q	G	Y
177	D	K	D	K	D	N	V	A	P	R	S	N	V	G	P	N	G	Y
178	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	Q	G	Hyp
179	D	K	D	K	D	N	V	A	P	R	S	K	I	G	P	Q	G	Hyp
180	N	N	F	G	A	-	I	L	P	S	T	K	I	G	S	N	T	Y
181	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
182	D	K	D	K	D	N	V	A	P	R	S	N	I	S	P	Q	G	Y
183	D	K	D	K	D	N	V	A	P	R	S	N	V	S	P	Q	G	Y
184	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	W
185	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	W	Hyp
186	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	Y	HYP
187	D	K	D	K	D	N	V	A	P	R	S	K	V	G	P	Q	G	Hyp
188	D	K	D	K	D	N	V	A	P	R	T	N	I	S	P	N	G	Y
189	D	K	D	K	D	N	V	A	P	R	T	K	I	S	P	Q	G	Hyp
190	D	K	D	K	D	N	V	A	P	R	T	K	I	S	P	N	G	Y
191	D	K	D	K	D	N	V	A	P	R	S	N	I	G	P	Q	G	Y
192	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
193	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
194	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
195	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
196	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
197	D	K	D	K	D	N	V	A	P	R	T	K	I	S	P	N	G	Hyp
198	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
199	D	K	D	K	D	N	V	A	P	R	T	N	I	S	P	Q	G	Y
200	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Y

201	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	H	Hyp
202	D	K	D	K	D	N	V	A	P	S	S	K	I	S	P	Q	T	Hyp
203	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	P	Hyp
204	D	K	D	K	D	N	V	A	P	R	S	K	V	S	P	N	G	Hyp
205	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
206	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	K	Hyp
207	N	N	F	G	A	-	I	L	P	S	T	K	I	G	S	N	G	Y
208	D	K	D	K	D	N	V	A	P	R	T	N	V	G	S	N	T	Y
209	D	K	D	K	D	N	V	A	P	R	T	K	V	S	P	Q	G	Y
210	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
211	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	F	Hyp
212	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
213	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
214	D	K	D	K	D	N	V	A	P	R	T	N	I	S	P	Q	G	Hyp
215	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	M
216	D	K	D	K	D	N	V	A	P	R	T	K	V	S	P	Q	G	Hyp
217	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
218	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	A	Hyp
219	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	H	Hyp
220	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	W	Hyp
221	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
222	D	K	D	K	D	N	V	A	P	S	S	K	I	S	P	Q	T	Hyp
223	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Y
224	D	K	D	K	D	N	V	A	P	R	S	N	V	S	P	Q	G	Hyp
225	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
226	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	W
227	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
228	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
229	D	K	D	K	D	N	V	A	P	R	S	N	I	G	P	Q	G	Hyp
230	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Y
231	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
232	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	Q	Hyp
233	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
234	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	G	Y
235	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	P
236	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	M	Hyp
237	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	M
238	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	F	Hyp
239	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	F
240	D	K	D	K	D	N	V	A	P	S	S	K	I	S	P	Q	T	Hyp
241	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	A
242	N	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	R
243	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp

244	N	K	D	K	A	Q	V	S	P	P	T	E	V	G	P	N	S	Hyp
245	N	K	D	K	A	Q	V	S	P	P	T	E	V	G	P	N	S	Hyp
246	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
247	D	K	D	K	A	N	V	S	P	P	T	E	V	G	P	N	S	Hyp
248	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Hyp
249	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
250	D	K	D	A	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
251	D	K	D	K	D	N	A	A	P	P	T	N	V	G	S	N	G	Hyp
252	D	K	D	K	D	N	V	A	P	A	T	N	V	G	S	N	G	Hyp
253	T	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
254	D	K	D	K	D	N	V	P	P	T	-	N	V	G	S	N	G	Hyp
255	D	K	D	K	D	N	V	A	P	T	-	N	V	G	S	N	G	Hyp
256	D	K	D	K	D	Q	V	A	P	P	T	N	V	G	S	N	S	Hyp
257	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Y
258	D	K	A	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
259	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Hyp
260	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Hyp
261	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Hyp
262	D	K	D	K	D	N	V	A	A	P	T	N	V	G	S	N	G	Hyp
263	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Y
264	D	K	D	K	D	N	V	A	P	R	T	N	V	G	S	N	T	Y
265	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
266	D	K	D	K	D	N	V	S	P	P	T	N	V	G	S	N	G	Hyp
267	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Hyp
268	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
269	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	N	G	Y
270	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	N	G	Hyp
271	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	N	G	Y
272	D	K	D	K	D	N	V	A	P	R	T	E	V	G	S	N	G	Y
273	D	K	D	K	D	N	V	A	P	R	T	N	V	G	P	Q	G	Y
274	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	Q	G	Hyp
275	D	K	D	K	D	N	V	A	P	R	T	K	I	S	P	N	G	Hyp
276	D	K	D	K	D	N	V	A	P	P	T	N	V	G	S	N	G	Hyp
277	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	N	G	Hyp
278	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	Q	G	Y
279	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Y
280	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Hyp
281	D	K	D	K	D	N	V	A	P	R	S	N	V	G	P	Q	G	Hyp
282	D	K	D	G	-	A	I	A	P	R	T	K	I	G	S	Q	G	Y
283	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	Q	G	Hyp
284	D	K	D	K	D	N	V	A	P	R	S	K	I	G	P	Q	G	Hyp
285	D	K	D	K	D	N	V	A	P	R	S	K	V	G	P	Q	G	Y
286	D	K	D	K	D	N	V	A	P	R	S	N	V	S	P	Q	G	Y

287	D	K	D	K	D	N	V	A	P	R	T	K	V	S	P	Q	G	Hyp
288	D	K	D	K	D	N	V	A	P	R	T	K	V	S	P	N	G	Hyp
289	D	K	D	K	D	N	V	A	P	R	S	N	V	G	P	Q	G	Hyp
290	D	K	D	K	D	N	V	A	P	R	S	K	V	G	P	N	G	Hyp
291	D	K	D	K	D	N	V	A	P	R	T	N	I	S	P	Q	G	Hyp
292	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Hyp
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295	D	K	F	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
296	D	K	D	K	D	N	V	A	P	R	S	K	I	S	P	Q	T	Hyp
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298	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Y
299	D	K	D	K	D	N	V	A	P	R	S	K	I	G	P	N	G	Hyp
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306	N	K	D	K	A	Q	V	S	P	P	T	E	V	G	P	N	S	Hyp
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319	D	K	D	K	D	N	V	A	P	T	-	N	V	G	S	N	G	Hyp
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334	D	K	D	K	D	N	V	A	P	R	T	E	V	G	S	N	G	Y
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341	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Hyp
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343	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	N	G	Hyp
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354	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Y
355	D	K	D	K	D	N	V	A	P	R	S	K	I	G	P	N	G	Hyp
356	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Y
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358	D	K	D	K	D	N	V	A	P	R	T	N	V	S	P	N	G	Hyp
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361	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Y
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373	D	K	D	K	D	N	V	A	P	R	S	N	V	G	P	N	G	Y
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377	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Y
278	D	K	D	K	D	N	V	A	P	R	T	K	V	G	S	N	G	Y
379	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Y
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381	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	N	G	Y
382	D	K	D	K	D	N	V	A	P	R	S	N	I	G	P	Q	G	Y
383	D	K	D	K	D	N	V	A	P	R	S	N	I	S	P	N	G	Y
384	D	K	D	K	D	N	V	A	P	R	S	K	V	S	P	N	G	Y
385	D	K	D	K	D	N	V	A	P	R	T	K	V	S	P	N	G	Y
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387	D	K	D	K	D	N	V	A	P	R	S	K	I	G	P	Q	G	Y
388	D	K	D	K	D	N	V	A	P	R	T	N	I	G	P	Q	G	Y
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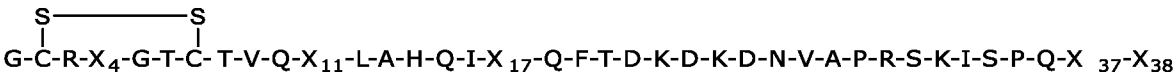
390	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	Q	G	Y
391	D	K	D	K	D	N	V	A	P	R	T	K	I	G	P	Q	G	Y
392	D	K	D	K	D	N	V	A	P	R	T	K	V	G	P	Q	G	Y

CLAIMS

1. An hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof comprising 38 amino acids (X_1-X_{38}) with an hAMY3R-EC_{50} ≤ 250 pM and an hAM1R-EC_{50} ≥ 25 nM, wherein the amino acid in position X_4 is selected as F, Y, W, T, M, I, A, or C; X_{37} is selected as G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected as Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; X_{11} is R, W, or Cit and wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position and further wherein the hAM_{15-52} analogue has at least 50 % homology (identity) to hAM_{15-52} (SEQ ID NO: 1).

2. An hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof according to claim 1, wherein the hAM_{15-52} analogue has at least 60 % homology to hAM_{15-52}, such as at least 70 % homology to hAM_{15-52}, preferably at least 80 % homology to hAM_{15-52} (SEQ ID NO: 1).

3. An hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof according to claim 1, comprising the amino acid sequence of formula (I):



(I)

wherein

X_{11} is selected from R, W, or Cit;

X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K;

X_4 is selected from F, Y, W, T, M, I, A, or C;

X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;

X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K;

and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position;

or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 % homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52}, preferably at least 95 % homology to hAM_{15-52}, wherein, in the derivative, X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

4. An hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof according to claim 1 with the sequence SEQ ID NOs: 3-360 or a derivative thereof with at least 50 % homology to hAM_{15-52}, such as at least 55 % homology to hAM_{15-52}, such as at least 60 % homology to hAM_{15-52}, such as at least 65 %

homology to hAM_{15-52}, preferably at least 70 % homology to hAM_{15-52}, such as at least 75 % homology to hAM_{15-52},, more preferably at least 80 % homology to hAM_{15-52}, such as at least 90 % homology to hAM_{15-52} (SEQ ID NO: 1), wherein, in the derivative, X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R, or K; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37}, or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

5. An hAM_{15-52} analogue or a pharmaceutically acceptable salt thereof according to claim 1 with the sequence SEQ ID NOs: 3-360 or a derivative thereof with at least 90 % homology (identity) to any one of SEQ ID NO: 3-360, preferably at least 95 % homology to any one of SEQ ID NO: 3-360, most preferably at least 97 % homology to anyone of SEQ ID NOs: 3-360, with the proviso that in the derivative X_{11} is selected from R, W, or Cit; X_{17} is selected as Y, W, T, Q, M, I, H, F, A, R or K; X_4 is selected from F, Y, W, T, M, I, A, or C; X_{37} is selected from G, Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K; X_{38} is selected from Hyp, Y, W, T, Q, P, M, I, H, F, E, A, R, or K; and further wherein at least one of the positions X_4, X_{37} or X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

6. An hAM_{15-52} analogue or a derivative thereof according to any of the preceding claims, wherein at least two of the positions X_4, X_{37}, and X_{38} is not the amino acid present in hAM_{15-52} (SEQ ID NO: 1) in said position.

7. An hAM_{15-52} analogue or a derivative thereof according to any of the preceding claims, wherein all of the positions X_4, X_{37} and X_{38} are selected as follows:
X_4 is selected from Y, W, T, M, I, A, or C;
X_{37} is selected from Y, S, W, T, Q, P, M, I, H, F, E, A, R, C, or K;
X_{38} is selected from Hyp, W, T, Q, P, M, I, H, F, E, A, R, or K;

8. An hAM_{15-52} analogue or a derivative thereof according to any of the preceding claims, wherein X_4 is selected as F, W, M, I, or C.

9. An hAM_{15-52} analogue or a derivative thereof according to any of the preceding claims, wherein X_{37} is selected as G, Y, W, P, H, or F.

10. An hAM_{15-52} analogue or a derivative thereof according to any of the preceding claims, wherein X_{38} is selected as Hyp, Y, W, M, or F.

11. An hAM_{15-52} analogue or a derivative thereof according to any of the preceding claims, wherein X_{17} is selected as W, or H.

12. An hAM_{15-52} analogue or a derivative thereof according to any of the preceding claims, wherein X_{11} is R.

13. An hAM_{15-52} analogue or a derivative thereof according to any of claims 1-12 for use as a medicament.

5

14. A pharmaceutical composition comprising an hAM_{15-52} analogue or a derivative thereof according to claims 1-12, a pharmaceutically acceptable carrier and optionally one or more excipient(s).

SEQUENCE LISTING

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Val Gly Pro Asn Ser Xaa
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 9

Arg Cys Asn Ala Ser Thr Cys Thr Val Asn Arg Leu Ala Asp Gln Ile
1   5   10   15

Thr Gln Phe Ser Asn Lys Asp Lys Ala Gln Val Ser Pro Pro Thr Glu
            20   25   30

Val Gly Pro Asn Ser Xaa
        35

<210> 10
<211> 38
<212> PRT
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 10

Lys Cys Asn Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Glu
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 11
<211> 38
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<220>
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<400> 11

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Asn Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 12
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<400> 12

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Lys Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 13
<211> 38
<212> PRT
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<220>
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<223> X = Hyp (L-hydroxyproline)

<400> 13

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Ala Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 14
<211> 38
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<220>
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<220>
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<400> 14

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 15
<211> 38
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 15

Lys Cys Asn Thr Ser Thr Cys Thr Val Ala Arg Leu Ala Asp Gln Ile
1   5   10   15

Thr Gln Phe Ser Asp Lys Asp Lys Ala Asn Val Ser Pro Pro Thr Glu
            20   25   30

Val Gly Pro Asn Ser Xaa
        35

<210> 16
<211> 38
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<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 16

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 17
<211> 38
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 17

Lys Cys Asn Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Glu
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 18
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 18

Lys Cys Asn Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Glu
            20   25   30

Val Gly Ser Asn Gly Pro
        35

<210> 19
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
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<400> 19

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Pro Arg Thr Lys Val
            20   25   30

Gly Ser Asn Gly Tyr
        35

<210> 20
<211> 38
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 20

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 21
<211> 38
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 21

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Asn Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 22
<211> 38
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<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 22

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Thr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 23
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
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<223> X = Hyp (L-hydroxyproline)

<400> 23

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Ala Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 24
<211> 38
<212> PRT
<213> Artificial Sequence

<220>

<223> Designed polypeptide

<220>
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<223> X = Hyp (L-hydroxyproline)

<400> 24

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Ala Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 25
<211> 38
<212> PRT
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 25

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Ala Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 26
<211> 38
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<213> Artificial Sequence

<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 26

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Ala Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 27
<211> 38
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 27

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Ala Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 28
<211> 38
<212> PRT
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 28

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Ala Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 29
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
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<220>

<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 29

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 30
<211> 37
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<220>
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<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 30

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 31
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 31

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa

35

<210> 32
<211> 38
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 32

Arg Cys Gln Thr Ser Thr Cys Thr Val Ala Arg Leu Ala Glu Gln Ile
1 5 10 15

Ala Gln Tyr Thr Asp Lys Asp Lys Asp Gln Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Ser Xaa
35

<210> 33
<211> 38
<212> PRT
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<220>
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 33

Arg Cys Gln Ala Ser Thr Cys Thr Val Ala Xaa Leu Ala Glu Gln Ile
1 5 10 15

Ala Gln Tyr Thr Asp Lys Asp Lys Asp Gln Val Ala Pro Pro Thr Glu
20 25 30

Val Gly Pro Asn Ser Xaa
35

<210> 34
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 34

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Ser Asn Gly Tyr
        35

<210> 35
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 35

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Gln Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 36
<211> 38
<212> PRT
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 36

Lys Cys Lys Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 37
<211> 38
<212> PRT
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<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 37

Lys Cys Asn Thr Ala Thr Cys Thr Val Ala Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 38
<211> 38
<212> PRT
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<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 38

Lys Cys Asn Thr Ala Thr Cys Thr Val Asn Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 39
<211> 38
<212> PRT
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 39

Arg Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 40
<211> 38
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 40

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Lys Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 41
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 41

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Lys Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 42
<211> 38

<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 42

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Ala Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 43
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 43

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Ala Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 44
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 44

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Tyr Asn
            20   25   30

Glu Gly Ser Asn Gly Xaa
        35

<210> 45
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 45

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 46
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 46

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 47
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 47

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Tyr Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 48
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 48

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Tyr Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 49
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 49

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn

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            20                  25                  30

Val Gly Pro Gln Gly Xaa
        35


<210>  50
<211>  38
<212>  PRT
<213>  Artificial Sequence

<220>
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<220>
<221>  misc_feature
<222>  (38)..(38)
<223>  X = Hyp (L-hydroxyproline)

<400>  50

Lys Cys Asn Thr Ser Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1               5                   10                  15


Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20                  25                  30


Val Gly Ser Asn Gly Xaa
        35


<210>  51
<211>  38
<212>  PRT
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<220>
<223>  Designed polypeptide

<220>
<221>  misc_feature
<222>  (38)..(38)
<223>  X = Hyp (L-hydroxyproline)

<400>  51

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1               5                   10                  15


Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20                  25                  30


Val Gly Ser Asn Gly Xaa
        35


<210>  52
<211>  38
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Designed polypeptide
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 52

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Ala Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 53
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 53

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Ala Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 54
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 54

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 55
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 55

Lys Cys Asn Thr Ala Thr Cys Thr Val Glu Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 56
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 56

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Ser Asn Thr Tyr
        35

<210> 57
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 57

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Ser Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 58
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 58

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Ser Ser Thr Lys Val
            20   25   30

Gly Ser Asn Thr Tyr
        35

<210> 59
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 59

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Pro Ser Thr Lys Val
            20   25   30

Gly Ser Asn Gly Tyr
        35

<210> 60
<211> 38
<212> PRT
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<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 60

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Lys
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 61
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 61

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 62
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 62

Lys Cys Asn Thr Ser Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 63
<211> 38
<212> PRT

<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 63

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Ala
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 64
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 64

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Ala Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 65
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 65

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 66
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 66

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ser Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 67
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 67

Lys Cys Asn Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Glu
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 68
<211> 38
<212> PRT
<213> Artificial Sequence

<220>

<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 68

Lys Cys Asn Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Glu
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 69
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 69

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Ser Xaa
        35

<210> 70
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 70

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 71
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 71

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Tyr Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 72
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 72

Lys Cys Gln Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 73
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>

<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 73

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Gln
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 74
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 74

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Lys Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 75
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 75

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa

35

<210> 76
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (14)..(14)
<223> X = Aad (L-homoglutamic acid)

<220>
<221> misc_feature
<222> (22)..(22)
<223> X = Sar (Sarcosine)

<220>
<221> misc_feature
<222> (24)..(24)
<223> X = (NMe)I (N-methyl-L-isoleucine)

<220>
<221> misc_feature
<222> (35)..(35)
<223> X = Hyp (L-hydroxyproline)

<400> 76

Arg Cys Gly Thr Ala Thr Cys Ala Thr Glu Arg Leu Ala Xaa Phe Leu
1 5 10 15

Gln Arg Ser Ser Phe Xaa Ala Xaa Leu Ser Ser Thr Glu Val Gly Ser
20 25 30

Asn Thr Xaa
35

<210> 77
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 77

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa

35

<210> 78
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 78

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1 5 10 15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 79
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 79

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Ala Gln Phe Ser Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 80
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (22)..(22)
<223> X = Sar (Sarcosine)

<220>
<221> misc_feature
<222> (24)..(24)
<223> X = (NMe)I (N-methyl-L-isoleucine)

<220>
<221> misc_feature
<222> (35)..(35)
<223> X = Hyp (L-hydroxyproline)

<400> 80

Arg Cys Gln Thr Ala Thr Cys Ala Thr Glu Arg Leu Ala His Phe Leu
1   5   10   15

Gln Arg Ser Ser Phe Xaa Ala Xaa Leu Ser Ser Thr Glu Val Gly Ser
            20   25   30

Asn Thr Xaa
        35

<210> 81
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 81

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 82
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 82

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 83
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 83

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Ala Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 84
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 84

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Asn Gly Tyr
        35

<210> 85
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>

<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 85

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Val Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 86
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 86

Lys Cys Asn Thr Ala Thr Cys Thr Val Ala Arg Leu Ala His Gln Ile
1   5   10   15

Asn Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 87
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 87

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asn Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa

35

<210> 88
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 88

Lys Cys Asn Thr Ser Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Pro Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 89
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 89

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1 5 10 15

Tyr Gln Phe Lys Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 90
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 90

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Val Gly Pro Asn Gly Xaa
35

<210> 91
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 91

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asn Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 92
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 92

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Pro Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 93
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 93

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Ala Pro Ser Thr Lys Val
            20   25   30

Gly Ser Asn Gly Tyr
        35

<210> 94
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 94

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Tyr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 95
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 95

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 96
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 96

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Thr Xaa
        35

<210> 97
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 97

Lys Cys Ala Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 98
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 98

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Asn Gly Tyr
        35

<210> 99
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 99

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 100
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 100

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Gln Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 101
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 101

Lys Cys Asn Ala Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 102
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 102

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Glu
            20   25   30

Val Gly Ser Asn Gly Tyr
        35

<210> 103
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 103

Lys Cys Asn Thr Ala Thr Cys Thr Val Val Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 104
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 104

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Tyr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 105
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 105

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Ala Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 106
<211> 38
<212> PRT
<213> Artificial Sequence

<220>

<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 106

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Ala Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 107
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 107

Lys Cys Asn Thr Ala Thr Cys Thr Val Ala Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 108
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 108

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Ala Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 109
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 109

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 110
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 110

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Glu Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 111
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 111

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 112
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 112

Lys Cys Asn Thr Ala Thr Cys Thr Val Asp Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 113
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 113

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Asn Gly Xaa
        35

<210> 114

<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 114

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Ala Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 115
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 115

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 116
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 116

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn

20 25 30

Val Ser Pro Gln Gly Tyr
35

<210> 117
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 117

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Ser Asn Gly Tyr
35

<210> 118
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 118

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Gly Pro Gln Gly Xaa
35

<210> 119
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (5)..(5)
<223> X = AIB (L-2-aminoisobutyric acid)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 119

Lys Cys Asn Thr Xaa Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 120
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 120

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Pro Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Ser Xaa
        35

<210> 121
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 121

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 122
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 122

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Ala Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 123
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 123

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Gly Ala Ile Ala Pro Arg Thr Lys Ile
            20   25   30

Gly Ser Gln Gly Tyr
        35

<210> 124
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 124

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 125
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 125

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 126
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 126

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 127
<211> 38

<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 127

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 128
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 128

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Ala Pro Ser Thr Lys Ile
            20   25   30

Gly Pro Asn Gly Tyr
        35

<210> 129
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 129

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 130
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 130

Lys Cys Asn Thr Ala Thr Cys Thr Val Asp Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Pro Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 131
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 131

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 132
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 132

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 133
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 133

Lys Cys Asn Thr Ala Thr Cys Thr Val Ala Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Pro Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 134
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 134

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Ser Pro Asn Gly Xaa
        35

<210> 135
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 135

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 136
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 136

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Lys Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 137
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 137

Lys Cys Asn Thr Ala Thr Cys Thr Val Ala Arg Leu Ala His Gln Ile
1   5   10   15

Asn Gln Phe Thr Asp Lys Asp Lys Asp Pro Val Ala Pro Pro Thr Asn

20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 138
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 138

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 139
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 139

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Val Gly Pro Asn Gly Xaa
35

<210> 140
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 140

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Ser Pro Gln Gly Tyr
35

<210> 141
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 141

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Ser Pro Gln Gly Xaa
35

<210> 142
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 142

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Gly Pro Asn Gly Tyr
35

<210> 143
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 143

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 144
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 144

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Pro Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 145
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 145

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 146
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 146

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Gln Gly Xaa
        35

<210> 147
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 147

Gly Cys Arg Ile Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 148
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 148

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Ser Ser Thr Lys Ile
            20   25   30

Gly Ser Asn Gly Tyr
        35

<210> 149
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 149

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Pro Ser Thr Lys Val
            20   25   30

Gly Pro Asn Gly Tyr
        35

<210> 150
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 150

Gly Cys Arg Trp Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 151
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 151

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 152
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 152

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 153
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 153

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala Glu Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 154
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 154

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Gly Tyr
        35

<210> 155
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 155

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 156
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 156

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 157
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 157

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 158
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 158

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Ser Pro Gln Gly Xaa
        35

<210> 159
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 159

Lys Cys Asn Thr Ala Thr Cys Thr Val Ile Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 160
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 160

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Gln Gly Tyr
        35

<210> 161
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 161

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa

35

<210> 162
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 162

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1 5 10 15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Pro Ser Thr Lys Ile
20 25 30

Gly Pro Asn Gly Tyr
35

<210> 163
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 163

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Val Ser Pro Asn Gly Xaa
35

<210> 164
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 164

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys

```
            20                  25                  30

Ile Ser Pro Gln Gly Tyr
        35


<210>  165
<211>  38
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Designed polypeptide

<220>
<221>  misc_feature
<222>  (38)..(38)
<223>  X = Hyp (L-hydroxyproline)

<400>  165

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1               5                   10                  15


Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20                  25                  30


Ile Gly Pro Gln Gly Xaa
        35


<210>  166
<211>  38
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Designed polypeptide

<220>
<221>  misc_feature
<222>  (38)..(38)
<223>  X = Hyp (L-hydroxyproline)

<400>  166

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1               5                   10                  15


Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20                  25                  30


Val Ser Pro Asn Gly Xaa
        35


<210>  167
<211>  38
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Designed polypeptide
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 167

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 168
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 168

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 169
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 169

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Gly Xaa
        35

<210> 170
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 170

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Ser Pro Asn Gly Xaa
        35

<210> 171
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 171

Gly Cys Arg Trp Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 172
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 172

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Asn Gly Tyr
        35

<210> 173
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 173

Gly Cys Arg Met Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 174
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 174

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 175
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 175

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Ser Pro Asn Gly Xaa
        35

<210> 176
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 176

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 177
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 177

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Gly Pro Asn Gly Tyr
        35

<210> 178
<211> 38
<212> PRT

<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 178

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 179
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 179

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 180
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 180

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Pro Ser Thr Lys Ile
            20   25   30

Gly Ser Asn Thr Tyr
        35

<210> 181
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 181

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 182
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 182

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Ser Pro Gln Gly Tyr
        35

<210> 183
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 183

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 184
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 184

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Trp
        35

<210> 185
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 185

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Trp Xaa
        35

<210> 186
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature

<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 186

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Tyr Xaa
        35

<210> 187
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 187

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 188
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 188

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Ser Pro Asn Gly Tyr
        35

<210> 189
<211> 38

<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 189

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Gln Gly Xaa
        35

<210> 190
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 190

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Asn Gly Tyr
        35

<210> 191
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 191

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Gly Pro Gln Gly Tyr
        35

<210> 192
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 192

Gly Cys Arg Met Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 193
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 193

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

His Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 194
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 194

Lys Cys Arg Met Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 195
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 195

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 196
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 196

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 197

<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 197

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Asn Gly Xaa
        35

<210> 198
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 198

Gly Cys Arg Ile Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 199
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 199

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn

20 25 30

Ile Ser Pro Gln Gly Tyr
35

<210> 200
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 200

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 201
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 201

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Ile Ser Pro Gln His Xaa
35

<210> 202
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 202

Gly Cys Arg Trp Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Ser Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 203
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 203

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Pro Xaa
        35

<210> 204
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 204

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Ser Pro Asn Gly Xaa
        35

<210> 205
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 205

Lys Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 206
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 206

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Lys Xaa
        35

<210> 207
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 207

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Pro Ser Thr Lys Ile
            20   25   30

Gly Ser Asn Gly Tyr
        35

<210> 208
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 208

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Ser Asn Thr Tyr
        35

<210> 209
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 209

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 210
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 210

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ala
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 211
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 211

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Phe Xaa
        35

<210> 212
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 212

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 213
<211> 38
<212> PRT

<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 213

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Trp Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 214
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 214

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Ser Pro Gln Gly Xaa
        35

<210> 215
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 215

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Met
        35

<210> 216
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 216

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 217
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 217

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 218
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature

<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 218

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Ala Xaa
        35

<210> 219
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 219

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln His Xaa
        35

<210> 220
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 220

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Trp Xaa
        35

<210> 221
<211> 38
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<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 221

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 222
<211> 38
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<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 222

Gly Cys Arg Met Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Ser Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 223
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 223

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Ser Asn Gly Tyr
        35

<210> 224
<211> 38
<212> PRT
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 224

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 225
<211> 38
<212> PRT
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 225

Lys Cys Asn Thr Leu Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 226
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<400> 226

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Trp
        35

<210> 227
<211> 38
<212> PRT
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 227

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

His Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 228
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 228

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

His Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa

35

<210> 229
<211> 38
<212> PRT
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<220>
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<220>
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<400> 229

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
20 25 30

Ile Gly Pro Gln Gly Xaa
35

<210> 230
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<400> 230

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Ile Ser Pro Gln Thr Tyr
35

<210> 231
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 231

Lys Cys Asn Thr Tyr Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 232
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 232

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Ile Ser Pro Gln Gln Xaa
35

<210> 233
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 233

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Arg Leu Ala Glu Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 234
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 234

Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1   5   10   15

Val Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Gly Tyr
        35

<210> 235
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 235

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Pro
        35

<210> 236
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 236

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Met Xaa
        35

<210> 237
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 237

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Met
        35

<210> 238
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 238

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Phe Xaa
        35

<210> 239
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 239

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Phe
35

<210> 240
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 240

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Ser Ser Lys
20 25 30

Ile Ser Pro Gln Thr Xaa
35

<210> 241
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 241

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Ile Ser Pro Gln Thr Ala
35

<210> 242
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 242

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asn Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Arg
        35

<210> 243
<211> 38
<212> PRT
<213> Artificial Sequence

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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 243

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala Ala Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 244
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (11)..(11)
<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 244

Lys Cys Asn Thr Ser Thr Cys Thr Val Ala Xaa Leu Ala Asp Gln Ile
1   5   10   15

Thr Gln Phe Ser Asn Lys Asp Lys Ala Gln Val Ser Pro Pro Thr Glu
            20   25   30

Val Gly Pro Asn Ser Xaa

35

<210> 245
<211> 38
<212> PRT
<213> Artificial Sequence

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<222> (11)..(11)
<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 245

Arg Cys Asn Ala Ser Thr Cys Thr Val Asn Xaa Leu Ala Asp Gln Ile
1 5 10 15

Thr Gln Phe Ser Asn Lys Asp Lys Ala Gln Val Ser Pro Pro Thr Glu
20 25 30

Val Gly Pro Asn Ser Xaa
35

<210> 246
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 246

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1 5 10 15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 247
<211> 38

<212> PRT
<213> Artificial Sequence

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<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 247

Lys Cys Asn Thr Ser Thr Cys Thr Val Ala Xaa Leu Ala Asp Gln Ile
1   5   10   15

Thr Gln Phe Ser Asp Lys Asp Lys Ala Asn Val Ser Pro Pro Thr Glu
            20   25   30

Val Gly Pro Asn Ser Xaa
        35

<210> 248
<211> 38
<212> PRT
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<223> X = Hyp (L-hydroxyproline)

<400> 248

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 249
<211> 38
<212> PRT
<213> Artificial Sequence

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<220>
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<223> X = Cit (L-citrulline)

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<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 249

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Ala Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 250
<211> 38
<212> PRT
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<220>
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 250

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Ala Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 251
<211> 38
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<220>
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<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 251

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Ala Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 252
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 252

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Ala Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 253
<211> 37
<212> PRT
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<220>
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<223> X = Hyp (L-hydroxyproline)

<400> 253

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 254
<211> 37
<212> PRT
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<223> X = Hyp (L-hydroxyproline)

<400> 254

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 255
<211> 37
<212> PRT
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<220>
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<223> X = Cit (L-citrulline)

<220>
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<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 255

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 256
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 256

Arg Cys Gln Thr Ser Thr Cys Thr Val Ala Xaa Leu Ala Glu Gln Ile
1   5   10   15

Ala Gln Tyr Thr Asp Lys Asp Lys Asp Gln Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Ser Xaa
        35

<210> 257
<211> 38
<212> PRT
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<220>
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<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 257

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Ser Asn Gly Tyr
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<210> 258
<211> 38
<212> PRT
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<223> X = Cit (L-citrulline)

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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 258

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Ala Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 259
<211> 38
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<223> X = Hyp (L-hydroxyproline)

<400> 259

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 260
<211> 38
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 260

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 261
<211> 38
<212> PRT
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<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 261

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 262
<211> 38
<212> PRT
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<220>
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<222> (11)..(11)
<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 262

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Ala Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 263
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 263

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 264
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 264

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn

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            20                  25                  30

Val Gly Ser Asn Thr Tyr
        35


<210>  265
<211>  37
<212>  PRT
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<220>
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<220>
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<222>  (37)..(37)
<223>  X = Hyp (L-hydroxyproline)

<400>  265

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1               5                   10                  15


Tyr Gln Phe Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn Val
            20                  25                  30


Gly Ser Asn Gly Xaa
        35


<210>  266
<211>  38
<212>  PRT
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<222>  (38)..(38)
<223>  X = Hyp (L-hydroxyproline)

<400>  266

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala Glu Gln Ile
1               5                   10                  15


Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ser Pro Pro Thr Asn
            20                  25                  30


Val Gly Ser Asn Gly Xaa
        35
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<210> 267
<211> 38
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 267

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 268
<211> 38
<212> PRT
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<222> (11)..(11)
<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 268

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 269
<211> 38
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<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 269

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Asn Gly Tyr
        35

<210> 270
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (11)..(11)
<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 270

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Asn Gly Xaa
        35

<210> 271
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 271

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Asn Gly Tyr
        35

<210> 272
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 272

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Glu
            20   25   30

Val Gly Ser Asn Gly Tyr
        35

<210> 273
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 273

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 274

<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 274

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 275
<211> 38
<212> PRT
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<220>
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<220>
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<220>
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<223> X = Hyp (L-hydroxyproline)

<400> 275

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Asn Gly Xaa
        35

<210> 276
<211> 38
<212> PRT
<213> Artificial Sequence

<220>

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<220>
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<220>
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<223> X = Hyp (L-hydroxyproline)

<400> 276

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Ala Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 277
<211> 38
<212> PRT
<213> Artificial Sequence

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<220>
<221> misc_feature
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<223> X = Hyp (L-hydroxyproline)

<400> 277

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 278
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<212> PRT
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<220>
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<220>
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<223> X = Cit (L-citrulline)

<400> 278

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 279
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> X = Cit (L-citrulline)

<400> 279

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Ser Asn Gly Tyr
        35

<210> 280
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<223> X = Hyp (L-hydroxyproline)

<400> 280

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 281
<211> 38
<212> PRT
<213> Artificial Sequence

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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 281

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 282
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 282

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Gly Ala Ile Ala Pro Arg Thr Lys Ile
            20   25   30

Gly Ser Gln Gly Tyr
        35

<210> 283
<211> 38
<212> PRT
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<220>
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<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 283

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 284
<211> 38
<212> PRT
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<220>
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<223> X = Hyp (L-hydroxyproline)

<400> 284

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 285
<211> 38
<212> PRT
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<220>
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<220>

<221> misc_feature
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<223> X = Cit (L-citrulline)

<400> 285

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 286
<211> 38
<212> PRT
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<220>
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<220>
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<400> 286

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 287
<211> 38
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<400> 287

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 288
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<400> 288

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Ser Pro Asn Gly Xaa
        35

<210> 289
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 289

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Gly Pro Gln Gly Xaa

35

<210> 290
<211> 38
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<223> X = Hyp (L-hydroxyproline)

<400> 290

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Val Gly Pro Asn Gly Xaa
35

<210> 291
<211> 38
<212> PRT
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<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 291

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Ser Pro Gln Gly Xaa
35

<210> 292
<211> 38

<212> PRT
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 292

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 293
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 293

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 294
<211> 38
<212> PRT
<213> Artificial Sequence

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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 294

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Gln Gly Xaa
        35

<210> 295
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 295

Gly Cys Arg Ile Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 296
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (11)..(11)
<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 296

Gly Cys Arg Trp Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 297
<211> 38
<212> PRT
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<220>
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<220>
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 297

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 298
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (11)..(11)
<223> X = Cit (L-citrulline)

<400> 298

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 299
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> X = Cit (L-citrulline)

<220>
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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 299

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 300
<211> 38
<212> PRT
<213> Artificial Sequence

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<220>
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<223> X = Cit (L-citrulline)

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<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 300

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Ser Pro Gln Gly Xaa
        35

<210> 301
<211> 38
<212> PRT
<213> Artificial Sequence

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<220>
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 301

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 302
<211> 38
<212> PRT
<213> Artificial Sequence

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<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 302

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Asn Gly Xaa
        35

<210> 303
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 303

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 304
<211> 38
<212> PRT
<213> Artificial Sequence

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<220>
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 304

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Asn Gly Xaa
        35

<210> 305
<211> 38
<212> PRT
<213> Artificial Sequence

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<220>
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<223> X = Cit (L-citrulline)

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 305

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Xaa Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Ser Pro Gln Gly Xaa
        35

<210> 306
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 306

Lys Cys Asn Thr Ser Thr Cys Thr Val Ala Trp Leu Ala Asp Gln Ile
1   5   10   15

Thr Gln Phe Ser Asn Lys Asp Lys Ala Gln Val Ser Pro Pro Thr Glu
            20   25   30

Val Gly Pro Asn Ser Xaa
        35

<210> 307
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 307

Arg Cys Asn Ala Ser Thr Cys Thr Val Asn Trp Leu Ala Asp Gln Ile
1   5   10   15

Thr Gln Phe Ser Asn Lys Asp Lys Ala Gln Val Ser Pro Pro Thr Glu
            20   25   30

Val Gly Pro Asn Ser Xaa
        35

<210> 308
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 308

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Ala Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 309
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 309

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Ala Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 310
<211> 38
<212> PRT

<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 310

Lys Cys Asn Thr Ser Thr Cys Thr Val Ala Trp Leu Ala Asp Gln Ile
1   5   10   15

Thr Gln Phe Ser Asp Lys Asp Lys Ala Asn Val Ser Pro Pro Thr Glu
            20   25   30

Val Gly Pro Asn Ser Xaa
        35

<210> 311
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 311

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala Asn Phe Leu
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 312
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 312

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 313
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 313

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Ala Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 314
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 314

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Ala Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 315
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature

<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 315

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Ala Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 316
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 316

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Ala Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 317
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 317

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 318
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 318

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 319
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 319

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 320
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 320

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Ala Lys Asp Asn Val Ala Pro Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 321
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 321

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala Glu Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Tyr Asn
20 25 30

Glu Gly Ser Asn Gly Xaa
35

<210> 322
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 322

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Pro Gln Gly Xaa
35

<210> 323

<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 323

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 324
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 324

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Ala Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 325
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 325

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Ala Pro Thr Asn
20 25 30

Val Gly Ser Asn Gly Xaa
35

<210> 326
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 326

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 327
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 327

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Val Gly Ser Asn Thr Tyr
35

<210> 328
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 328

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Ala Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 329
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (37)..(37)
<223> X = Hyp (L-hydroxyproline)

<400> 329

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn Val
            20   25   30

Gly Ser Asn Gly Xaa
        35

<210> 330
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 330

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 331
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 331

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 332
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 332

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Asn Gly Tyr
        35

<210> 333
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 333

Lys Cys Asn Ala Ala Thr Cys Thr Val Gln Trp Leu Ala Glu Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 334
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 334

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Glu
            20   25   30

Val Gly Ser Asn Gly Tyr
        35

<210> 335
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 335

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 336
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 336

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 337
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 337

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Asn Gly Xaa
        35

<210> 338
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 338

Lys Cys Asn Thr Ala Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Ala Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Pro Thr Asn
            20   25   30

Val Gly Ser Asn Gly Xaa
        35

<210> 339
<211> 38
<212> PRT

<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 339

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 340
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 340

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 341
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 341

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 342
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 342

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 343
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 343

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 344
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 344

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 345
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 345

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Ser Pro Gln Gly Tyr
        35

<210> 346
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 346

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 347
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature

<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 347

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Gly Pro Asn Gly Xaa
        35

<210> 348
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 348

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Asn Gly Tyr
        35

<210> 349
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 349

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 350
<211> 38

<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 350

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Ser Pro Gln Gly Xaa
        35

<210> 351
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 351

Gly Cys Arg Ile Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Phe Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Ser Pro Gln Thr Xaa
        35

<210> 352
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 352

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 353
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 353

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Val Gly Pro Gln Gly Xaa
        35

<210> 354
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 354

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Val Gly Pro Gln Gly Tyr
        35

<210> 355
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>

<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 355

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
            20   25   30

Ile Gly Pro Asn Gly Xaa
        35

<210> 356
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 356

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Ile Gly Pro Gln Gly Tyr
        35

<210> 357
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 357

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 358

<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 358

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
            20   25   30

Val Ser Pro Asn Gly Xaa
        35

<210> 359
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 359

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile
1   5   10   15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
            20   25   30

Ile Gly Pro Gln Gly Xaa
        35

<210> 360
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<220>
<221> misc_feature
<222> (38)..(38)
<223> X = Hyp (L-hydroxyproline)

<400> 360

Gly Cys Arg Thr Gly Thr Cys Thr Val Gln Trp Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
20 25 30

Val Ser Pro Asn Gly Xaa
35

<210> 361
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 361

Lys Cys Asn Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Ser Asn Gly Tyr
35

<210> 362
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 362

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 363
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 363

Lys Cys Asn Phe Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu

1 5 10 15

Val Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 364
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 364

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 365
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 365

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 366
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 366

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Ser Pro Asn Gly Tyr
35

<210> 367
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 367

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Ile Gly Pro Asn Gly Tyr
35

<210> 368
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 368

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 369
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 369

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 370
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 370

Lys Cys Asn Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Glu
20 25 30

Val Gly Ser Asn Gly Tyr
35

<210> 371
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 371

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Ile Ser Pro Asn Gly Tyr
35

<210> 372
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 372

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala Asn Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 373
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 373

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
20 25 30

Val Gly Pro Asn Gly Tyr
35

<210> 374
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 374

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 375
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 375

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 376
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 376

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Ile Gly Ser Asn Gly Tyr
35

<210> 377
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 377

Gly Cys Arg Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 378
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 378

Lys Cys Asn Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Ser Asn Gly Tyr
35

<210> 379
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 379

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 380
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 380

Gly Cys Arg Phe Ala Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 381
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 381

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Gly Pro Asn Gly Tyr
35

<210> 382
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 382

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 383
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 383

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Asn
20 25 30

Ile Ser Pro Asn Gly Tyr
35

<210> 384
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 384

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Val Ser Pro Asn Gly Tyr
35

<210> 385
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 385

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Ser Pro Asn Gly Tyr
35

<210> 386
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 386

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala Asn Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Val Gly Pro Gln Gly Tyr
35

<210> 387
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 387

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 388
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 388

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Asn
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 389
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 389

Lys Cys Asn Phe Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe Leu
1 5 10 15

Val Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 390
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 390

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu

1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 391
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 391

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Gln Ile
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Ile Gly Pro Gln Gly Tyr
35

<210> 392
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed polypeptide

<400> 392

Gly Cys Arg Phe Gly Thr Cys Thr Val Gln Arg Leu Ala His Phe Leu
1 5 10 15

Tyr Gln Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Thr Lys
20 25 30

Val Gly Pro Gln Gly Tyr
35