

METHODS AND COMPOSITIONS FOR GENOMIC INTEGRATION

CROSS REFERENCE

[0001] This Application claims the benefit of U.S. Provisional Application No. 62/895,441, filed on September 3, 2019, U.S. Provisional Application No. 62/908,800, filed on October 1, 2019, and U.S. Provisional Application No. 63/039,261, filed on June 15, 2020, each of which is incorporated herein by reference in its entirety.

BACKGROUND

[0002] Cell therapy is a rapidly developing field for addressing difficult to treat diseases, such as cancer, persistent infections and certain diseases that are refractory to other forms of treatment. Cell therapy often utilizes cells that are engineered ex vivo and administered to an organism to correct deficiencies within the body. An effective and reliable system for manipulation of a cell's genome is crucial, in the sense that when the engineered cell is administered into an organism, it functions optimally and with prolonged efficacy. Likewise, reliable mechanisms of genetic manipulation form the cornerstone in the success of gene therapy. However, severe deficiencies exist in methods for delivering nucleic acid cargo (e.g., large cargo) in a therapeutically safe and effective manner. Viral delivery mechanisms are frequently used to deliver large nucleic acid cargo in a cell but are tied to safety issues and cannot be used to express the cargo in some cell types. Additionally, subjecting a cell to repeated gene manipulation can affect cell health, induce alterations of cell cycle and render the cell unsuitable for therapeutic use. Advancements are continually sought in the area for efficacious delivery and stabilization of an exogenously introduced genetic material for therapeutic purposes.

SUMMARY

[0002a] In one aspect, provided herein is a composition comprising one or more exogenous RNA molecules, wherein the one or more exogenous RNA molecules comprise: (a) an RNA sequence encoding an exogenous human therapeutic polypeptide or an RNA sequence that is the reverse complement of a sequence encoding the exogenous human therapeutic polypeptide, and (b) an RNA sequence encoding an ORF2p polypeptide comprising a reverse transcription (RT) domain, and wherein the ORF2p polypeptide does not have endonuclease activity, and (c) a sequence encoding a CRISPR-Cas protein comprising an endonuclease domain, and (d) a guide RNA or a polynucleotide encoding the guide RNA, wherein the guide RNA targets a target site of a genome of a target human cell.

[0002b] In another aspect, provided herein is a method of expressing an exogenous human therapeutic polypeptide from a genomically integrated DNA sequence of a target human cell population, the method comprising: (a) contacting one or more exogenous RNA molecules to the target human cell population, wherein the one or more exogenous RNA molecules comprise: (i) an RNA sequence that (I) encodes the human therapeutic polypeptide or (II) an RNA sequence that is the reverse complement of a DNA sequence encoding the exogenous human therapeutic polypeptide, (ii) an RNA sequence encoding an ORF2p polypeptide comprising a reverse transcription (RT) domain, and wherein the ORF2p polypeptide does not have endonuclease activity, (iii) an RNA sequence encoding a CRISPR-Cas protein comprising an endonuclease domain, and (iv) a guide RNA or a polynucleotide encoding the guide RNA, wherein the guide RNA targets a target site of the genome.

[0002c] In another aspect, provided herein is use of the composition as described herein in the manufacture of a medicament for treating a disease or condition in a human subject.

[0002d] In another aspect, provided herein is the composition as described herein for use in therapy.

[0003] Provided herein are compositions and methods for stable, non-viral transfer and integration of genetic material into a cell. In one aspect, the genetic material is a self-integrating polynucleotide. The genetic material can be stably integrated in the genome of the cell. The cell may be a human cell. The method is designed for a safe and reliable integration of a genetic material into the genome of a cell.

[0004] In one aspect, provided herein are compositions and methods that allow integration of genetic material into the genome of a cell, wherein the genetic material that can be integrated is not specifically restricted by size. In some aspects, the method described herein provides a one-step, single polynucleotide-mediated delivery and integration of genetic "cargo" in the genome of a cell. The genetic material may comprise a coding sequence, e.g., a sequence encoding a transgene, a peptide, a recombinant protein, or an antibody or fragments thereof, wherein the method and compositions ensure stable expression of the transcribed product encoded by the coding sequence. The genetic material may comprise a non-coding sequence, for example, a regulatory RNA sequences, e.g., a regulatory small inhibitory RNA (siRNA), microRNA (miRNA), long non-coding RNA (lncRNA), or one or more transcription regulators such as a

Claims

What is claimed is:

1. A composition comprising one or more exogenous RNA molecules, wherein the one or more exogenous RNA molecules comprise:
 - (a) an RNA sequence encoding an exogenous human therapeutic polypeptide or an RNA sequence that is the reverse complement of a sequence encoding the exogenous human therapeutic polypeptide, and
 - (b) an RNA sequence encoding an ORF2p polypeptide comprising a reverse transcription (RT) domain, and wherein the ORF2p polypeptide does not have endonuclease activity, and
 - (c) a sequence encoding a CRISPR-Cas protein comprising an endonuclease domain, and
 - (d) a guide RNA or a polynucleotide encoding the guide RNA, wherein the guide RNA targets a target site of a genome of a target human cell..
2. A method of expressing an exogenous human therapeutic polypeptide from a genomically integrated DNA sequence of a target human cell population, the method comprising:
 - (a) contacting one or more exogenous RNA molecules to the target human cell population, wherein the one or more exogenous RNA molecules comprise:
 - (i) an RNA sequence that (I) encodes the human therapeutic polypeptide or (II) an RNA sequence that is the reverse complement of a DNA sequence encoding the exogenous human therapeutic polypeptide,
 - (ii) an RNA sequence encoding an ORF2p polypeptide comprising a reverse transcription (RT) domain, and wherein the ORF2p polypeptide does not have endonuclease activity,
 - (iii) an RNA sequence encoding a CRISPR-Cas protein comprising an endonuclease domain, and
 - (iv) a guide RNA or a polynucleotide encoding the guide RNA, wherein the guide RNA targets a target site of the genome.
3. The composition of claim 1 or the method of claim 2, wherein the one or more RNA molecules further comprise a sequence having homology to the target site.
4. The method of claim 2, wherein the method comprises expressing the exogenous human therapeutic polypeptide solely from the sequence integrated into the genomic DNA in the target human cell.
5. The composition of claim 3 or the method of claims 2 or 4, wherein the exogenous human therapeutic polypeptide is expressed in at least 2% of the cells in the human cell population.
6. The composition of claim 1, 3 or 5 or the method of claim 2, 4, or 5, wherein the RNA molecule is an in vitro transcribed RNA molecule, a synthetic RNA molecule, a purified RNA molecule, or an isolated RNA molecule.

7. The composition of any one of claims 1, 3 and 5-6 or the method of any one of claims 2 and 4-6, wherein the one or more exogenous RNA molecules comprise an mRNA molecule.
8. The composition of any one of claims 1, 3 and 5-7 or the method of any one of claims 2 and 4-7, wherein the ORF2p polypeptide comprises a human ORF2p.
9. The composition of claim 8 or the method of claim 8, wherein the one or more exogenous RNA molecules comprise a sequence encoding a human ORF1p.
10. The composition of claim 9 or the method of claim 9, wherein the one or more exogenous RNA molecules comprise a first RNA molecule and a second RNA molecule, wherein the first RNA molecule comprises the sequence encoding a human ORF1p, and the second RNA molecule encodes the human ORF2p, and wherein the ratio of the first RNA molecule to the second RNA molecule in the composition is (a) at least 2:1, (b) at most 5:1, or (c) about 3:1.
11. The composition of claim 10 or the method of claim 10, wherein the first RNA molecule comprises a first number of copies of a sequence encoding the human ORF1p or functional fragment thereof and the second RNA molecule comprises a second number of copies of a sequence encoding the human ORF2p or functional fragment thereof, wherein the ratio of the first number of copies to the second number of copies is at least 2:1.
12. The composition of any one of claims 8-11 or the method of any one of claims 8-11, wherein the ORF2p polypeptide comprises a sequence with at least 90% sequence identity to SEQ ID NO: 55.
13. The composition of any one of claims 1, 3, 5-12 or the method of any one of claims 2 and 4-12, wherein the ORF2p polypeptide comprises a nuclear localization signal (NLS).
14. The composition of any one of claims 1, 3, 5-13 or the method of any one of claims 2 and 4-13, wherein the human cell is an immune cell selected from the group consisting of a T cell, a B cell, a myeloid cell, a monocyte, a macrophage and a dendritic cell.
15. The method of any one of claims 2 and 4-14, wherein the method comprises translating the RNA sequence of (ii) and the RNA sequence of (iii);
reverse transcribing the RNA sequence of (i), thereby producing the DNA sequence encoding the exogenous human therapeutic polypeptide;
integrating the DNA sequence encoding the exogenous human therapeutic polypeptide into the genome;
and
expressing the exogenous human therapeutic polypeptide from the genomically integrated DNA sequence.
16. The method of any claim 15, wherein integrating comprises integrating the sequence encoding the exogenous human therapeutic polypeptide into the genomic DNA at a locus that is not a ribosomal DNA (rDNA) locus.
17. The composition of any one of claims 1, 3, and 5-14 or the method of any one of claims 2 and 4-16, wherein the exogenous human therapeutic polypeptide is a ligand, an antibody, a receptor, an enzyme, a

transport protein, a structural protein, a hormone, a contractile protein, a storage protein, a transcription factor, a chimeric antigen receptor (CAR) or a T cell receptor (TCR).

18. The composition of any one of claims 1, 3, 5-14, and 17 or the method of any one of claims 2 and 4-17, wherein the RNA molecule comprises a 5' UTR sequence, a 3' UTR sequence and a poly A sequence; wherein:
 - (i) the 5' UTR sequence is upstream of the sequence of the RNA sequence encoding the ORF2p polypeptide,
 - (ii) the 3' UTR sequence is downstream of the sequence encoding the exogenous human therapeutic polypeptide; and
 - (iii) the 3' UTR is upstream of the poly A sequence; andwherein the 5' UTR sequence, the 3' UTR sequence or the poly A sequence comprises a binding site for the ORF2p polypeptide.
19. The composition of any one of claims 1, 3, 5-14, 17, and 18 or the method of any one of claims 2 and 4-18, wherein the RNA molecule comprises a 5' UTR sequence and a 3' UTR sequence, wherein
 - (a) the 5' UTR comprises a 5' UTR from LINE-1; and/or
 - (b) the 3' UTR comprises a 3' UTR from LINE-1.
20. The composition of any one of claims 1, 3, 5-14, and 17-19 or the method of any one of claims 2 and 4-19, wherein the CRISPR-Cas protein comprises a Cas9 protein.
21. The composition of claim 20 or the method of claim 20, wherein the Cas9 is a Cas9 nickase.
22. The composition of any one of claims 1, 3, 5-14, and 17-21 or the method of any one of claims 2 and 4-21, wherein the ORF2p polypeptide comprises an endonuclease (EN) domain and wherein the EN domain comprises a mutation that inactivates the endonuclease activity of the ORF2p polypeptide.
23. The composition of claim 22 or the method of claim 22, wherein the mutation is a D205 mutation, a S228 mutation, a D145 mutation, or a H230 mutation.
24. Use of the composition of any one of claims 1, 3, 5-14, and 17-23 in the manufacture of a medicament for treating a disease or condition in a human subject.
25. The composition of any one of claims 1, 3, 5-14, and 17-23 for use in therapy.

SEQUENCE LISTING

<110> MYELOID THERAPEUTICS, INC.

<120> METHODS AND COMPOSITIONS FOR GENOMIC INTEGRATION

<130> 56371-706.601

<140> PCT/US2020/049240

<141> 2020-09-03

<150> 63/039,261

<151> 2020-06-15

<150> 62/908,800

<151> 2019-10-01

<150> 62/895,441

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<170> PatentIn version 3.5

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Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser Phe
50 55 60

Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val
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polypeptide

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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Thr Leu Ile
35 40 45

Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Tyr
65 70 75 80

Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln Tyr Asp Glu Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
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<223> Description of Artificial Sequence: Synthetic polypeptide

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

Ser Tyr Glu Lys Ser Asp Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn
20 25 30

Gln Glu Thr Tyr Glu Thr Leu Lys His Glu Lys Pro Pro Gln
35 40 45

<210> 4

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<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic polypeptide

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Tyr Glu Asp Met Arg Gly Ile Leu Tyr Ala Ala Pro Gln Leu Arg Ser
1 5 10 15

Ile Arg Gly Gln Pro Gly Pro Asn His Glu Glu Asp Ala Asp Ser Tyr
20 25 30

Glu Asn Met
35

<210> 5

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Lys Lys Val Ala Lys Lys Pro Thr Asn Lys Ala Pro His Pro Lys Gln
1 5 10 15

Glu Pro Gln Glu Ile Asn Phe Pro Asp Asp Leu Pro Gly Ser Asn Thr
20 25 30

Ala Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr Gln
35 40 45

Glu Asp Gly Lys Glu Ser Arg Ile Ser Val Gln Glu Arg Gln
50 55 60

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1 5 10 15

Ser Leu Val Ile Thr
20

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Ala Leu Ser Asn Ser Ile Met Tyr Phe Ser His Phe Val Pro Val Phe
1 5 10 15

Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
20 25 30

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
35 40 45

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
50 55 60

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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly Ser Thr
100 105 110

Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Glu Val Gln Leu
115 120 125

Val Glu
130

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<400> 9

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1 5 10 15

Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly
20 25 30

Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr
35 40 45

Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr
50 55 60

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
65 70 75 80

Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala
85 90 95

Met Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val
100 105

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Ser

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20 25 30

Gly Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn
35 40 45

Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Met Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser
65 70 75 80

Phe Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala
85 90 95

Tyr Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe
100 105 110

Cys Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly
115 120 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
145 150 155 160

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
165 170 175

Gln Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys
180 185 190

Ala Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val
195 200 205

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
210 215 220

Ile Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln
225 230 235 240

Tyr Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
245 250 255

Lys Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn Ser Ile Met Tyr
260 265 270

Phe Ser His Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr
275 280 285

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
290 295 300

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
305 310 315 320

His Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
325 330 335

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Arg Arg
340 345 350

Leu Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser
355 360 365

Asp Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu
370 375 380

Thr Leu Lys His Glu Lys Pro Pro Gln Gly Ser Gly Ser Tyr Glu Asp
385 390 395 400

Met Arg Gly Ile Leu Tyr Ala Ala Pro Gln Leu Arg Ser Ile Arg Gly
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Gln Pro Gly Pro Asn His Glu Glu Asp Ala Asp Ser Tyr Glu Asn Met
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<210> 15

<211> 436

<212> PRT

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<400> 15

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile
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Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
20 25 30

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr
35 40 45

Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
50 55 60

Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser
65 70 75 80

Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
85 90 95

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro
100 105 110

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly Ser
115 120 125

Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Glu Val Gln
130 135 140

Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
145 150 155 160

Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His
165 170 175

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile
180 185 190

Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg
195 200 205

Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met
 210 215 220

Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg Trp
 225 230 235 240

Gly Gly Asp Gly Phe Tyr Ala Met Asp Val Trp Gly Gln Gly Thr Leu
 245 250 255

Val Thr Val Ser Ser Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn
 260 265 270

Ser Ile Met Tyr Phe Ser His Phe Val Pro Val Phe Leu Pro Ala Lys
 275 280 285

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
 290 295 300

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
 305 310 315 320

Gly Gly Ala Val His Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro
 325 330 335

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
 340 345 350

Tyr Cys Arg Arg Leu Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser
 355 360 365

Tyr Glu Lys Ser Asp Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln
 370 375 380

Glu Thr Tyr Glu Thr Leu Lys His Glu Lys Pro Pro Gln Gly Ser Gly
 385 390 395 400

Ser Tyr Glu Asp Met Arg Gly Ile Leu Tyr Ala Ala Pro Gln Leu Arg
 405 410 415

Ser Ile Arg Gly Gln Pro Gly Pro Asn His Glu Glu Asp Ala Asp Ser
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Tyr Glu Asn Met
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<400> 16

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20 25 30

Gly Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn
35 40 45

Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Met Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser
65 70 75 80

Phe Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala
85 90 95

Tyr Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe
100 105 110

Cys Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly
115 120 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
145 150 155 160

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
165 170 175

Gln Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys
180 185 190

Ala Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val
195 200 205

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
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Ile Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln
225 230 235 240

Tyr Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
245 250 255

Lys Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn Ser Ile Met Tyr
260 265 270

Phe Ser His Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr
275 280 285

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
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Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
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His Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
325 330 335

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Arg Leu
340 345 350

Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp
355 360 365

Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr
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Leu Lys His Glu Lys Pro Pro Gln Lys Lys Val Ala Lys Lys Pro Thr
385 390 395 400

Asn Lys Ala Pro His Pro Lys Gln Glu Pro Gln Glu Ile Asn Phe Pro
405 410 415

Asp Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu Thr Leu
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peptide

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20 25 30

Pro Asn Pro Ser Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly
35 40 45

Phe Ser Pro Val Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr
50 55 60

Pro Gly Asp Cys Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro
65 70 75 80

Pro Tyr Gln Gly Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp
85 90 95

Pro Ile Pro Asn Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro
100 105 110

Gln Ser Leu Asp Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu
115 120 125

Asn Val Pro Pro Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu
130 135 140

Ser Asp His Glu Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu
145 150 155 160

Arg Glu Ala Gln Tyr Ser Met Leu Ala Thr Trp Arg Arg Arg Thr Pro
165 170 175

Arg Arg Glu Ala Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met
180 185 190

Asp Leu Leu Gly Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys Gly Pro
195 200 205

Ala Ala Leu Pro Pro Ala Pro Ser Leu Leu Arg
 210 215

<210> 22
 <211> 171
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 22
 Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro Ala Asp
 1 5 10 15

Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu Ile Thr
 20 25 30

Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu
 35 40 45

Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu
 50 55 60

Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser
 65 70 75 80

Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn
 85 90 95

Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser
 100 105 110

Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp
 115 120 125

Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu
 130 135 140

Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro
 145 150 155 160

Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
165 170

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

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 23
Met Ser Asn Gly Tyr Ser Thr Asp Glu Asn Phe Arg Tyr Leu Ile Ser
1 5 10 15

Cys Phe Arg Ala Arg Val Lys Met Tyr Ile Gln Val Glu Pro Val Leu
20 25 30

Asp Tyr Leu Thr Phe Leu Pro Ala Glu Val Lys Glu Gln Ile Gln Arg
35 40 45

Thr Val Ala Thr Ser Gly Asn Met Gln Ala Val Glu Leu Leu Leu Ser
50 55 60

Thr Leu Glu Lys Gly Val Trp His Leu Gly Trp Thr Arg Glu Phe Val
65 70 75 80

Glu Ala Leu Arg Arg Thr Gly Ser Pro Leu Ala Ala Arg Tyr Met Asn
85 90 95

Pro Glu Leu Thr Asp Leu Pro Ser Pro Ser Phe Glu Asn Ala His Asp
100 105 110

Glu Tyr Leu Gln Leu Leu Asn Leu Leu Gln Pro Thr Leu Val Asp Lys
115 120 125

Leu Leu Val Arg Asp Val Leu Asp Lys Cys Met Glu Glu Glu Leu Leu
130 135 140

Thr Ile Glu Asp Arg Asn Arg Ile Ala Ala Ala Glu Asn Asn Gly Asn
145 150 155 160

Glu Ser Gly Val Arg Glu Leu Leu Lys Arg Ile Val Gln Lys Glu Asn
165 170 175

Trp Phe Ser Ala Phe Leu Asn Val Leu Arg Gln Thr Gly Asn Asn Glu
180 185 190

Leu Val Gln Glu Leu Thr Gly Ser Asp Cys Ser Glu Ser Asn Ala Glu
195 200 205

Ile Glu Asn
210

<210> 24

<211> 607

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 24

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile
1 5 10 15

Ser Glu Ile Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly
20 25 30

Gly Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn
35 40 45

Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
50 55 60

Met Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser
65 70 75 80

Phe Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala
85 90 95

Tyr Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe
100 105 110

Cys Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly
115 120 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
145 150 155 160

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
165 170 175

Gln Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys
180 185 190

Ala Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val
195 200 205

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
210 215 220

Ile Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln
225 230 235 240

Tyr Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
245 250 255

Lys Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn Ser Ile Met Tyr
260 265 270

Phe Ser His Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr
275 280 285

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
290 295 300

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
305 310 315 320

His Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
325 330 335

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Arg Leu
340 345 350

Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp
355 360 365

Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr
370 375 380

Leu Lys His Glu Lys Pro Pro Gln Gly Ser Gly Ser Met Ser Asn Gly
385 390 395 400

Tyr Ser Thr Asp Glu Asn Phe Arg Tyr Leu Ile Ser Cys Phe Arg Ala
405 410 415

Arg Val Lys Met Tyr Ile Gln Val Glu Pro Val Leu Asp Tyr Leu Thr
420 425 430

Phe Leu Pro Ala Glu Val Lys Glu Gln Ile Gln Arg Thr Val Ala Thr
435 440 445

Ser Gly Asn Met Gln Ala Val Glu Leu Leu Leu Ser Thr Leu Glu Lys
450 455 460

Gly Val Trp His Leu Gly Trp Thr Arg Glu Phe Val Glu Ala Leu Arg
465 470 475 480

Arg Thr Gly Ser Pro Leu Ala Ala Arg Tyr Met Asn Pro Glu Leu Thr
485 490 495

Asp Leu Pro Ser Pro Ser Phe Glu Asn Ala His Asp Glu Tyr Leu Gln
500 505 510

Leu Leu Asn Leu Leu Gln Pro Thr Leu Val Asp Lys Leu Leu Val Arg
515 520 525

Asp Val Leu Asp Lys Cys Met Glu Glu Glu Leu Leu Thr Ile Glu Asp
530 535 540

Arg Asn Arg Ile Ala Ala Ala Glu Asn Asn Gly Asn Glu Ser Gly Val
 545 550 555 560

Arg Glu Leu Leu Lys Arg Ile Val Gln Lys Glu Asn Trp Phe Ser Ala
 565 570 575

Phe Leu Asn Val Leu Arg Gln Thr Gly Asn Asn Glu Leu Val Gln Glu
 580 585 590

Leu Thr Gly Ser Asp Cys Ser Glu Ser Asn Ala Glu Ile Glu Asn
 595 600 605

<210> 25

<211> 615

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 25

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile
 1 5 10 15

Ser Glu Ile Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly
 20 25 30

Gly Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn
 35 40 45

Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
 50 55 60

Met Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser
 65 70 75 80

Phe Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala
 85 90 95

Tyr Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe
 100 105 110

Cys Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly
115 120 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
145 150 155 160

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
165 170 175

Gln Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys
180 185 190

Ala Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val
195 200 205

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
210 215 220

Ile Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln
225 230 235 240

Tyr Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
245 250 255

Lys Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn Ser Ile Met Tyr
260 265 270

Phe Ser His Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr
275 280 285

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
290 295 300

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
305 310 315 320

His Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
325 330 335

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Arg Leu
340 345 350

Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp
355 360 365

Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr
370 375 380

Leu Lys His Glu Lys Pro Pro Gln Gly Ser Gly Ser Gln Arg Trp Lys
385 390 395 400

Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu
405 410 415

Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser
420 425 430

Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val
435 440 445

Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr Pro Gly Asp Cys
450 455 460

Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly
465 470 475 480

Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn
485 490 495

Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp
500 505 510

Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro
515 520 525

Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu
530 535 540

Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln
 545 550 555 560

Tyr Ser Met Leu Ala Thr Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala
 565 570 575

Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly
 580 585 590

Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys Gly Pro Ala Ala Leu Pro
 595 600 605

Pro Ala Pro Ser Leu Leu Arg
 610 615

<210> 26
 <211> 567
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 26
 Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile
 1 5 10 15

Ser Glu Ile Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly
 20 25 30

Gly Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn
 35 40 45

Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
 50 55 60

Met Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser
 65 70 75 80

Phe Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala
 85 90 95

Tyr Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe
100 105 110

Cys Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly
115 120 125

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
145 150 155 160

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
165 170 175

Gln Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys
180 185 190

Ala Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val
195 200 205

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
210 215 220

Ile Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln
225 230 235 240

Tyr Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
245 250 255

Lys Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn Ser Ile Met Tyr
260 265 270

Phe Ser His Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr
275 280 285

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
290 295 300

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
 305 310 315 320

His Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
 325 330 335

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Arg Leu
 340 345 350

Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp
 355 360 365

Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr
 370 375 380

Leu Lys His Glu Lys Pro Pro Gln Gly Ser Gly Ser Pro Leu Cys Leu
 385 390 395 400

Gln Arg Glu Ala Lys Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly
 405 410 415

Thr Gln Gly Pro Glu Gln Gln His Leu Leu Ile Thr Ala Pro Ser Ser
 420 425 430

Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg Arg Ala
 435 440 445

Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala
 450 455 460

Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly
 465 470 475 480

His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser
 485 490 495

Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly
 500 505 510

Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro
 515 520 525

Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu
530 535 540

Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro
545 550 555 560

Asp Ala Gly Met Lys Pro Ser
565

<210> 27
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 27
Arg Leu Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys
1 5 10 15

Ser Asp Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr
20 25 30

Glu Thr Leu Lys His Glu Lys Pro Pro Gln
35 40

<210> 28
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 28
Arg Leu Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys
1 5 10 15

Ser Asp Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr
20 25 30

Glu Thr Leu Lys His Glu Lys Pro Pro Gln
35 40

<210> 29

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 29

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1 5 10 15

Ser Leu Val Ile Thr Leu Tyr Cys
20

<210> 30

<211> 86

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 30

Ala Leu Ser Asn Ser Ile Met Tyr Phe Ser His Phe Val Pro Val Phe
1 5 10 15

Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
20 25 30

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
35 40 45

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Ile Tyr
50 55 60

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
65 70 75 80

Val Ile Thr Leu Tyr Cys
85

<210> 31
<211> 83
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 31
Ala Leu Ser Asn Ser Ile Met Tyr Phe Ser His Phe Val Pro Val Phe
1 5 10 15

Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
20 25 30

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
35 40 45

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Ile Tyr
50 55 60

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
65 70 75 80

Val Ile Thr

<210> 32
<211> 255
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 32
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly Ser Thr
 100 105 110

Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Glu Val Gln Leu
 115 120 125

Val Glu Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 130 135 140

Gly Gly Ser Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
 145 150 155 160

Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg Gln
 165 170 175

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn
 180 185 190

Gly Tyr Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
 195 200 205

Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg
 210 215 220

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly
 225 230 235 240

Phe Tyr Ala Met Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val
 245 250 255

<210> 33

<211> 240

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 33

Glu Ile Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser Phe
50 55 60

Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
130 135 140

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
145 150 155 160

Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ala
165 170 175

Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val Pro
180 185 190

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
195 200 205

Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln Tyr
210 215 220

Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
225 230 235 240

<210> 34
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 34
Ile Tyr Leu Ile Ile Gly Ile Cys Gly Gly Gly Ser Leu Leu Met Val
1 5 10 15

Phe Val Ala Leu Leu Val Phe Tyr Ile Thr
20 25

<210> 35
<211> 1075
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polynucleotide

<400> 35
taatacgaact cactataggg agaaagacgc caccatgggc aagaagcaaa atcgcaagac 60
ggggaattcc aagacacaat ccgctagccc accacctaaa gagcgttcta gctcccctgc 120
tactgagcag tcctggatgg aaaacgactt cgatgaactc cggaagagg gatttaggcg 180
atccaactat tcagaactcc gcgaagatat ccagacaaag gggaaggaag tcgagaattt 240

cgagaagaac ctcgaggagt gcatcacccg tatcacaac actgagaaat gtctcaaaga	300
actcatggaa cttagacaa aagccaggga gcttcgagag gagtgtcgga gtctgagatc	360
caggtgtgac cagctcgagg agcgcgtgag cgcgatggaa gacgagatga acgagatgaa	420
aagagagggc aaattcaggg agaagcgc atagaggaac gaacagagtc tgcaggagat	480
ttgggattac gtcaagaggc ctaacctgcg gttgatcggc gtccccgaga gcgacgtaga	540
aaacgggact aaactggaga atacacttca agacatcatt caagaaaatt ttccaaacct	600
ggctcggcaa gctaattgtc aaatccaaga gatccaacgc acacccagc ggtatagctc	660
tcggcgtgcc acccctaggc atattatcgt gcgctttact aaggtggaga tgaaagagaa	720
gatgctgcga gccgctcggg aaaaggggaag ggtgactttg aaggggcaaac ctattcggct	780
gacggttgac cttagcgccg agacactcca ggcacgccgg gaatggggcc ccatctttaa	840
tatcctgaag gagaagaact tccagccacg aatctcttac cctgcaaagt tgagttttat	900
ctccgagggt gagattaagt atttcacga taaacagatg ctgcgagact tcgtgacaac	960
tcgccagct ctcaaggaac tgctcaaaga ggctcttaat atggagcgca ataatagata	1020
tcaacccttg cagaaccacg caaagatgga ttataaggat gacgatgata aatga	1075

<210> 36

<211> 5751

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<400> 36

taatacgact cactataggg agaaagacgc caccatgaca ggttcaaata gtcacattac	60
gattctcact ctgaatataa atgggctgaa ttctgcaatt aaacggcaca ggcttgcttc	120
ctggataaag tctcaagacc cctcagtgtg ctgtattcag gaaacgcac tcacgtgcag	180
ggacacccat cggctgaaaa taaaaggctg gcggaagatc taccaagcca atggaaaaca	240
aaagaaggct ggggtggcga tacttgtaag cgataaaaaca gactttaaac caactaagat	300
caaacgggac aaagagggcc attacatcat ggtaaagggt agtattcaac aagaggagct	360
gactatcctg aatatttatg cacctaatac tggagcccc agattcataa agcaagtgtt	420
gagtgcctt caacgcgacc tcgactcca cactctgac atgggagact ttaacacccc	480

gctgtccact ctcgacagat ctactagaca gaaagtcaac aaggatacac aggaactgaa	540
cagtgtcttc caccaagcgg accttatcga catctacaga acactccacc ccaaaagcac	600
agaatatacc ttcttttcag cccctcacca cacctattcc aaaattgacc acattgtggg	660
gagtaaagcc cttctctcca aatgtaaagc gaccgaaatt atcactaact atctctccga	720
ccacagtgcataaaaaacttg aattgcgaat taagaatctc actcaaagta gatccacgac	780
atggaaactg aacaatctcc tcttgaatga ctactgggtg cataacgaaa tgaaggctga	840
aataaagatg ttctttgaga ccaacgaaaa caaagacacc acgtaccaga atctctggga	900
cgctttcaaa gcagtgtgtc gaggaaaatt tattgcaactg aatgcttaca agcgggaagca	960
ggaaagatcc aaaatagaca ccctgactag ccaacttaaa gaactggaaa agcaagagca	1020
aactcatagc aaagctagcc gtcgccaaga aattacgaaa atcagagctg aactgaagga	1080
aattgagaca cagaaaaccc tgcaaaagat aaatgaaagc cgcagctggt tctttgaacg	1140
catcaacaaa atcgataggc cacttgctcg ctttatcaag aagaaaaggg agaagaatca	1200
aatcgacact ataaagaatg ataaaggcga tataaccacc gatcccacag aaattcaaac	1260
aaccatacgc gaatactaca aacacctcta cgccaataaa ctcgaaaatc tcgaggaaat	1320
ggatacattc ctcgacacgt acacccttcc caggctgaac caggaagaag ttgaatcact	1380
gaatcggcct atcacgggga gtgaaatagt agctatcatc aattcactcc ctaccaagaa	1440
gtcaccggga cctgatggat tcaccgccga attctaccag agatacatgg aagaactggt	1500
gcccttcttg ctgaaacttt tccaaagtat tgagaaagag ggaatacttc caaactcatt	1560
ttatgaggca tccatcattc tgatcccgaa gcccggcagg gacacgacca agaaagagaa	1620
ttttcgacca atctcattga tgaacattga tgcaaagatc ctcaataaaa tactggcaaa	1680
tcggattcag cagcacataa agaagctgat ccacatgat caagtaggct tcatccccgg	1740
tatgcaaggt tggttcaata tacgaaaatc aatcaatggt atccagcata taaaccgggc	1800
caaagacaag aaccacatga ttattagtat cgatgctgag aaagcctttg acaaaataca	1860
acaacccttc atgctgaaaa cattgaataa gctgggaatt gatggcacct acttcaaaat	1920
catcagagcc atatatgaca aaccaacagc aaatatcatt ctgaatggtc agaaattgga	1980
agcattcccc ttgaaaaccg gcacacggca gggttgccct ctgtcaccac tcctcttcaa	2040
catcgtgttg gaagttcttg cccgcgcaat ccggcaggaa aaggaaatca agggcattca	2100

actgggcaaa gaggaagtta aattgagcct gtttgcagac gacatgatcg tctatttgga	2160
aaaccccata gttagtgcac aaaatctgct gaagttgatc agtaatttct ccaaagtgag	2220
tgggtacaaa atcaatgtgc aaaagagcca agctttcttg tacaccaaca acaggcaaac	2280
tgagtctcaa atcatgggcg aactccccctt cgtgattgca tccaagcggg tcaaatacct	2340
ggggattcaa ttgactcgtg atgtgaagga cctcttcaag gagaactaca aaccctgct	2400
caaggaaatc aaagaggaca caaacaatg gaagaacatt ccatgctctt ggggtgggaag	2460
gatcaatatc gtcaaaatgg ccatcctgcc caaggtaatt tacaggttca atgctatacc	2520
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<223> Description of Artificial Sequence: Synthetic polynucleotide

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<223> Description of Artificial Sequence: Synthetic polynucleotide

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<210> 51
 <211> 19
 <212> DNA
 <213> Unknown

<220>
 <223> Description of Unknown: transposon end
 sequence

<400> 51	
agatgtgtat aagagacag	19

<210> 52
 <211> 19
 <212> DNA
 <213> Unknown

<220>

<223> Description of Unknown: transposon end
sequence

<400> 52

ctgtctctta tacacatct

19

<210> 53

<211> 338

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 53

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Ala	Ser	Pro	Pro	Pro	Lys	Glu	Arg	Ser	Ser	Ser	Pro	Ala	Thr	Glu	Gln
			20					25					30		

Ser	Trp	Met	Glu	Asn	Asp	Phe	Asp	Glu	Leu	Arg	Glu	Glu	Gly	Phe	Arg
		35					40					45			

Arg	Ser	Asn	Tyr	Ser	Glu	Leu	Arg	Glu	Asp	Ile	Gln	Thr	Lys	Gly	Lys
	50					55					60				

Glu	Val	Glu	Asn	Phe	Glu	Lys	Asn	Leu	Glu	Glu	Cys	Ile	Thr	Arg	Ile
65					70					75					80

Thr	Asn	Thr	Glu	Lys	Cys	Leu	Lys	Glu	Leu	Met	Glu	Leu	Lys	Thr	Lys
				85					90					95	

Ala	Arg	Glu	Leu	Arg	Glu	Glu	Cys	Arg	Ser	Leu	Arg	Ser	Arg	Cys	Asp
			100					105					110		

Gln	Leu	Glu	Glu	Arg	Val	Ser	Ala	Met	Glu	Asp	Glu	Met	Asn	Glu	Met
		115					120					125			

Lys	Arg	Glu	Gly	Lys	Phe	Arg	Glu	Lys	Arg	Ile	Lys	Arg	Asn	Glu	Gln
	130					135					140				

Ser Leu Gln Glu Ile Trp Asp Tyr Val Lys Arg Pro Asn Leu Arg Leu
 145 150 155 160

Ile Gly Val Pro Glu Ser Asp Val Glu Asn Gly Thr Lys Leu Glu Asn
 165 170 175

Thr Leu Gln Asp Ile Ile Gln Glu Asn Phe Pro Asn Leu Ala Arg Gln
 180 185 190

Ala Asn Val Gln Ile Gln Glu Ile Gln Arg Thr Pro Gln Arg Tyr Ser
 195 200 205

Ser Arg Arg Ala Thr Pro Arg His Ile Ile Val Arg Phe Thr Lys Val
 210 215 220

Glu Met Lys Glu Lys Met Leu Arg Ala Ala Arg Glu Lys Gly Arg Val
 225 230 235 240

Thr Leu Lys Gly Lys Pro Ile Arg Leu Thr Val Asp Leu Ser Ala Glu
 245 250 255

Thr Leu Gln Ala Arg Arg Glu Trp Gly Pro Ile Phe Asn Ile Leu Lys
 260 265 270

Glu Lys Asn Phe Gln Pro Arg Ile Ser Tyr Pro Ala Lys Leu Ser Phe
 275 280 285

Ile Ser Glu Gly Glu Ile Lys Tyr Phe Ile Asp Lys Gln Met Leu Arg
 290 295 300

Asp Phe Val Thr Thr Arg Pro Ala Leu Lys Glu Leu Leu Lys Glu Ala
 305 310 315 320

Leu Asn Met Glu Arg Asn Asn Arg Tyr Gln Pro Leu Gln Asn His Ala
 325 330 335

Lys Met

<210> 54
 <211> 1017

<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<400> 54

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gaactccggg aagagggatt taggcgatcc aactattcag aactccgcga agatatccag	180
acaaagggga aggaagtcga gaatttcgag aagaacctcg aggagtgcac caccgtatc	240
acaaacactg agaaatgtct caaagaactc atggaactta agacaaaagc caggagagctt	300
cgagaggagt gtcggagtct gagatccagg tgtgaccagc tcgaggagcg cgtgagcgcg	360
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caacgcacac cccagcggta tagctctcgg cgtgccaccc ctaggcatat tatcgtgcgc	660
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cagatgctgc gagacttcgt gacaactcgc ccagctctca aggaactgct caaagaggct	960
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<210> 55

<211> 1275

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 55

Met Thr Gly Ser Asn Ser His Ile Thr Ile Leu Thr Leu Asn Ile Asn

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Gly	Leu	Asn	Ser
	20		
Ala	Ile	Lys	Arg
		25	
His	Arg	Leu	Ala
		30	
Ser	Gln	Asp	Pro
	35		
Ser	Val	Cys	Cys
		40	
Ile	Gln	Glu	Thr
		45	
His	Leu	Thr	Cys
Arg	Asp	Thr	His
	50		
Arg	Leu	Lys	Ile
		55	
Lys	Gly	Trp	Arg
		60	
Lys	Ile	Tyr	Gln
Ala	Asn	Gly	Lys
	65		
Gln	Lys	Lys	Ala
	70		
Gly	Val	Ala	Ile
	75		
Leu	Val	Ser	Asp
		80	
Lys	Thr	Asp	Phe
		85	
Lys	Pro	Thr	Lys
Ile	Lys	Arg	Asp
	90		
Lys	Glu	Gly	His
		95	
Tyr	Ile	Met	Val
		100	
Lys	Gly	Ser	Ile
Gln	Gln	Glu	Glu
	105		
Leu	Thr	Ile	Leu
		110	
Asn	Ile	Tyr	Ala
	115		
Pro	Asn	Thr	Gly
Ala	Pro	Arg	Phe
		120	
Ile	Lys	Gln	Val
		125	
Leu	Ser	Asp	Leu
	130		
Gln	Arg	Asp	Leu
		135	
Asp	Ser	His	Thr
		140	
Leu	Ile	Met	Gly
Asp	Phe	Asn	Thr
	145		
Pro	Leu	Ser	Thr
	150		
Leu	Asp	Arg	Ser
		155	
Thr	Arg	Gln	Lys
		160	
Val	Asn	Lys	Asp
Thr	Gln	Glu	Leu
	165		
Asn	Ser	Ala	Leu
		170	
His	Gln	Ala	Asp
		175	
Leu	Ile	Asp	Ile
Tyr	Arg	Thr	Leu
His	Pro	Lys	Ser
	180		
Thr	Glu	Tyr	Thr
		185	
Phe	Phe	Ser	Ala
Pro	His	His	Thr
Tyr	Ser	Lys	Ile
Asp	His	Ile	Val
	190		
Gly	Ser	Lys	Ala
Leu	Leu	Ser	Lys
		200	
Cys	Lys	Arg	Thr
Glu	Ile	Ile	Thr
Gly	Ser	Lys	Ala
	210		
Leu	Leu	Ser	Lys
		215	
Cys	Lys	Arg	Thr
Glu	Ile	Ile	Thr
Gly	Ser	Lys	Ala
Leu	Leu	Ser	Lys
		220	
Cys	Lys	Arg	Thr
Glu	Ile	Ile	Thr

Asn Tyr Leu Ser Asp His Ser Ala Ile Lys Leu Glu Leu Arg Ile Lys
 225 230 235 240

Asn Leu Thr Gln Ser Arg Ser Thr Thr Trp Lys Leu Asn Asn Leu Leu
 245 250 255

Leu Asn Asp Tyr Trp Val His Asn Glu Met Lys Ala Glu Ile Lys Met
 260 265 270

Phe Phe Glu Thr Asn Glu Asn Lys Asp Thr Thr Tyr Gln Asn Leu Trp
 275 280 285

Asp Ala Phe Lys Ala Val Cys Arg Gly Lys Phe Ile Ala Leu Asn Ala
 290 295 300

Tyr Lys Arg Lys Gln Glu Arg Ser Lys Ile Asp Thr Leu Thr Ser Gln
 305 310 315 320

Leu Lys Glu Leu Glu Lys Gln Glu Gln Thr His Ser Lys Ala Ser Arg
 325 330 335

Arg Gln Glu Ile Thr Lys Ile Arg Ala Glu Leu Lys Glu Ile Glu Thr
 340 345 350

Gln Lys Thr Leu Gln Lys Ile Asn Glu Ser Arg Ser Trp Phe Phe Glu
 355 360 365

Arg Ile Asn Lys Ile Asp Arg Pro Leu Ala Arg Leu Ile Lys Lys Lys
 370 375 380

Arg Glu Lys Asn Gln Ile Asp Thr Ile Lys Asn Asp Lys Gly Asp Ile
 385 390 395 400

Thr Thr Asp Pro Thr Glu Ile Gln Thr Thr Ile Arg Glu Tyr Tyr Lys
 405 410 415

His Leu Tyr Ala Asn Lys Leu Glu Asn Leu Glu Glu Met Asp Thr Phe
 420 425 430

Leu Asp Thr Tyr Thr Leu Pro Arg Leu Asn Gln Glu Glu Val Glu Ser

435

440

445

Leu Asn Arg Pro Ile Thr Gly Ser Glu Ile Val Ala Ile Ile Asn Ser
 450 455 460

Leu Pro Thr Lys Lys Ser Pro Gly Pro Asp Gly Phe Thr Ala Glu Phe
 465 470 475 480

Tyr Gln Arg Tyr Met Glu Glu Leu Val Pro Phe Leu Leu Lys Leu Phe
 485 490 495

Gln Ser Ile Glu Lys Glu Gly Ile Leu Pro Asn Ser Phe Tyr Glu Ala
 500 505 510

Ser Ile Ile Leu Ile Pro Lys Pro Gly Arg Asp Thr Thr Lys Lys Glu
 515 520 525

Asn Phe Arg Pro Ile Ser Leu Met Asn Ile Asp Ala Lys Ile Leu Asn
 530 535 540

Lys Ile Leu Ala Asn Arg Ile Gln Gln His Ile Lys Lys Leu Ile His
 545 550 555 560

His Asp Gln Val Gly Phe Ile Pro Gly Met Gln Gly Trp Phe Asn Ile
 565 570 575

Arg Lys Ser Ile Asn Val Ile Gln His Ile Asn Arg Ala Lys Asp Lys
 580 585 590

Asn His Met Ile Ile Ser Ile Asp Ala Glu Lys Ala Phe Asp Lys Ile
 595 600 605

Gln Gln Pro Phe Met Leu Lys Thr Leu Asn Lys Leu Gly Ile Asp Gly
 610 615 620

Thr Tyr Phe Lys Ile Ile Arg Ala Ile Tyr Asp Lys Pro Thr Ala Asn
 625 630 635 640

Ile Ile Leu Asn Gly Gln Lys Leu Glu Ala Phe Pro Leu Lys Thr Gly
 645 650 655

Thr Arg Gln Gly Cys Pro Leu Ser Pro Leu Leu Phe Asn Ile Val Leu
660 665 670

Glu Val Leu Ala Arg Ala Ile Arg Gln Glu Lys Glu Ile Lys Gly Ile
675 680 685

Gln Leu Gly Lys Glu Glu Val Lys Leu Ser Leu Phe Ala Asp Asp Met
690 695 700

Ile Val Tyr Leu Glu Asn Pro Ile Val Ser Ala Gln Asn Leu Leu Lys
705 710 715 720

Leu Ile Ser Asn Phe Ser Lys Val Ser Gly Tyr Lys Ile Asn Val Gln
725 730 735

Lys Ser Gln Ala Phe Leu Tyr Thr Asn Asn Arg Gln Thr Glu Ser Gln
740 745 750

Ile Met Gly Glu Leu Pro Phe Val Ile Ala Ser Lys Arg Ile Lys Tyr
755 760 765

Leu Gly Ile Gln Leu Thr Arg Asp Val Lys Asp Leu Phe Lys Glu Asn
770 775 780

Tyr Lys Pro Leu Leu Lys Glu Ile Lys Glu Asp Thr Asn Lys Trp Lys
785 790 795 800

Asn Ile Pro Cys Ser Trp Val Gly Arg Ile Asn Ile Val Lys Met Ala
805 810 815

Ile Leu Pro Lys Val Ile Tyr Arg Phe Asn Ala Ile Pro Ile Lys Leu
820 825 830

Pro Met Thr Phe Phe Thr Glu Leu Glu Lys Thr Thr Leu Lys Phe Ile
835 840 845

Trp Asn Gln Lys Arg Ala Arg Ile Ala Lys Ser Ile Leu Ser Gln Lys
850 855 860

Asn Lys Ala Gly Gly Ile Thr Leu Pro Asp Phe Lys Leu Tyr Tyr Lys

865		870		875		880
Ala Thr Val Thr	Lys Thr Ala Trp Tyr Trp Tyr Gln Asn Arg Asp Ile					
	885		890		895	
Asp Gln Trp Asn Arg Thr Glu Pro Ser Glu Ile Met Pro His Ile Tyr						
	900		905		910	
Asn Tyr Leu Ile Phe Asp Lys Pro Glu Lys Asn Lys Gln Trp Gly Lys						
	915		920		925	
Asp Ser Leu Phe Asn Lys Trp Cys Trp Glu Asn Trp Leu Ala Ile Cys						
	930		935		940	
Arg Lys Leu Lys Leu Asp Pro Phe Leu Thr Pro Tyr Thr Lys Ile Asn						
	945		950		955	960
Ser Arg Trp Ile Lys Asp Leu Asn Val Lys Pro Lys Thr Ile Lys Thr						
	965		970		975	
Leu Glu Glu Asn Leu Gly Ile Thr Ile Gln Asp Ile Gly Val Gly Lys						
	980		985		990	
Asp Phe Met Ser Lys Thr Pro Lys Ala Met Ala Thr Lys Asp Lys Ile						
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Asp Lys Trp Asp Leu Ile Lys Leu Lys Ser Phe Cys Thr Ala Lys						
	1010		1015		1020	
Glu Thr Thr Ile Arg Val Asn Arg Gln Pro Thr Thr Trp Glu Lys						
	1025		1030		1035	
Ile Phe Ala Thr Tyr Ser Ser Asp Lys Gly Leu Ile Ser Arg Ile						
	1040		1045		1050	
Tyr Asn Glu Leu Lys Gln Ile Tyr Lys Lys Lys Thr Asn Asn Pro						
	1055		1060		1065	
Ile Lys Lys Trp Ala Lys Asp Met Asn Arg His Phe Ser Lys Glu						
	1070		1075		1080	

Asp Ile Tyr Ala Ala Lys Lys His Met Lys Lys Cys Ser Ser Ser
 1085 1090 1095

Leu Ala Ile Arg Glu Met Gln Ile Lys Thr Thr Met Arg Tyr His
 1100 1105 1110

Leu Thr Pro Val Arg Met Ala Ile Ile Lys Lys Ser Gly Asn Asn
 1115 1120 1125

Arg Cys Trp Arg Gly Cys Gly Glu Ile Gly Thr Leu Leu His Cys
 1130 1135 1140

Trp Trp Asp Cys Lys Leu Val Gln Pro Leu Trp Lys Ser Val Trp
 1145 1150 1155

Arg Phe Leu Arg Asp Leu Glu Leu Glu Ile Pro Phe Asp Pro Ala
 1160 1165 1170

Ile Pro Leu Leu Gly Ile Tyr Pro Asn Glu Tyr Lys Ser Cys Cys
 1175 1180 1185

Tyr Lys Asp Thr Cys Thr Arg Met Phe Ile Ala Ala Leu Phe Thr
 1190 1195 1200

Ile Ala Lys Thr Trp Asn Gln Pro Lys Cys Pro Thr Met Ile Asp
 1205 1210 1215

Trp Ile Lys Lys Met Trp His Ile Tyr Thr Met Glu Tyr Tyr Ala
 1220 1225 1230

Ala Ile Lys Asn Asp Glu Phe Ile Ser Phe Val Gly Thr Trp Met
 1235 1240 1245

Lys Leu Glu Thr Ile Ile Leu Ser Lys Leu Ser Gln Glu Gln Lys
 1250 1255 1260

Thr Lys His Arg Ile Phe Ser Leu Ile Gly Gly Asn
 1265 1270 1275

<210> 56

<211> 3828

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polynucleotide

<400> 56

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aagatttatc aggcgacgg taagcagaag aaagccggag tcgcaattct ggtctcagac	240
aagacggatt tcaagccac caaataaag cgtgataagg aaggtcacta tattatgggtg	300
aaaggcagca tacagcagga agaacttacc atattgaaca tctacgcgcc aaacaccggc	360
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gtaaataaag acacgcaaga gctcaatagc gactgcatc aggcagatct cattgatatt	540
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gagataatta caaattacct gtcagatcat agcgcatca agctcgagct gagaatcaag	720
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atttccttcg ttgggacctg gatgaagctg gagactatta ttctgagcaa gctgtctcag 3780
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<210> 57

<211> 1290

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 57

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Gln Asp Pro Tyr Ile Cys Cys Leu Gln Glu Thr His Phe Arg Pro Arg
35 40 45

Asp Thr Tyr Arg Leu Lys Val Arg Gly Trp Lys Lys Ile Phe His Ala
50 55 60

Asn Gly Asn Gln Lys Lys Ala Gly Val Ala Ile Leu Ile Ser Asp Lys
65 70 75 80

Ile Asp Phe Lys Ile Lys Asn Val Thr Arg Asp Lys Glu Gly His Tyr
85 90 95

Ile Met Ile Gln Gly Ser Ile Gln Glu Glu Asp Ile Thr Ile Ile Asn
100 105 110

Ile Tyr Ala Pro Asn Ile Gly Ala Pro Gln Tyr Ile Arg Gln Leu Leu
115 120 125

Thr Ala Ile Lys Glu Glu Ile Asp Ser Asn Thr Ile Ile Val Gly Asp
130 135 140

Phe Asn Thr Ser Leu Thr Pro Met Asp Arg Ser Ser Lys Met Lys Ile
145 150 155 160

Asn Lys Glu Thr Glu Ala Leu Asn Asp Thr Ile Asp Gln Ile Asp Leu
165 170 175

Ile Asp Ile Tyr Arg Thr Phe His Pro Lys Thr Ala Asp Tyr Thr Phe
180 185 190

Phe Ser Ser Ala His Gly Thr Phe Ser Arg Ile Asp His Ile Leu Gly
195 200 205

His Lys Ser Ser Leu Ser Lys Phe Lys Lys Ile Glu Ile Ile Ser Ser
210 215 220

Ile Phe Ser Asp His Asn Ala Met Arg Leu Glu Met Asn His Arg Glu
225 230 235 240

Lys Asn Val Lys Lys Thr Asn Thr Trp Arg Leu Asn Asn Thr Leu Leu
245 250 255

Asn Asn Gln Glu Ile Thr Glu Glu Ile Lys Gln Glu Ile Lys Lys Tyr
260 265 270

Leu Glu Thr Asn Asp Asn Glu Asn Thr Thr Thr Gln Asn Leu Trp Asp
275 280 285

Ala Ala Lys Ala Val Leu Arg Gly Lys Phe Ile Ala Ile Gln Ala Tyr
290 295 300

Leu Lys Lys Gln Glu Lys Ser Gln Val Asn Asn Leu Thr Leu His Leu
305 310 315 320

Lys Lys Leu Glu Lys Glu Glu Gln Thr Lys Pro Lys Val Ser Arg Arg
325 330 335

Lys Glu Ile Ile Lys Ile Arg Ala Glu Ile Asn Glu Ile Glu Thr Lys
340 345 350

Lys Thr Ile Ala Lys Ile Asn Lys Thr Lys Ser Trp Phe Phe Glu Lys
355 360 365

Ile Asn Lys Ile Asp Lys Pro Leu Ala Arg Leu Ile Lys Lys Lys Arg
370 375 380

Glu Arg Thr Gln Ile Asn Lys Ile Arg Asn Glu Lys Gly Glu Val Thr
385 390 395 400

Thr Asp Thr Ala Glu Ile Gln Asn Ile Leu Arg Asp Tyr Tyr Lys Gln
405 410 415

Leu Tyr Ala Asn Lys Met Asp Asn Leu Glu Glu Met Asp Lys Phe Leu
420 425 430

Glu Arg Tyr Asn Leu Pro Arg Leu Asn Gln Glu Glu Thr Glu Asn Ile
435 440 445

Asn Arg Pro Ile Thr Ser Asn Glu Ile Glu Thr Val Ile Lys Asn Leu
450 455 460

Pro Thr Asn Lys Ser Pro Gly Pro Asp Gly Phe Thr Gly Glu Phe Tyr
465 470 475 480

Gln Thr Phe Arg Glu Glu Leu Thr Pro Ile Leu Leu Lys Leu Phe Gln
485 490 495

Lys Ile Ala Glu Glu Gly Thr Leu Pro Asn Ser Phe Tyr Glu Ala Thr
500 505 510

Ile Thr Leu Ile Pro Lys Pro Asp Lys Asp Thr Thr Lys Lys Glu Asn
515 520 525

Tyr Arg Pro Ile Ser Leu Met Asn Ile Asp Ala Lys Ile Leu Asn Lys
530 535 540

Ile Leu Ala Asn Arg Ile Gln Gln His Ile Lys Arg Ile Ile His His
545 550 555 560

Asp Gln Val Gly Phe Ile Pro Gly Met Gln Gly Phe Phe Asn Ile Arg
565 570 575

Lys Ser Ile Asn Val Ile His His Ile Asn Lys Leu Lys Lys Lys Asn
580 585 590

His Met Ile Ile Ser Ile Asp Ala Glu Lys Ala Phe Asp Lys Ile Gln
595 600 605

His Pro Phe Met Ile Lys Thr Leu Gln Lys Val Gly Ile Glu Gly Thr
610 615 620

Tyr Leu Asn Ile Ile Lys Ala Ile Tyr Asp Lys Pro Thr Ala Asn Ile
625 630 635 640

Ile Leu Asn Gly Glu Lys Leu Lys Ala Phe Pro Leu Arg Ser Gly Thr
645 650 655

Arg Gln Gly Cys Pro Leu Ser Pro Leu Leu Phe Asn Ile Val Leu Glu
660 665 670

Val Leu Ala Thr Ala Ile Arg Glu Glu Lys Glu Ile Lys Gly Ile Gln
675 680 685

Ile Gly Lys Glu Glu Val Lys Leu Ser Leu Phe Ala Asp Asp Met Ile
690 695 700

Leu Tyr Ile Glu Asn Pro Lys Thr Ala Thr Arg Lys Leu Leu Glu Leu
705 710 715 720

Ile Asn Glu Tyr Gly Lys Val Ala Gly Tyr Lys Ile Asn Ala Gln Lys
725 730 735

Ser Leu Ala Phe Leu Tyr Thr Asn Asp Glu Lys Ser Glu Arg Glu Ile
740 745 750

Met Glu Thr Leu Pro Phe Thr Ile Ala Thr Lys Arg Ile Lys Tyr Leu
755 760 765

Gly Ile Asn Leu Pro Lys Glu Thr Lys Asp Leu Tyr Ala Glu Asn Tyr
770 775 780

Lys Thr Leu Met Lys Glu Ile Lys Asp Asp Thr Asn Arg Trp Arg Asp
785 790 795 800

Ile Pro Cys Ser Trp Ile Gly Arg Ile Asn Ile Val Lys Met Ser Ile
805 810 815

Leu Pro Lys Ala Ile Tyr Arg Phe Asn Ala Ile Pro Ile Lys Leu Pro
820 825 830

Met Ala Phe Phe Thr Glu Leu Glu Gln Ile Ile Leu Lys Phe Val Trp
835 840 845

Arg His Lys Arg Pro Arg Ile Ala Lys Ala Val Leu Arg Gln Lys Asn
850 855 860

Gly Ala Gly Gly Ile Arg Leu Pro Asp Phe Arg Leu Tyr Tyr Lys Ala
865 870 875 880

Thr Val Ile Lys Thr Ile Trp Tyr Trp His Lys Asn Arg Asn Ile Asp
885 890 895

Gln Trp Asn Lys Ile Glu Ser Pro Glu Ile Asn Pro Arg Thr Tyr Gly
900 905 910

Gln Leu Ile Tyr Asp Lys Gly Gly Lys Asp Ile Gln Trp Arg Lys Asp
915 920 925

Ser Leu Phe Asn Lys Trp Cys Trp Glu Asn Trp Thr Ala Thr Cys Lys
930 935 940

Arg Met Lys Leu Glu Tyr Ser Leu Thr Pro Tyr Thr Lys Ile Asn Ser
945 950 955 960

Lys Trp Ile Arg Asp Leu Asn Ile Arg Leu Asp Thr Ile Lys Leu Leu
965 970 975

Glu Glu Asn Ile Gly Arg Thr Leu Phe Asp Ile Asn His Ser Lys Ile
980 985 990

Phe Phe Asp Pro Pro Pro Arg Val Met Glu Ile Lys Thr Lys Ile Asn
995 1000 1005

Lys Trp Asp Leu Met Lys Leu Gln Ser Phe Cys Thr Ala Lys Glu
1010 1015 1020

Thr Ile Asn Lys Thr Lys Arg Gln Pro Ser Glu Trp Glu Lys Ile
1025 1030 1035

Phe Ala Asn Glu Ser Thr Asp Lys Gly Leu Ile Ser Lys Ile Tyr
1040 1045 1050

Lys Gln Leu Ile Gln Leu Asn Ile Lys Glu Thr Asn Thr Pro Ile
1055 1060 1065

Gln Lys Trp Ala Glu Asp Leu Asn Arg His Phe Ser Lys Glu Asp
1070 1075 1080

Ile Gln Thr Ala Thr Lys His Met Lys Arg Cys Ser Thr Ser Leu
1085 1090 1095

Ile Ile Arg Glu Met Gln Ile Lys Thr Thr Met Arg Tyr His Leu
1100 1105 1110

Thr Pro Val Arg Met Gly Ile Ile Arg Lys Ser Thr Asn Asn Lys
1115 1120 1125

Cys Trp Arg Gly Cys Gly Glu Lys Gly Thr Leu Leu His Cys Trp
1130 1135 1140

Trp Glu Cys Lys Leu Ile Gln Pro Leu Trp Arg Thr Ile Trp Arg
1145 1150 1155

Phe Leu Lys Lys Leu Lys Ile Glu Leu Pro Tyr Asp Pro Ala Ile
1160 1165 1170

Pro Leu Leu Gly Ile Tyr Pro Glu Lys Thr Val Ile Gln Lys Asp
1175 1180 1185

Thr Cys Thr Arg Met Phe Ile Ala Ala Leu Phe Thr Ile Ala Arg
1190 1195 1200

Ser Trp Lys Gln Pro Lys Cys Pro Ser Thr Asp Glu Trp Ile Lys
1205 1210 1215

Lys Met Trp Tyr Ile Tyr Thr Met Glu Tyr Tyr Ser Ala Ile Lys
1220 1225 1230

Arg Asn Glu Ile Gly Ser Phe Leu Glu Thr Trp Met Asp Leu Glu
1235 1240 1245

Thr Val Ile Gln Ser Glu Val Ser Gln Lys Glu Lys Asn Lys Tyr
1250 1255 1260

Arg Ile Leu Thr His Ile Cys Gly Thr Trp Lys Asn Gly Thr Asp
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Glu Pro Val Cys Arg Thr Glu Ile Glu Thr Gln Met
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<210> 58

<211> 3873

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polynucleotide

<400> 58

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gagaaaaccg taattcaaaa agacacatgc acccgaatgt tcattgcagc actatttaca	3600
atagccaggt catggaagca acctaaatgc ccatcgacag acgaatggat aaagaagatg	3660
tggtagatat atacaatgga atattactca gccataaaaa ggaacgaaat tgggtcattt	3720
ttagagacgt ggatggatct agagactgtc atacagagtg aagtaagtca gaaagagaaa	3780
aacaaatatc gtatattaac gcatatatgt ggaacctgga aaaatggtac agatgaaccg	3840
gtctgcagga cagaaattga gacacaaatg taa	3873

<210> 59
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 59
 Pro Ala Ala Lys Arg Val Lys Leu Asp
 1 5

<210> 60
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 60
 Asp Tyr Lys Asp Asp Asp Asp Lys
 1 5

<210> 61
 <211> 234
 <212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 61

Ala Ser Asn Phe Thr Gln Phe Val Leu Val Asp Asn Gly Gly Thr Gly
1 5 10 15

Asp Val Thr Val Ala Pro Ser Asn Phe Ala Asn Gly Ile Ala Glu Trp
20 25 30

Ile Ser Ser Asn Ser Arg Ser Gln Ala Tyr Lys Val Thr Cys Ser Val
35 40 45

Arg Gln Ser Ser Ala Gln Asn Arg Lys Tyr Thr Ile Lys Val Glu Val
50 55 60

Pro Lys Gly Ala Trp Arg Ser Tyr Leu Asn Met Glu Leu Thr Ile Pro
65 70 75 80

Ile Phe Ala Thr Asn Ser Asp Cys Glu Leu Ile Val Lys Ala Met Gln
85 90 95

Gly Leu Leu Lys Asp Gly Asn Pro Ile Pro Ser Ala Ile Ala Ala Asn
100 105 110

Ser Gly Ile Tyr Ala Met Ala Ser Asn Phe Thr Gln Phe Val Leu Val
115 120 125

Asp Asn Gly Gly Thr Gly Asp Val Thr Val Ala Pro Ser Asn Phe Ala
130 135 140

Asn Gly Ile Ala Glu Trp Ile Ser Ser Asn Ser Arg Ser Gln Ala Tyr
145 150 155 160

Lys Val Thr Cys Ser Val Arg Gln Ser Ser Ala Gln Asn Arg Lys Tyr
165 170 175

Thr Ile Lys Val Glu Val Pro Lys Gly Ala Trp Arg Ser Tyr Leu Asn
180 185 190

Met Glu Leu Thr Ile Pro Ile Phe Ala Thr Asn Ser Asp Cys Glu Leu
195 200 205

Ile Val Lys Ala Met Gln Gly Leu Leu Lys Asp Gly Asn Pro Ile Pro
210 215 220

Ser Ala Ile Ala Ala Asn Ser Gly Ile Tyr
225 230

<210> 62
<211> 9
<212> PRT
<213> Unknown

<220>
<223> Description of Unknown: "LAGLIDADG" family motif
peptide

<400> 62
Leu Ala Gly Leu Ile Asp Ala Asp Gly
1 5

<210> 63
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 63
Glu Ile Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser Phe
50 55 60

Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala Tyr

65				70				75				80			
Leu	Gln	Ile	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Phe	Cys
			85						90					95	
Thr	Arg	Arg	Gly	Tyr	Asp	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Gln	Gly	Thr
			100					105					110		
Thr	Val	Thr	Val												
			115												

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<210> 64
<211> 107
<212> PRT
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 64
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Thr Leu Ile
35 40 45

Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Tyr
65 70 75 80

Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln Tyr Asp Glu Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 65

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

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 65
Leu Tyr Cys Arg Arg Leu Lys Ile Gln Val Arg Lys Ala Ala Ile Thr
1 5 10 15

Ser Tyr Glu Lys Ser Asp Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn
20 25 30

Gln Glu Thr Tyr Glu Thr Leu Lys His Glu Lys Pro Pro
35 40 45

<210> 66
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 66
Tyr Glu Asp Met Arg Gly Ile Leu Tyr Ala Ala Pro Gln Leu Arg Ser
1 5 10 15

Ile Arg Gly Gln Pro Gly Pro Asn His Glu Glu Asp Ala Asp Ser Tyr
20 25 30

Glu Asn Met
35

<210> 67
<211> 61
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 67
Lys Val Ala Lys Lys Pro Thr Asn Lys Ala Pro His Pro Lys Gln Glu

1				5				10				15				
Pro	Gln	Glu	Ile	Asn	Phe	Pro	Asp	Asp	Leu	Pro	Gly	Ser	Asn	Thr	Ala	
				20					25					30		
Ala	Pro	Val	Gln	Glu	Thr	Leu	His	Gly	Cys	Gln	Pro	Val	Thr	Gln	Glu	
				35					40					45		
Asp	Gly	Lys	Glu	Ser	Arg	Ile	Ser	Val	Gln	Glu	Arg	Gln				
				50					55					60		

Ser Leu Val Ile Thr
20

<210> 69
<211> 62
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 69
Ala Leu Ser Asn Ser Ile Met Tyr Phe Ser His Phe Val Pro Val Phe
1 5 10 15

Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro
20 25 30

Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys
35 40 45

Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
50 55 60

<210> 70

<211> 415

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 70

Glu Ile Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser Phe
50 55 60

Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
130 135 140

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
145 150 155 160

Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ala
165 170 175

Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val Pro
180 185 190

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
195 200 205

Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln Tyr
210 215 220

Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
225 230 235 240

Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn Ser Ile Met Tyr Phe
245 250 255

Ser His Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro
260 265 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
275 280 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
290 295 300

Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305 310 315 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Arg Arg Leu
325 330 335

Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp
340 345 350

Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr
355 360 365

Leu Lys His Glu Lys Pro Pro Gln Gly Ser Gly Ser Tyr Glu Asp Met

370

375

380

Arg Gly Ile Leu Tyr Ala Ala Pro Gln Leu Arg Ser Ile Arg Gly Gln
 385 390 395 400

Pro Gly Pro Asn His Glu Glu Asp Ala Asp Ser Tyr Glu Asn Met
 405 410 415

<210> 71

<211> 437

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 71

Glu Ile Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1 5 10 15

Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser Phe
 50 55 60

Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala Tyr
 65 70 75 80

Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
 85 90 95

Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr
 100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu

130

135

140

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
 145 150 155 160

Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ala
 165 170 175

Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val Pro
 180 185 190

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
 195 200 205

Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln Tyr
 210 215 220

Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 225 230 235 240

Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn Ser Ile Met Tyr Phe
 245 250 255

Ser His Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro
 260 265 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
 275 280 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
 290 295 300

Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
 305 310 315 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Arg Leu Lys
 325 330 335

Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp Gly
 340 345 350

Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr Leu
355 360 365

Lys His Glu Lys Pro Pro Gln Lys Lys Val Ala Lys Lys Pro Thr Asn
370 375 380

Lys Ala Pro His Pro Lys Gln Glu Pro Gln Glu Ile Asn Phe Pro Asp
385 390 395 400

Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu Thr Leu His
405 410 415

Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser
420 425 430

Val Gln Glu Arg Gln
435

<210> 72

<211> 438

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 72

Glu Ile Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Val Arg Ile Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr His Thr Gly Glu Pro Thr Tyr Ala Asp Ser Phe
50 55 60

Lys Gly Arg Phe Thr Phe Ser Leu Asp Asp Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Thr Arg Arg Gly Tyr Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu
130 135 140

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
145 150 155 160

Asp Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ala
165 170 175

Pro Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Glu Ser Gly Val Pro
180 185 190

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
195 200 205

Ser Ser Leu Gln Tyr Glu Asp Phe Gly Ile Tyr Tyr Cys Gln Gln Tyr
210 215 220

Asp Glu Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
225 230 235 240

Ser Gly Gly Gly Gly Ser Gly Ala Leu Ser Asn Ser Ile Met Tyr Phe
245 250 255

Ser His Phe Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro
260 265 270

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
275 280 285

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His

290

295

300

Thr Arg Gly Leu Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
 305 310 315 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Arg Arg Leu
 325 330 335

Lys Ile Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp
 340 345 350

Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr
 355 360 365

Leu Lys His Glu Lys Pro Pro Gln Lys Lys Val Ala Lys Lys Pro Thr
 370 375 380

Asn Lys Ala Pro His Pro Lys Gln Glu Pro Gln Glu Ile Asn Phe Pro
 385 390 395 400

Asp Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu Thr Leu
 405 410 415

His Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile
 420 425 430

Ser Val Gln Glu Arg Gln
 435

<210> 73

<211> 44

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 73

Met Arg Asn Lys Lys Ile Leu Lys Glu Asp Glu Leu Leu Ser Glu Thr
 1 5 10 15

Gln Gln Ala Ala Phe His Gln Ile Ala Met Glu Pro Phe Glu Ile Asn

20

25

30

Val Pro Lys Pro Lys Arg Arg Asn Gly Val Asn Phe
 35 40

<210> 74

<211> 50

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 74

Met Glu Gln Trp Asp His Phe His Asn Gln Gln Glu Asp Thr Asp Ser
 1 5 10 15

Cys Ser Glu Ser Val Lys Phe Asp Ala Arg Ser Met Thr Ala Leu Leu
 20 25 30

Pro Pro Asn Pro Lys Asn Ser Pro Ser Leu Gln Glu Lys Leu Lys Ser
 35 40 45

Phe Lys
 50

<210> 75

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 75

Gly Ala Ala Pro Ala Ala Ala Pro Ala Lys Gln Glu Ala Ala Ala Pro
 1 5 10 15

Ala Pro Ala Ala Lys Ala Glu Ala Pro Ala Ala Ala Pro Ala Ala Lys
 20 25 30

Ala

<210> 76
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<220>
<221> MISC_FEATURE
<222> (1)..(20)
<223> This sequence may encompass 1-4 "Gly Gly Gly Gly Ser" repeating units

<220>
<223> See specification as filed for detailed description of substitutions and preferred embodiments

<400> 76
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 77
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 77
Gly Gly Gly Gly Gly
1 5

<210> 78
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 78

Gly Gly Gly Gly Gly Gly Gly Gly
1 5

<210> 79
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<220>
<221> MISC_FEATURE
<222> (1)..(20)
<223> This sequence may encompass 1-4 "Glu Ala Ala Ala Lys"
repeating units

<220>
<223> See specification as filed for detailed description of
substitutions and preferred embodiments

<400> 79
Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Glu
1 5 10 15

Ala Ala Ala Lys
20

<210> 80
<211> 48
<212> RNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 80
cuaggaaucu ggaaguaccg aggaaacucg guacuuccug uguccuag

48

<210> 81
<211> 37
<212> RNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 81

auauggaaga uccuggggaa cugggaucuu ccuaagu

37