

RELAXIN-2 FUSION PROTEIN ANALOGS AND METHODS OF USING SAME**RELATED APPLICATIONS**

[0001] This application claims priority to U.S. Provisional Patent Application Serial Nos. 63/503,101, filed May 18, 2023, 63/585,849, filed September 27, 2023, 63/586,868, filed September 29, 2023, 63/611,732, filed December 18, 2023, and 63/617,398, filed January 3, 2024, the entire disclosures of which are hereby incorporated by reference herein.

REFERENCE TO SEQUENCE LISTING

[0002] This application contains a sequence listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety (said XML copy, created May 16, 2024, is named "209634_seqlist.xml" and is 727,648 bytes in size).

BACKGROUND

[0003] Relaxin-2 exhibits strong antifibrotic activity. In injured tissues, fibroblast activation and proliferation cause increased collagen production and interstitial fibrosis. Fibrosis in the heart is increased by biomechanical overload, and influences ventricular dysfunction, remodeling, and arrhythmogenesis. However, due to the limited *in vivo* half-life of relaxin, compound administration has to be performed as a continuous infusion for at least 48 hours. Further, the synthesis of relaxin-2 is difficult. Due to the low solubility of the B-chain and the requirement for the laborious, specific introduction of cysteine bridges between the A and B-chains, yields of active peptide obtained by these methods are extremely low.

[0004] There is a need for an engineered relaxin-2 analog with greater half-life and greater ease in production.

SUMMARY

[0005] This disclosure provides fusion proteins that are engineered relaxin-2 analogs with improved pharmacokinetic properties. This disclosure also provides methods of using these fusion proteins to enhance relaxin-2 related activity in a subject and to treat or prevent relaxin-2 related diseases. The structure of the fusion proteins described herein is based, at least in part, upon the surprising discovery that reducing the isoelectric point (pI) of relaxin-2 fusion protein analogs increases their circulating half-life and improves their pharmacokinetic and pharmacodynamic properties.

[0006] Accordingly, in one aspect, the present disclosure provides a fusion protein comprising, from N-terminus to C-terminus, a first peptide; a linker peptide; and a second peptide, wherein: (a) the first peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 502 and the second peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 503 or 504; or the first peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 503 or 504 and the second peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 502; and optionally, (b) the fusion protein has a pI from 6.0 to 8.2.

[0007] In some embodiments, the fusion protein has a pI from about 6.0 to about 9.4. In some embodiments, the fusion protein has a pI from about 6.0 to about 8.2. In some embodiments, the fusion protein has a pI that is less than about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, or 6.1. In some embodiments, the fusion protein has a pI that is less than 9.0. In some embodiments, the fusion protein has a pI that is less than about 8.2. In some embodiments, the fusion protein has a pI of about 6.8. In some embodiments, the fusion protein has a pI of about 7.0. In some embodiments, the fusion protein has a pI of about 7.1. In some embodiments, the fusion protein has a pI of about 7.4. In some embodiments, the fusion protein has a pI of about 7.5. In some embodiments, the fusion protein has a pI of about 7.9. In some embodiments, the fusion protein has a pI of about 8.0. In some embodiments, the fusion protein has a pI of about 8.4. In some embodiments, the fusion protein has a pI of about 8.5. In some embodiments, the fusion protein has a pI of about 8.8. In some embodiments, the fusion protein has a pI of about 8.9.

[0008] In some embodiments, the first peptide comprises the amino acid sequence X₁₁LCGRELVRQAIC (SEQ ID NO: 505), wherein X₁₁ is K, Q, D, E, L, I or Y. In some embodiments, the first peptide consists of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, or 29 amino acids.

[0009] In some embodiments, the first peptide comprises the amino acid sequence X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein: X₁₂ is K, Q, D, E, L, I, or Y; X₁₃ is any amino acid except M, W, or C; X₁₄ is K, Q, D, E, L, I, or Y; X₁₅ is Q, D, E, L, I, Y or R; and X₁₆ is R or Q. In some embodiments, the first peptide comprises the amino acid sequence X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein: X₁₂ is K, Q, D, E,

L, I, or Y; X₁₃ is H, K, Q, Y, L, N, I, S, T, or F; X₁₄ is K, Q, D, E, L, I, or Y; X₁₅ is Q, D, E, L, I, Y or R; and X₁₆ is R or Q. In some embodiments, X₁₃ is Q. In some embodiments, the first peptide consists of 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids.

[0010] In some embodiments, the second peptide comprises the amino acid sequence X₁₁LCGRELVRQAIC (SEQ ID NO: 505), wherein X₁₁ is K, Q, D, E, L, I or Y. In some embodiments, the second peptide consists of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, or 29 amino acids.

[0011] In some embodiments, the second peptide comprises the amino acid sequence X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein: X₁₂ is K, Q, D, E, L, I, or Y; X₁₃ is any amino acid except M, W, or C; X₁₄ is K, Q, D, E, L, I, or Y; X₁₅ is Q, D, E, L, I, Y or R; and X₁₆ is R or Q. In some embodiments, the second peptide comprises the amino acid sequence X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein: X₁₂ is K, Q, D, E, L, I, or Y; X₁₃ is H, K, Q, Y, L, N, I, S, T, or F; X₁₄ is K, Q, D, E, L, I, or Y; X₁₅ is Q, D, E, L, I, Y or R; and X₁₆ is R or Q. In some embodiments, X₁₃ is Q. In some embodiments, the second peptide consists of 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids.

[0012] In some embodiments, the linker peptide comprises an amino acid sequence with 12-15 amino acids. In some embodiments, the linker peptide comprises the amino acid sequence ASDAAGAX₈AX₉AGA (SEQ ID NO: 17), wherein: X₈ is D, E, N, or Q; and X₉ is D, E, N, or Q; or the linker peptide comprises the amino acid sequence GGEGSGGEGX₁₀GGG (SEQ ID NO: 25), wherein: X₁₀ is E or S. In some embodiments, X₈ is D, E, N, or Q, and X₉ is D, E, or Q; or X₈ is D, E, or Q, and X₉ is D, E, N, or Q. In some embodiments, the linker peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 18, 19, 20, 21, 22, 23, 24, 26, and 27.

[0013] In another aspect, the present disclosure provides a fusion protein comprising, from N-terminus to C-terminus, a first peptide; a linker peptide; and a second peptide, wherein: (a) the first peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 1, wherein the amino acid at at least one of positions 4 or 25 of the first peptide is not M; and the second peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 8, wherein the amino acid at position 22 of the second peptide is not R; or the first peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 8, wherein the amino acid at position 22 of the second peptide is not R; and the second peptide comprises an

amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 1, wherein the amino acid at at least one of positions 4 or 25 of the first peptide is not M; and optionally, (b) the fusion protein has a pI from 6.0 to 8.2.

[0014] In some embodiments, the fusion protein has a pI from about 6.0 to about 9.4. In some
5 embodiments, the fusion protein has a pI from about 6.0 to about 8.2. In some embodiments,
the fusion protein has a pI that is less than about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1,
8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, or 6.1. In
some embodiments, the fusion protein has a pI that is less than 9.0. In some embodiments, the
fusion protein has a pI that is less than about 8.2. In some embodiments, the fusion protein has
10 a pI of about 6.8. In some embodiments, the fusion protein has a pI of about 7.0. In some
embodiments, the fusion protein has a pI of about 7.1. In some embodiments, the fusion protein
has a pI of about 7.4. In some embodiments, the fusion protein has a pI of about 7.5. In some
embodiments, the fusion protein has a pI of about 7.9. In some embodiments, the fusion protein
has a pI of about 8.0. In some embodiments, the fusion protein has a pI of about 8.4. In some
15 embodiments, the fusion protein has a pI of about 8.5. In some embodiments, the fusion protein
has a pI of about 8.8. In some embodiments, the fusion protein has a pI of about 8.9.

[0015] In some embodiments, the linker peptide comprises an amino acid sequence with 12-
15 amino acids. In some embodiments, the linker peptide comprises the amino acid sequence
ASDAAGAX₈AX₉AGA (SEQ ID NO: 17), wherein: X₈ is D, E, N, or Q; and X₉ is D, E, N, or
20 Q; or the linker peptide comprises the amino acid sequence GGEGSGGEGX₁₀GGG (SEQ ID
NO: 25), wherein: X₁₀ is E or S. In some embodiments, X₈ is D, E, N, or Q, and X₉ is D, E, or
Q; or X₈ is D, E, or Q, and X₉ is D, E, N, or Q.

[0016] In another aspect, the present disclosure provides a fusion protein comprising, from N-
terminus to C-terminus: a first peptide; a linker peptide; and a second peptide, wherein: the
25 linker peptide comprises the amino acid sequence ASDAAGAX₈AX₉AGA (SEQ ID NO: 17),
wherein: X₈ is D, E, N, or Q; and X₉ is D, E, N, or Q; or the linker peptide comprises the amino
acid sequence GGEGSGGEGX₁₀GGG (SEQ ID NO: 25), wherein: X₁₀ is E or S.

[0017] In some embodiments, X₈ is D, E, N, or Q, and X₉ is D, E, or Q; or X₈ is D, E, or Q,
and X₉ is D, E, N, or Q. In some embodiments, the linker peptide comprises an amino acid
30 sequence selected from the group consisting of SEQ ID NOs: 18, 19, 20, 21, 22, 23, 24, 26,
and 27.

[0018] In some embodiments, the first peptide comprises the amino acid sequence
DSX₁QEEVIX₂LCGRELVRAQIAICGX₃ST (SEQ ID NO: 7), wherein: X₁ is not M, H, or C;

X₂ is K, Q, D, E, L, I or Y; and X₃ is K or Q. In some embodiments, the first peptide comprises the amino acid sequence DSX₁QEEVIX₂LCGRELVRAQIAICGX₃ST (SEQ ID NO: 7), wherein: X₁ is W, Y, F, L, I, V or A; X₂ is K, Q, D, E, L, I or Y; and X₃ is K or Q. In some embodiments, X₁ is Y. In some embodiments, the first peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, 5, and 6. In some embodiments, the first peptide consists of 27, 28, or 29 amino acids.

[0019] In some embodiments, the first peptide comprises the amino acid sequence QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein: X₄ is K, Q, D, E, L, I, or Y; X₅ is any amino acid except M, W, or C; X₆ is K, Q, D, E, L, I, or Y; and X₇ is Q, D, E, L, I, Y or R. In some embodiments, the first peptide comprises the amino acid sequence QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein: X₄ is K, Q, D, E, L, I, or Y; X₅ is H, K, Q, Y, L, N, I, S, T, or F; X₆ is K, Q, D, E, L, I, or Y; and X₇ is Q, D, E, L, I, Y or R. In some embodiments, X₅ is Q. In some embodiments, the first peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, and 507. In some embodiments, the first peptide consists of 24 or 25 amino acids.

[0020] In some embodiments, the second peptide comprises the amino acid sequence DSX₁QEEVIX₂LCGRELVRAQIAICGX₃ST (SEQ ID NO: 7), wherein: X₁ is not M, H, or C; X₂ is K, Q, D, E, L, I or Y; and X₃ is K or Q. In some embodiments, the second peptide comprises the amino acid sequence DSX₁QEEVIX₂LCGRELVRAQIAICGX₃ST (SEQ ID NO: 7), wherein: X₁ is W, Y, F, L, I, V or A; X₂ is K, Q, D, E, L, I, or Y; and X₃ is K or Q. In some embodiments, X₁ is Y. In some embodiments, the second peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, 5, and 6. In some embodiments, the second peptide consists of 27, 28, or 29 amino acids.

[0021] In some embodiments, the second peptide comprises the amino acid sequence QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein: X₄ is K, Q, D, E, L, I, or Y; X₅ is any amino acid except M, W, or C; X₆ is K, Q, D, E, L, I, or Y; and X₇ is Q, D, E, L, I, Y or R. In some embodiments, the second peptide comprises the amino acid sequence QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein: X₄ is K, Q, D, E, L, I, or Y; X₅ is H, K, Q, Y, L, N, I, S, T, or F; X₆ is K, Q, D, E, L, I, or Y; and X₇ is Q, D, E, L, I, Y or R. In some embodiments, X₅ is Q. In some embodiments, the second peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, and 507. In some embodiments, the second peptide consists of 24 or 25 amino acids.

[illegible]

[illegible]

[illegible]

[illegible]

the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 1; the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 2; the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 3; the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 4; the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 5; or the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 6.

[0024] In some embodiments, the fusion protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 28-75 and 508-515.

[0025] In some embodiments, the fusion protein further comprises an IgG Fc. In some embodiments, the IgG Fc comprises the amino acid alanine at each of EU positions 234 and 235. In some embodiments, the IgG Fc comprises the amino acid alanine at EU position 329. In some embodiments, the IgG Fc comprises the amino acid alanine at each of EU positions 234, 235, and 329. In some embodiments, the IgG Fc comprises the amino acids alanine, alanine, alanine, leucine, and serine at EU positions 234, 235, 329, 428, and 434, respectively. In some embodiments, the IgG Fc comprises the amino acids lysine, phenylalanine, and tyrosine at EU positions 433, 434, and 436, respectively. In some embodiments, the IgG Fc comprises the amino acids tyrosine, threonine, and glutamate at EU positions 252, 254, and 256, respectively. In some embodiments, the IgG Fc comprises the amino acids leucine and serine at EU positions 428 and 434, respectively.

[0026] In some embodiments, the IgG Fc comprises an amino acid sequence at least 85% identical to the amino acid sequence of a human IgG1 Fc. In some embodiments, the IgG Fc comprises the amino acid sequence of a human IgG1 Fc.

[0027] In some embodiments, the IgG Fc comprises an amino acid sequence at least 95% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 76-83. In some embodiments, the IgG Fc comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 76-83.

[0028] In some embodiments, the IgG Fc is linked to the N-terminus of the first peptide. In some embodiments, the IgG Fc is linked to the C-terminus of the second peptide.

[0029] In some embodiments, the fusion protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 84-138 and 516-523. In some embodiments, the fusion protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 139-193, 524-531, and 549.

- 5 [0030] In another aspect, the present disclosure provides a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-6, 8-15, 18-24, 26-75, 84-193, 507-531, and 549-558.

[0031] In another aspect, the present disclosure provides a polynucleotide comprising a nucleotide sequence encoding any one of the fusion proteins described herein, or any one of
10 the polypeptides described herein.

[0032] In some embodiments, the polynucleotide is a DNA molecule. In some embodiments, the polynucleotide comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs: 194-248, 410-464, and 532-547.

[0033] In some embodiments, the polynucleotide is an RNA molecule.

- 15 [0034] In another aspect, the present disclosure provides an expression vector comprising the any one of the polynucleotides described herein.

[0035] In some embodiments, the expression vector is a plasmid. In some embodiments, the expression vector is a viral vector.

- [0036] In another aspect, the present disclosure provides a host cell comprising any one of the
20 polynucleotides described herein, or any one of the expression vectors described herein.

[0037] In some embodiments, the host cell is a prokaryotic cell. In some embodiments, the prokaryotic cell is an *E. coli* cell or a *Bacillus* cell. In some embodiments, the host cell is a eukaryotic cell. In some embodiments, the eukaryotic cell is selected from the group consisting of a yeast cell, an insect cell, and a mammalian cell. In some embodiments, the mammalian
25 cell is selected from the group consisting of a CHO cell, a HeLa cell, and a 293 cell.

[0038] In another aspect, the present disclosure provides a population of cells comprising two or more of any of the host cells described herein.

- [0039] In another aspect, the present disclosure provides a method of producing any one of the fusion proteins described herein, or any one of the polypeptides described herein, comprising
30 culturing any one of the host cells described herein, under conditions such that the fusion protein is produced.

[0040] In another aspect, the present disclosure provides a pharmaceutical composition comprising an effective amount of any one of the fusion proteins described herein, any one of

the polypeptides described herein, any one of the polynucleotides described herein, or any one of the expression vectors described herein.

[0041] In some embodiments, the fusion protein has a circulating half-life of at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21 days, at least 22 days, or at least 23 days. In some embodiments, the fusion protein has a circulating half-life of at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21 days, at least 22 days, or at least 23 days when administered (*e.g.*, to a human).
In some embodiments, the fusion protein has bioavailability of at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, or at least 70% when administered (*e.g.*, to a human). In some embodiments, administration of the pharmaceutical composition is via intravenous administration or subcutaneous administration.

[0042] In another aspect, the present disclosure provides a method of enhancing a relaxin-2-related activity in a primary cell, comprising contacting the primary cell with any one of the fusion proteins described herein, thereby enhancing relaxin-2-related activity in the cell.

[0043] In some embodiments, the fusion protein activates relaxin-2 receptor (RXFP1) on a cell surface.

[0044] In some embodiments, the method elevates cAMP levels in the primary cell, inducing vasodilation, inducing the expression of angiogenic factors, inducing the expression of MMPs, and inducing collagen degradation.

[0045] In some embodiments, the primary cell is selected from the group consisting of endothelial cells, vascular smooth muscle cells, other vascular cells, cardiomyocytes, other cardiac cells, and fibroblasts.

[0046] In some embodiments, the primary cell is within a subject. In some embodiments, the subject has a relaxin-2-associated disorder. In some embodiments, the relaxin-2-associated disorder is selected from the group consisting of kidney diseases, fibrotic diseases, and cardiovascular diseases. In some embodiments, the disorder is selected from the group consisting of pulmonary hypertension, pulmonary arterial hypertension (PAH), pulmonary hypertension due to left heart disease (PH-LHD), combined precapillary and postcapillary pulmonary hypertension (CpcPH), isolated postcapillary pulmonary hypertension (IpcPH), heart failure, heart failure with preserved ejection fraction (HFpEF), heart failure with mid-range ejection fraction (HFmrEF), heart failure with reduced ejection fraction (HFrEF),

valvular heart disease, joint disease, frozen shoulder (also known as adhesive capsulitis), kidney disease, chronic kidney disease, and hypertensive kidney disease.

[0047] In some embodiments, the disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH) with heart failure with preserved ejection fraction (HFpEF).

5 In some embodiments, the disorder is isolated postcapillary pulmonary hypertension (IpcPH) with heart failure with preserved ejection fraction (HFpEF). In some embodiments, the disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH) with heart failure with mid-range ejection fraction (HFmrEF). In some embodiments, the disorder is isolated postcapillary pulmonary hypertension (IpcPH) with heart failure with mid-range
10 ejection fraction (HFmrEF).

[0048] In another aspect, the present disclosure provides a method of treating a relaxin-associated disorder in a subject in need thereof, comprising administering to the subject an effective amount of any one of the fusion proteins described herein, any one of the polynucleotides described herein, any one of the expression vectors described herein, or any
15 one of the pharmaceutical compositions described herein, thereby treating the relaxin-associated disorder.

[0049] In some embodiments, the relaxin-2-associated disorder is selected from the group consisting of kidney diseases, fibrotic diseases, and cardiovascular diseases. In some embodiments, the disorder is selected from the group consisting of pulmonary hypertension, pulmonary arterial hypertension (PAH), pulmonary hypertension due to left heart disease (PH-LHD), combined precapillary and postcapillary pulmonary hypertension (CpcPH), isolated postcapillary pulmonary hypertension (IpcPH), heart failure, heart failure with preserved ejection fraction (HFpEF), heart failure with mid-range ejection fraction (HFmrEF), heart failure with reduced ejection fraction (HFrEF), kidney disease, chronic kidney disease, and
20 hypertensive kidney disease. In some embodiments, the method decreases arterial pressure, increases renal artery blood flow, increases cardiac filling at diastole, resolves established fibrosis, and/or suppresses new fibrosis development in the subject.

[0050] In some embodiments, the method increases renal plasma flow in the subject. In some embodiments, the increase in the renal plasma flow in the subject persists after 1 week, 2 weeks,
30 3 weeks, 4 weeks, 5 weeks, or 1 month after a single administration of the fusion protein. In some embodiments, the increase in the renal plasma flow in the subject is maintained by at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about

95% 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 1 month after a single administration of the fusion protein.

[0051] In some embodiments, the disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH) with heart failure with preserved ejection fraction (HFpEF).

5 In some embodiments, the disorder is isolated postcapillary pulmonary hypertension (IpcPH) with heart failure with preserved ejection fraction (HFpEF). In some embodiments, the disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH) with heart failure with mid-range ejection fraction (HFmrEF). In some embodiments, the disorder is isolated postcapillary pulmonary hypertension (IpcPH) with heart failure with mid-range
10 ejection fraction (HFmrEF).

[0052] In some embodiments, the subject is administered the fusion protein by intravenous administration. In some embodiments, the subject is administered from about 0.1 mg/kg to about 20 mg/kg of the fusion protein. In some embodiments, the subject is administered about 0.3 mg/kg of the fusion protein. In some embodiments, the subject is administered about 1
15 mg/kg of the fusion protein. In some embodiments, the subject is administered about 3 mg/kg of the fusion protein. In some embodiments, the subject is administered about 10 mg/kg of the fusion protein.

[0053] In some embodiments, the subject is administered the fusion protein by intravenous infusion. In some embodiments, the subject is administered the fusion protein by intravenous
20 infusion over 30 minutes. In some embodiments, the subject is administered the fusion protein by intravenous infusion over 60 minutes. In some embodiments, the subject is administered the fusion protein by intravenous infusion over 30 to 60 minutes.

[0054] In some embodiments, the subject is administered the fusion protein by subcutaneous administration. In some embodiments, the subject is administered about 100 mg to about 1500
25 mg of the fusion protein. In some embodiments, the subject is administered about 150 mg of the fusion protein. In some embodiments, the subject is administered at least 150 mg of the fusion protein. In some embodiments, the subject is administered about 300 mg of the fusion protein. In some embodiments, the subject is administered about 600 mg of the fusion protein.

[0055] In some embodiments, the subject is administered the fusion protein once every 1 week,
30 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 1 month.

BRIEF DESCRIPTION OF THE DRAWINGS

[0056] **FIGs. 1A-1C** are graphs depicting cAMP response induced by SEQ ID NO: 87 and wild-type (WT) human relaxin-2 in HEK293 cells transiently expressing human (FIG. 1A), rat (FIG. 1B), and monkey (FIG. 1C) RXFP1, respectively.

5 [0057] **FIGs. 2A-2C** are graphs depicting the pharmacokinetic (PK) values obtained by measuring the concentration of the various relaxin-2 fusion protein analogs (using human Fc levels as a proxy) as indicated in the serum of rats following a 5 mg/kg intravenous (IV) injection of the respective protein analog over time.

10 [0058] **FIG. 3** is a graph depicting the change in renal arterial blood flow (RABF) compared to baseline, over time, in rats administered the various relaxin-2 fusion protein analogs as indicated.

15 [0059] **FIGs. 4A and 4B** are graphs depicting the changes to RABF (FIG. 4A) and serum levels of fusion protein (FIG. 4B; using human Fc levels as a proxy) in response to dose of SEQ ID NO: 87 or SEQ ID NO: 497 as indicated, over time. **FIG. 4C** is a graph depicting serum PK as a function of increase in RABF (baseline subtracted).

20 [0060] **FIGs. 5A and 5B** are graphs depicting that a low dose of SEQ ID NO: 87 increases and maintains RABF in treated rats significantly more than SEQ ID NO: 497. **FIG. 5A** shows the increase in RABF in rats treated with SEQ ID NO: 87 or SEQ ID NO: 497 over time. **FIG. 5B** shows that rats treated with SEQ ID NO: 87 demonstrate significant increase in RABF compared to SEQ ID NO: 497 by area under the curve analysis.

25 [0061] **FIGs. 6A and 6B** are graphs depicting the effect of SEQ ID NO: 87 on right ventricular systolic pressure (RVSP) following 10 mg/kg intravenous treatment of SEQ ID NO: 87 for three weeks in MCT-induced rats (MCT), with (FIG. 6A) or without (FIG. 6B) B cell depletion using an anti-CD20 antibody (no CD20 or +CD20). Sildenafil was used as a positive control in the non-B cell depleted animals.

30 [0062] **FIGs. 7A and 7B** are graphs depicting the effect of SEQ ID NO: 87 on mean pulmonary arterial pressure (mPAP) following 10 mg/kg intravenous treatment of SEQ ID NO: 87 for three weeks in MCT-induced rats (MCT), with (FIG. 7A) or without (FIG. 7B) B cell depletion using an anti-CD20 antibody (no CD20 or +CD20). Sildenafil was used as a positive control in the non-B cell depleted animals.

[0063] **FIGs. 8A and 8B** are graphs depicting the effect of SEQ ID NO: 87 on the Fulton Index following 10 mg/kg intravenous treatment of SEQ ID NO: 87 for three weeks in MCT-induced rats (MCT), with (FIG. 8A) or without (FIG. 8B) B cell depletion using an anti-CD20 antibody

(no CD20 or +CD20). Sildenafil was used as a positive control in the non-B cell depleted animals.

[0064] FIGs. 9A and 9B are graphs depicting the effect of SEQ ID NO: 87 on serum NT-pro-BNP levels following 10 mg/kg intravenous treatment of SEQ ID NO: 87 for three weeks in MCT-induced rats (MCT), with (FIG. 9A) or without (FIG. 9B) B cell depletion using an anti-CD20 antibody (no CD20 or +CD20). Sildenafil was used as a positive control in the non-B cell depleted animals.

[0065] FIGs. 10A and 10B are graphs depicting the results of histopathological analysis of the effect of SEQ ID NO: 87 on lung inflammation (FIG. 10A) and pulmonary arterial muscularization (FIG. 10B) following 10 mg/kg intravenous treatment of SEQ ID NO: 87 for three weeks in MCT-induced rats (MCT), with B cell depletion using an anti-CD20 antibody (+anti-CD20). *: $p < 0.05$; **: $p < 0.01$; ****: $p < 0.0001$ using a nonparametric 1-way analysis of variance with post hoc Dunn's multiple comparisons tests.

[0066] FIG. 11 is a graph depicting the effect of SEQ ID NO: 87 on mortality following 10 mg/kg intravenous treatment of SEQ ID NO: 87 for three weeks in MCT-induced rats (MCT), with or without B cell depletion using an anti-CD20 antibody (no CD20 or +CD20). Sildenafil was used as a positive control in the non-B cell depleted animals.

[0067] FIG. 12 is a graph depicting the effect of SEQ ID NO: 496 and SEQ ID NO: 313 on collagen deposition in renal parenchyma in a mouse unilateral ureteral obstruction (UUO) model, according to aspects of the present disclosure. Mice underwent UUO surgery and were treated with vehicle (PBS; $n=10$), 20 mg/kg SEQ ID NO: 496 ($n=10$), 10 mg/kg SEQ ID NO: 313 ($n=10$), or 20 mg/kg SEQ ID NO: 313 ($n=10$). Also shown are control mice that underwent a sham surgery and were treated with vehicle (PBS; $n=5$). Following treatment, obstructed kidneys were harvested and fixed for histology. Collagen was detected via immunolabeling. Depicted is a quantification of collagen levels as a percentage of total immunolabeled area. *: $p < 0.05$; ****: $p < 0.0001$.

[0068] FIG. 13 is a graph depicting the effect of SEQ ID NO: 87 on collagen deposition in kidney cortex in a mouse UUO model, according to aspects of the present disclosure. Mice underwent UUO surgery and were treated with vehicle (PBS; $n=8$) or 10 mg/kg SEQ ID NO: 87 ($n=8$). Also shown are control mice that underwent a sham surgery and were treated with vehicle (PBS; $n=8$). Following treatment, obstructed kidneys were harvested and fixed for histology. Collagen was detected via immunolabeling. Depicted is a quantification of collagen levels as a percentage of total immunolabeled area. ****: $p < 0.0001$; *: $p = 0.02$.

[0069] FIG. 14 is a graph depicting the effect of SEQ ID NO: 87 on TNF α levels in kidney cortex in a mouse UVO model, according to aspects of the present disclosure. Mice were treated as described for FIG. 13, and TNF α levels were quantified in protein lysates via electrochemiluminescence assay. ****: $p < 0.0001$; ***: $p < 0.001$.

5 [0070] FIG. 15 is a graph depicting the effect of SEQ ID NO: 87 on isoproterenol-induced cardiac hypertrophy, according to aspects of the present disclosure. Mice were treated with vehicle (n=10), isoproterenol (n=10), or isoproterenol and SEQ ID NO: 87 (n=6). Following treatment, body weight and heart rate was measured for each mouse. Depicted is heart weight normalized by body weight (HW/BW) for each group. ****: $p < 0.0001$.

10 [0071] FIG. 16 is a graph depicting the effect of SEQ ID NO: 87 on isoproterenol-induced fibrosis, according to aspects of the present disclosure. Mice were treated as described for FIG. 15, and collagen content was quantified using a hydroxyproline assay. ****: $p < 0.0001$; ***: $p < 0.001$.

[0072] FIGs. 17A and 17B are graphs depicting PK (FIG. 17A) and PD (FIG. 17B) data of
15 healthy human patients administered a single 0.3 mg/kg IV dose of SEQ ID NO: 87. FIG. 17A shows the concentration of SEQ ID NO: 87 over time in dosed patients (solid lines), as well as the PK profile of SEQ ID NO: 87 as predicted using non-human primate modeling (dashed line). FIG. 17B shows the change in renal plasma flow over baseline on days 2, 8, and 17, in healthy patients dosed with SEQ ID NO: 87 or placebo (PBO).

20 [0073] FIG. 18 is a graph depicting PK data of healthy human patients administered a single 150 mg SC dose of SEQ ID NO: 87, showing the concentration of SEQ ID NO: 87 over time in dosed patients.

DETAILED DESCRIPTION

[0074] The therapeutic potential of relaxin-2 was highlighted in the RELAX-AHF trials (*see*,
25 *e.g.*, Teerlink *et al.*, (2013) *Lancet* 381(9860):29-39). However, the therapeutic protein used, human relaxin-2 (Serelaxin), had not been modified in any way to extend half-life *in vivo*, and the protein had to be administered by continuous IV infusion over a 48-hour period. Half-life extended versions of relaxin-2 have been generated via fusion of the peptide hormone to human IgG1 Fc or to an albumin binding nanobody, but such fusion proteins have shown extremely
30 rapid clearance from plasma. The present disclosure is based in part on the discovery by the inventors that reducing the positive charge and heparin binding of relaxin-2 results in greatly improved pharmacokinetic and pharmacodynamic profiles.

[0075] The disclosure provides fusion proteins comprising a human relaxin-2 B chain, or a derivative thereof, and a human relaxin-2 A chain, or a derivative thereof, joined by a peptide linker, wherein the fusion proteins have high *in vivo* circulating half-life when administered to mammals. In some embodiments, the *in vivo* circulating half-life of the fusion proteins
5 provided in this disclosure is greater than 2 hours. In some embodiments, the fusion proteins provided in this disclosure have low pI. In some embodiments, the pI of the fusion proteins provided in this disclosure is less than 8.5. In some embodiments, the low pI of the fusion proteins provided in this disclosure is caused by acidic amino acid residues present in the peptide linker. In some embodiments, the peptide linker of the fusion protein comprises 2 or
10 more acidic amino acids. In some embodiments, the peptide linker is 10-15 total amino acids in length.

Definitions

[0076] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which the claimed subject
15 matter belongs. It is to be understood that the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of any subject matter claimed. In this application, the use of the singular includes the plural unless specifically stated otherwise. It must be noted that, as used in the specification and the appended claims, the singular forms “a,” “an,” and “the” include plural referents unless the context clearly
20 dictates otherwise. In this application, the use of “or” means “and/or” unless stated otherwise. Furthermore, use of the term “including” as well as other forms, such as “include,” “includes,” and “included,” is not limiting. The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

[0077] The term “polynucleotide” as used herein refers to a polymer of DNA or RNA. The
25 polynucleotide sequence can be single-stranded or double-stranded; contain natural, non-natural, or altered nucleotides; and contain a natural, non-natural, or altered internucleotide linkage, such as a phosphoroamidate linkage or a phosphorothioate linkage, instead of the phosphodiester found between the nucleotides of an unmodified polynucleotide sequence. Polynucleotide sequences include, but are not limited to, all polynucleotide sequences which
30 are obtained by any means available in the art, including, without limitation, recombinant means, *e.g.*, the cloning of polynucleotide sequences from a recombinant library or a cell genome, using ordinary cloning technology and polymerase chain reaction, and the like, and by synthetic means.

[0078] The terms “protein” and “polypeptide” are used interchangeably herein and refer to a polymer of amino acids connected by one or more peptide bonds. As used herein, “amino acid sequence” refers to the information describing the relative order and identity of amino acid residues which make up a polypeptide.

- 5 [0079] As used herein, the term “an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications” with reference to an amino acid sequence, refers to an amino acid sequence that comprises up to 5 amino acid substitutions, alterations, inversions, additions, or deletions compared to a reference amino acid sequence.

- [0080] The determination of “percent identity” between two sequences (*e.g.*, amino acid sequences or nucleic acid sequences) can be accomplished using a mathematical algorithm. A specific, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin S & Altschul S F, (1990) *PNAS* 87: 2264-2268, modified as in Karlin S & Altschul SF, (1993) *PNAS* 90: 5873-5877, each of which is herein incorporated by reference in its entirety. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul SF *et al.*, (1990) *J Mol Biol* 215: 403, which is herein incorporated by reference in its entirety. BLAST nucleotide searches can be performed with the NBLAST nucleotide program parameters set, *e.g.*, at score=100, wordlength=12 to obtain nucleotide sequences homologous to a nucleic acid molecule described herein. BLAST protein searches can be performed with the XBLAST program parameters set, *e.g.*, at score=50, wordlength=3 to obtain amino acid sequences homologous to a protein molecule described herein. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul S F *et al.*, (1997) *Nuc Acids Res* 25: 3389-3402, which is herein incorporated by reference in its entirety. Alternatively, PSI BLAST can be used to perform an iterated search which detects distant relationships between molecules. *Id.* When utilizing BLAST, Gapped BLAST, and PSI BLAST programs, the default parameters of the respective programs (*e.g.*, of XBLAST and NBLAST) can be used (*see, e.g.*, National Center for Biotechnology Information (NCBI) on the worldwide web, ncbi.nlm.nih.gov). Another specific, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, (1988) *CABIOS* 4:11-17, which is herein incorporated by reference in its entirety.
- 25 Such an algorithm is incorporated in the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.
- 30

[0081] The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, typically only exact matches are counted.

5 [0082] As used herein, the term “linked to” refers to covalent or noncovalent binding between two molecules or moieties. The skilled worker will appreciate that when a first molecule or moiety is linked to a second molecule or moiety, the linkage need not be direct, but instead, can be via an intervening molecule or moiety.

[0083] As used herein, the terms “human relaxin-2 B chain” or “relaxin B chain” or “relaxin B” or “rel B” refer to a peptide comprising or consisting of the amino acid sequence as set forth
10 in DSWMEEVIKLCGRELVRAQIAICGMSTWS (SEQ ID NO: 249) or derivatives thereof. In some embodiments, a derivative of a relaxin B chain comprises the amino acid sequence of SEQ ID NO: 154 with 1, 2, 3, 4, or 5 amino acid changes.

[0084] As used herein, the terms “human relaxin-2 A chain” or “relaxin A chain” or “relaxin A” or “rel A” refer to a peptide comprising or consisting of the amino acid sequence as set
15 forth in QLYSALANKCCHVGCTKRSLARFC (SEQ ID NO: 257) or derivatives thereof. In some embodiments, a derivative of a relaxin A chain comprises the amino acid sequence of SEQ ID NO: 155 with 1, 2, 3, 4, or 5 amino acid changes.

[0085] As used herein, the term “linker peptide” refers to a peptide that links the relaxin A chain and the relaxin B chain in the fusion proteins described herein.

20 [0086] As used herein, the term “acidic amino acid” refers to an amino acid that has a carboxylic acid in its side chain. In some embodiments, the acidic amino acid is aspartate, glutamate, 2-aminoadipic acid, 2-aminobutyric acid or 2-aminopimelic acid. In some embodiments, acid amino acids include aspartate and glutamate.

[0087] As used herein, the term “non-acidic amino acid” refers to amino acids that are not
25 acidic amino acids. In some embodiments, non-acidic amino acids include glycine, proline, and serine. In some embodiments, non-specific amino acids also include arginine, histidine, lysine, threonine, asparagine, glutamine, cysteine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, tyrosine, and tryptophan.

[0088] As used herein, the term “IgG Fc” refers to the immunoglobulin G (IgG) fragment
30 crystallizable (Fc) region. In some embodiments, the IgG Fc is the human IgG1, IgG2, IgG3, or IgG4 Fc region. In some embodiments, the IgG Fc is the IgG1 Fc region.

[0089] As used herein, the term “EU numbering system” refers to the EU numbering convention for the constant regions of an antibody, as described in Edelman, G. M. *et al.*, Proc.

Natl. Acad. USA, 63, 78-85 (1969) and Kabat *et al.*, Sequences of Proteins of Immunological Interest, U.S. Dept. Health and Human Services, 5th edition, 1991, each of which is herein incorporated by reference in its entirety.

[0090] As used herein, the term “relaxin-2 receptor,” “human relaxin-2 receptor,” “human relaxin receptor 1,” “RXFP1,” or “LGR7” is the native receptor of relaxin-2 in humans. In some embodiments, RXFP1 comprises the amino acid sequence shown in NCBI Reference Sequence: NP_067647.2, NP_001240656.1, NP_001240657.1, NP_001240658.1, NP_001240659.1, NP_001240661.1, NP_001240662.1, or NP_001350705.1 incorporated herein by reference in its entirety.

[0091] As used herein, the terms “treat,” “treating,” and “treatment” refer to therapeutic or preventative measures described herein. In some embodiments, the methods of “treatment” employ administration of a fusion protein to a subject having a disease or disorder, or predisposed to having such a disease or disorder, in order to prevent, cure, delay, reduce the severity of, or ameliorate one or more symptoms of the disease or disorder or recurring disease or disorder, or in order to prolong the survival of a subject beyond that expected in the absence of such treatment.

[0092] As used herein, the term “effective amount” in the context of the administration of a therapy to a subject refers to the amount of a therapy that achieves a desired prophylactic or therapeutic effect.

[0093] As used herein, the term “subject” includes any human or non-human animal. In one embodiment, the subject is a human or non-human mammal. In one embodiment, the subject is a human.

[0094] As used herein, the term “pI” means the isoelectric point, *i.e.*, the pH of a solution at which the net charge on a fusion protein is zero. In some embodiments, the pI is the calculated or theoretical pI. In some embodiments, the pI is measured experimentally by an instrument.

Fusion Proteins

[0095] The disclosure provides fusion proteins comprising a human relaxin-2 B chain, or a derivative thereof, and a human relaxin-2 A chain, or a derivative thereof, linked by a peptide linker, wherein the fusion proteins have high *in vivo* circulating half-life when administered to mammals. In some embodiments, the fusion protein comprises, from N-terminus to C-terminus, a human relaxin-2 B chain, or a derivative thereof, a peptide linker and a human relaxin-2 A chain, or a derivative thereof. In some embodiments, the fusion protein comprises, from N-terminus to C-terminus, a human relaxin-2 A chain, or a derivative thereof, a peptide

linker and a human relaxin-2 B chain, or a derivative thereof. In some embodiments, the fusion protein further comprises an IgG Fc. The IgG Fc is linked to the N-terminus or C-terminus of the human relaxin B chain-linker protein-human relaxin A chain fusion protein or the human relaxin A chain-linker protein-human relaxin B chain fusion protein. In some embodiments, the fusion proteins form homodimers via interaction between IgG Fc moieties. In some
5 embodiments, the IgG Fc described above is replaced with PEG.

Human Relaxin-2 B Chain Derivatives

[0096] The disclosure provides human relaxin-2 B chain derivatives, wherein the derivatives have 1, 2, 3, 4, or 5 amino acid changes when compared to the amino acid sequence of SEQ
10 ID NO: 249. In some embodiments, the amino acid that corresponds with position 13 of SEQ ID NO: 249 must be arginine. In some embodiments, the amino acid that corresponds with position 17 of SEQ ID NO: 249 must be arginine. In some embodiments, the amino acid that corresponds with position 20 of SEQ ID NO: 249 must be isoleucine. In some embodiments, the amino acid that corresponds with position 13 of SEQ ID NO: 249 must be arginine; the
15 amino acid that corresponds with position 17 of SEQ ID NO: 249 must be arginine; and the amino acid that corresponds with position 20 of SEQ ID NO: 249 must be isoleucine.

[0097] In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of the following formula: $DSWX_{19}EEVIKLCGRELVRQAIAICGX_{20}ST$ (SEQ ID NO: 250), wherein X_{19} and X_{20} are absent or any amino acid. In some embodiments, X_{19} is methionine
20 (M), glutamine (Q), glutamic acid (E), asparagine (N), aspartic acid (D), serine (S), or threonine (T). In some embodiments, X_{19} is methionine (M), lysine (K) or glutamine (Q). In some embodiments, X_{20} is methionine (M), lysine (K), glutamine (Q), or asparagine (N). In some embodiments, X_{20} is methionine (M) or lysine (K). In some embodiments, X_{20} is lysine (K). In some embodiments, X_{19} is methionine (M), lysine (K) or glutamine (Q), and X_{20} is
25 methionine (M) or lysine (K).

[0098] The disclosure provides human relaxin-2 B chain derivatives, wherein the derivatives comprise an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 1, wherein the amino acid at position 4 is not methionine (M), or the amino acid at position 25 of is not methionine (M). In some
30 embodiments, the derivatives comprise an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 1, wherein the amino acid at position 4 is not methionine (M), and the amino acid at position 25 of is not methionine (M). In some embodiments, the derivatives comprise an amino acid sequence that has 0, 1, 2,

3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 1, wherein the amino acid at at least one of positions 4 or 25 of the first peptide is not methionine (M).

[0099] In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of the following formula: $DSX_1QEEVIX_2LCGRELVRQAIAICGX_3ST$ (SEQ ID NO: 7), wherein X₁ is tryptophan (W), tyrosine (Y), phenylalanine (F), leucine (L), isoleucine (I), valine (V), or alanine (A); X₂ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and X₃ is lysine (K) or glutamine (Q). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of the following formula: $DSX_1QEEVIX_2LCGRELVRQAIAICGX_3ST$ (SEQ ID NO: 7), wherein X₁ is tryptophan (W), tyrosine (Y), phenylalanine (F), leucine (L), isoleucine (I), valine (V), or alanine (A); X₂ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and X₃ is methionine (M), lysine (K), glutamine (Q), or asparagine (N). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of the following formula: $DSX_1QEEVIX_2LCGRELVRQAIAICGX_3ST$ (SEQ ID NO: 7), wherein X₁ is any amino acid except for methionine (M), histidine (H), and cysteine (C); X₂ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and X₃ is lysine (K) or glutamine (Q). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of the following formula: $DSX_1QEEVIX_2LCGRELVRQAIAICGX_3ST$ (SEQ ID NO: 7), wherein X₁ is any amino acid except for methionine (M), histidine (H), and cysteine (C); X₂ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and X₃ is methionine (M), lysine (K), glutamine (Q), or asparagine (N).

[0100] In some embodiments, the human relaxin-2 B chain derivatives comprise an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 502. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of the following formula: $X_{11}LCGRELVRQAIAIC$ (SEQ ID NO: 505), wherein X₁₁ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y).

[0101] In some embodiments, the human relaxin-2 B chain derivatives used in the fusion proteins described herein do not include the amino acid sequences of SEQ ID NOs: 251-254 as set forth below:

DSWKEEVIKLCGRELVRQAIAICGKSTAS (SEQ ID NO: 251);

DSWKEEVIKLCGRELVRAQIAICGKSTWS (SEQ ID NO: 252);
DSWMEEVIKLCGRELVRAQIAICGKSTAS (SEQ ID NO: 253); and
DSWMEEVIKLCGRELVRAQIAICGKSTWS (SEQ ID NO: 254.

[0102] In some embodiments, the human relaxin-2 B chain derivatives are from 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, or 32 amino acids in length. In some embodiments, the human relaxin-2 B chain derivatives are 25, 26, 27, 28, or 29 amino acids in length. In some embodiments, the human relaxin-2 B chain derivatives are 27 amino acids in length. In some embodiments, the human relaxin-2 B chain derivatives are 15-29 amino acids in length. In some embodiments, the human relaxin-2 B chain derivatives are 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, or 29 amino acids in length.

[0103] In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of the amino acid sequences shown in Table 1, below.

Table 1. Human Relaxin-2 B Chain Derivative Sequences

SEQ ID NO:	Amino Acid Sequence
1	DSWQEEVIKLCGRELVRAQIAICGKST
2	DSWQEEVIKLCGRELVRAQIAICGQST
3	DSYQEEVIKLCGRELVRAQIAICGKST
4	DSFQEEVIKLCGRELVRAQIAICGKST
5	DSLQEEVIKLCGRELVRAQIAICGKST
6	DSIQEEVIKLCGRELVRAQIAICGKST
249	DSWMEEVIKLCGRELVRAQIAICGMSTWS
255	DSWKEEVIKLCGRELVRAQIAICGKST
256	DSWMEEVIKLCGRELVRAQIAICGKST
502	KLCGRELVRAQIAIC

[0104] In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 1. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 2. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 3. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 4. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 5. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 6. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 249. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 255. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of

SEQ ID NO: 256. In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 502.

- [0105]** In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 1, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 2, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 3, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 4, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 5, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 6, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 249, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 255, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 256, wherein the amino acid at position 9 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y). In some embodiments, the human relaxin-2 B chain derivatives comprise or consist of SEQ ID NO: 502, wherein the amino acid at position 1 is lysine, (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y).
- [0106]** In some embodiments, the human relaxin-2 B chain derivatives further comprise two residues at the C-terminal end. For example, SEQ ID NOs: 1-7, 250, 255, and 256 can further comprise two residues at the C-terminal end, *e.g.*, the tryptophan (W) and serine (S) at the C-terminal end of SEQ ID NO: 249. In some embodiments, the human relaxin-2 B chain

derivatives further comprise an X amino acid and serine (S) at the C-terminal end, wherein the X amino acid can be any amino acid except cysteine (C). Accordingly, in some embodiments, the C-terminal end of the human relaxin-2 B chain derivatives are XS, wherein X is any amino acid except cysteine (C).

- 5 [0107] In some embodiments, the human relaxin-2 B chain derivatives further comprise one or more substitutions that improve the stability of the relaxin-2 B chain derivatives, e.g., stability of the relaxin-2 B chain derivatives after light or heat exposure, as measured by methods known in the art, e.g., SEC to assess aggregate formation, and CE-SDS to assess purity. In some embodiments, the amino acid in the human relaxin-2 B chain derivatives
10 corresponding to amino acid position 3 in SEQ ID NO: 3 is a tyrosine (Y).

Human Relaxin-2 A Chain Derivatives

- [0108] The disclosure provides human relaxin-2 A chain derivatives, wherein the derivatives have 1, 2, 3, 4, or 5 amino acid changes when compared to the amino acid sequence of SEQ
15 ID NO: 257. In some embodiments, the amino acid that corresponds with position 3 of SEQ ID NO: 257 must be tyrosine. In some embodiments, the amino acid that corresponds with position 23 of SEQ ID NO: 257 must be phenylalanine. In some embodiments, the amino acid that corresponds with position 3 of SEQ ID NO: 257 must be tyrosine; and the amino acid that corresponds with position 23 of SEQ ID NO: 257 must be phenylalanine.

- 20 [0109] In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of the following formula: $X_{21}QX_{22}YSALANKCCHVGCTKRSLAX_{23}FC$ (SEQ ID NO: 258), wherein X_{21} , X_{22} , and X_{23} are absent or any amino acid. In some embodiments, X_{21} is arginine (R), lysine (K), glutamine (Q), asparagine (N), histidine (H), serine (S), threonine (T), proline (P), glycine (G), or absent. In some embodiments, X_{21} is arginine (R), glycine (G), or absent.
25 In some embodiments, X_{21} is arginine (R) or absent. In some embodiments, X_{22} is leucine (L), aspartic acid (D), glutamic acid (E), asparagine (N), glutamine (Q), serine (S), or threonine (T). In some embodiments, X_{22} is leucine (L) or aspartic acid (D). In some embodiments, X_{23} is arginine (R), glutamine (Q), glutamic acid (E), aspartic acid (D), asparagine (N), serine (S), or threonine (T). In some embodiments, X_{23} is arginine (R), glutamine (Q), or glutamic acid (E).
30 In some embodiments, X_{21} is arginine (R) or absent, X_{22} is leucine (L) or aspartic acid (D), and X_{23} is arginine (R), glutamine (Q), or glutamic acid (E).

[0110] The disclosure provides human relaxin-2 A chain derivatives, wherein the derivatives comprise an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative

to the amino acid sequence of SEQ ID NO: 8 wherein the amino acid at position 22 of the second peptide is not arginine (R).

[0111] In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of the following formula: QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein X₄ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₅ is histidine (H), lysine (K), glutamine (Q), tyrosine (Y), leucine (L), asparagine (N), isoleucine (I), serine (S), threonine (T), or phenylalanine (F); X₆ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and X₇ is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of the following formula: QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein X₄ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₅ is any amino acid except methionine (M), tryptophan (W), and cysteine (C); X₆ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and X₇ is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R).

[0112] In some embodiments, the human relaxin-2 A chain derivatives comprise an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 503 or 504. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of the following formula: X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein X₁₂ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₁₃ is histidine (H), lysine (K), glutamine (Q), tyrosine (Y), leucine (L), asparagine (N), isoleucine (I), serine (S), threonine (T), or phenylalanine (F); X₁₄ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₁₅ is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R); and X₁₆ is arginine (R) or glutamine (Q). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of the following formula: X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein X₁₂ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₁₃ is histidine (H), lysine (K), glutamine (Q), tyrosine (Y), leucine (L), asparagine (N), isoleucine (I), serine (S), threonine (T), or phenylalanine (F); X₁₄ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₁₅ is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R); and X₁₆ is arginine (R) or glutamine (Q).

(R); and X₁₆ is arginine (R), glutamine (Q), glutamic acid (E), aspartic acid (D), asparagine (N), serine (S), or threonine (T). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of the following formula: X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein X₁₂ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₁₃ is any amino acid except methionine (M), tryptophan (W), and cysteine (C); X₁₄ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₁₅ is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R); and X₁₆ is arginine (R) or glutamine (Q). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of the following formula: X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein X₁₂ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₁₃ is any amino acid except methionine (M), tryptophan (W), and cysteine (C); X₁₄ is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); X₁₅ is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R); and X₁₆ is arginine (R), glutamine (Q), glutamic acid (E), aspartic acid (D), asparagine (N), serine (S), or threonine (T).

[0113] In some embodiments, the human relaxin-2 A chain derivatives are from 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 amino acids in length. In some embodiments, the human relaxin-2 A chain derivatives are 22, 23, 24, 25, or 26 amino acids in length. In some embodiments, the human relaxin-2 A chain derivatives are 24 amino acids in length. In some embodiments, the human relaxin-2 A chain derivatives are 25 amino acids in length. In some embodiments, the human relaxin-2 A chain derivatives are 16-25 amino acids in length. In some embodiments, the human relaxin-2 A chain derivatives are 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids in length.

[0114] In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of the amino acid sequences shown in Table 2, below.

Table 2. Human Relaxin-2 A Chain Derivative Sequences

SEQ ID NO:	Amino Acid Sequence
8	QLYSALANKCCHVGCTKRSLAQFC
9	QLYSALANKCCHVGCTKQSLAQFC
10	QLYSALANKCCYVGCTKRSLAQFC
11	QLYSALANKCCLVGCTKRSLAQFC
12	QLYSALANKCCQVGCTKRSLAQFC
13	QLYSALANKCCKVGCTKRSLAQFC

SEQ ID NO:	Amino Acid Sequence
14	QLYSALANKCCYVGCTKQSLAQFC
15	QLYSALANKCCKVGCTKQSLAQFC
257	QLYSALANKCCHVGCTKRSLARFC
259	RQLYSALANKCCHVGCTKRSLARFC
260	RQLYSALANKCCHVGCTKRSLAQFC
261	RQLYSALANKCCHVGCTKRSLAEFC
503	KCCHVGCTKRSLARFC
504	KCCHVGCTKRSLAQFC
507	QLYSALANKCCQVGCTKQSLAQFC
550	QLYSALANKCCHVGCTKRSLAEFC
551	RQLYSALANKCCHVGCTKQSLAQFC
552	RQLYSALANKCCYVGCTKRSLAQFC
553	RQLYSALANKCCLVGCTKRSLAQFC
554	RQLYSALANKCCQVGCTKRSLAQFC
555	RQLYSALANKCCKVGCTKRSLAQFC
556	RQLYSALANKCCYVGCTKQSLAQFC
557	RQLYSALANKCCKVGCTKQSLAQFC
558	RQLYSALANKCCQVGCTKQSLAQFC

[0115] In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 8. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 9. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 10. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 11. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 12. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 13. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 14. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 15. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 257. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 259. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 260. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 261. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 503. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 504. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 507. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 550. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of

SEQ ID NO: 551. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 552. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 553. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 554. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 555. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 556. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 557. In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 558.

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10 [0116] In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 8, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 9, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 10, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 11, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 12,

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wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 13, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 14, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 15, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 257, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 259, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some

embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 260, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 261, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 503, wherein the amino acid at position 1 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 10 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 504, wherein the amino acid at position 1 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 10 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 507, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 550, wherein the amino acid at position 9 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 17 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the

amino acid at position 18 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 550, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 551, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 553, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 554, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 555, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 556, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid

at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 557, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R). In some embodiments, the human relaxin-2 A chain derivatives comprise or consist of SEQ ID NO: 558, wherein the amino acid at position 10 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); the amino acid at position 18 is lysine (K), glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), or tyrosine (Y); and the amino acid at position 19 is glutamine (Q), aspartic acid (D), glutamic acid (E), leucine (L), isoleucine (I), tyrosine (Y), or arginine (R).

[0117] In some embodiments, the human relaxin-2 A chain derivatives further comprise one or more substitutions that improve the stability of the relaxin-2 A chain derivatives, *e.g.*, stability of the relaxin-2 A chain derivatives after light or heat exposure, as measured by methods known in the art, *e.g.*, SEC to assess aggregate formation, and CE-SDS to assess purity. In some embodiments, the amino acid in the human relaxin-2 A chain derivatives corresponding to amino acid position 12 in SEQ ID NO: 12 is a glutamine (Q).

Linker Peptides

[0118] The disclosure provides linker peptides, wherein the peptides have at least two acidic amino acids. In some embodiments, the acidic amino acid is glutamate. In some embodiments, the acidic amino acid is aspartate. In some embodiments, the acidic amino acid is a non-standard amino acid. In some embodiments, the acidic amino acid is 2-aminoadipic acid, 2-aminobutyric acid or 2-aminopimelic acid. In some embodiments, the linker peptide has 2, 3, 4, 5, 6, 7, 8, 9, or 10 acidic amino acids.

[0119] In some embodiments, the linker peptide is 8, 9, 10, 11, 12, 13, 14, or 15 amino acids in length. In some embodiments, the linker peptide is 12, 13, 14, or 15 amino acids in length. In some embodiments, the linker peptide has 2, 3, 4, or 5 acidic amino acids. In some embodiments, the linker peptide is 12, 13, 14, or 15 amino acids in length and has 2, 3, 4, or 5

acidic amino acids. In some embodiments, the remaining amino acids are non-acidic amino acids. In some embodiments, the non-acidic amino acids can be any standard amino acid that is not aspartate or glutamate. In some embodiments, non-acidic amino acids can be any amino acid that does not have a carboxylic acid in its side chain. In some embodiments, the non-acidic amino acid is glycine, proline, serine, arginine, histidine, lysine, threonine, asparagine, glutamine, cysteine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, tyrosine, or tryptophan. In some embodiments, the non-acidic amino acid is glycine, proline, or cysteine. In some embodiments, the non-acidic amino acid is glycine.

[0120] In some embodiments, the linker peptide comprises acidic amino acids, wherein all the acidic amino acids are the same amino acids. In some embodiments, the acidic amino acids in the linker peptide are both/all glutamates. In some embodiments, the acidic amino acids in the linker peptide are both/all aspartates. In some embodiments, the linker peptide comprises amino acids that are a mixture of acidic amino acids. In some embodiments, the linker peptide comprises both glutamate and aspartate as acidic amino acids.

[0121] In some embodiments, the linker peptide comprises an amino acid sequence selected from the group consisting of

$X_{17}X_{17}X_{17}X_{18}X_{17}X_{17}X_{17}X_{18}X_{17}X_{17}X_{17}X_{18}X_{17}$;

$X_{17}/X_{17}/X_{17}/X_{18}X_{17}/X_{17}/X_{17}/X_{18}X_{17}/X_{17}/X_{17}/X_{18}X_{17}/X_{17}/X_{17}$;

$X_{17}X_{17}X_{18}X_{17}X_{17}X_{17}X_{18}X_{18}X_{17}X_{17}X_{17}X_{18}X_{17}X_{17}$;

$X_{17}X_{17}X_{17}X_{18}X_{18}X_{17}X_{17}X_{17}X_{18}X_{18}X_{17}X_{17}X_{17}$; and

$X_{17}/X_{17}/X_{18}X_{17}/X_{18}X_{17}/X_{17}/X_{18}X_{17}/X_{18}X_{17}/X_{17}/X_{17}$,

wherein X_{17} is a non-acidic amino acid and X_{18} is an acidic amino acid.

[0122] In some embodiments, the linker peptide comprises non-acidic amino acids, wherein all the non-acidic amino acids are the same amino acids. In some embodiments, the non-acidic amino acids in the linker peptide are all glycine. In some embodiments, the linker peptide comprises amino acids that are a mixture of non-acidic amino acids. In some embodiments, the linker peptide comprises 2, 3, 4, 5, 6, 7, 8, 9, or 10 different types of non-acidic amino acids.

[0123] In some embodiments, the linker peptide comprises the amino acid sequence ASDAAGAX₈AX₉AGA (SEQ ID NO: 17), wherein X₈ is aspartic acid (D), glutamic acid (E), asparagine (N), or glutamine (Q); and X₉ is aspartic acid (D), glutamic acid (E), asparagine (N), or glutamine (Q). In some embodiments, X₈ is aspartic acid (D), glutamic acid (E), asparagine (N), or glutamine (Q), and X₉ is aspartic acid (D), glutamic acid (E), or glutamine

(Q). In some embodiments, X₈ is aspartic acid (D), glutamic acid (E), or glutamine (Q), and X₉ is aspartic acid (D), glutamic acid (E), asparagine (N), or glutamine (Q).

[0124] In some embodiments, the linker peptide comprises GGEGSGGEGX₁₀GGG (SEQ ID NO: 25), wherein X₁₀ is glutamic acid (E) or serine (S).

- 5
- [0125] In some embodiments, the linker peptide comprises or consists of the amino acid sequences shown in Table 3, below.

Table 3. Linker Peptide Sequences

SEQ ID NO:	Amino Acid Sequence
18	ASDAAGADADAGA
19	ASDAAGADANAGA
20	ASDAAGADAQAGA
21	ASDAAGAEAEAGA
22	ASDAAGANADAGA
23	ASDAAGAQADAGA
24	ASDAAGAQAQAGA
26	GGEGSGGEGEGGG
27	GGEGSGGEGSGGG
267	GGGE
268	GEGE
269	GGEG
270	GEGG
271	GGEE
272	GGGEGGGEGGGEG
273	GGGEGGGEGGGEGGG
274	GEGGGEEGGGEGG
275	GGGEEGGGEEGGG
276	GGEGEGGEGEGGS

- 10
- [0126] In some embodiments, the linker peptide comprises 2, 3, 4, or 5 repeats of SEQ ID NO: 267, 268, 269, 270, or 271. For example, 3 repeats of SEQ ID NO: 267 would be the amino acid sequence of GGGEGGGEGGGGE (SEQ ID NO: 277).

- [0127] In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 18. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 19. In some
- 15
- embodiments, the linker peptide comprises or consists of SEQ ID NO: 20. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 21. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 22. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 23. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 24. In some

embodiments, the linker peptide comprises or consists of SEQ ID NO: 26. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 27. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 267. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 268. In some
 5 embodiments, the linker peptide comprises or consists of SEQ ID NO: 269. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 270. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 271. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 272. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 273. In some
 10 embodiments, the linker peptide comprises or consists of SEQ ID NO: 274. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 275. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 276. In some embodiments, the linker peptide comprises or consists of SEQ ID NO: 277.

Relaxin/Linker Peptide Combinations for the Fusion Protein

15 **[0128]** In some embodiments, the fusion protein comprises an N-terminal or first peptide, a linker peptide, and a C-terminal or second peptide. In some embodiments, the N-terminal peptide comprises a human relaxin-2 A chain or a derivative thereof (RelA) and the C-terminal peptide comprises a human relaxin-2 B chain or a derivative thereof (RelB). In some
 20 embodiments, the N-terminal peptide comprises a human relaxin-2 B chain or a derivative thereof and the C-terminal peptide comprises a human relaxin-2 A chain or a derivative thereof. Any combination of any of the embodiments of the human relaxin-2 A chain or a derivative thereof, with a human relaxin-2 A chain or a derivative thereof linked by any of the linker peptides disclosed herein can be used to construct embodiments of the fusion proteins described herein. In some embodiments, at least one of the N-terminal peptide and the C-terminal peptide
 25 is a derivative of a human relaxin-2 A chain or a human relaxin-2 B chain. In some embodiments, the N-terminal peptide comprises a human relaxin-2 A chain derivative and the C-terminal peptide comprises a human relaxin-2 B chain derivative. In some embodiments, the N-terminal peptide comprises a human relaxin-2 B chain derivative and the C-terminal peptide comprises a human relaxin-2 A chain derivative.

30 **[0129]** In some embodiments, the human relaxin-2 B chain derivative consists of 15 amino acids and the human relaxin-2 A chain derivative consists of 16-25 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 16 amino acids and the human relaxin-2 A chain derivative consists of 16-25 amino acids. In some embodiments, the human

[illegible]

[0130] In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 16 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 17 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 18 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 19 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 20 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino

- acids and the human relaxin-2 A chain derivative consists of 21 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 22 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 23 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 24 amino acids. In some embodiments, the human relaxin-2 B chain derivative consists of 15-29 amino acids and the human relaxin-2 A chain derivative consists of 25 amino acids.
- 10 [0131] Specific embodiments of the fusion proteins provided in this disclosure are shown below in Table 4.

Table 4. Fusion Proteins

RelB-linker (SEQ ID NO: 18)-RelA			RelB-linker (SEQ ID NO: 19)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	18	8	1	19	8
2	18	8	2	19	8
3	18	8	3	19	8
4	18	8	4	19	8
5	18	8	5	19	8
6	18	8	6	19	8
249	18	8	249	19	8
255	18	8	255	19	8
256	18	8	256	19	8
502	18	8	502	19	8
1	18	9	1	19	9
2	18	9	2	19	9
3	18	9	3	19	9
4	18	9	4	19	9
5	18	9	5	19	9
6	18	9	6	19	9
249	18	9	249	19	9
255	18	9	255	19	9
256	18	9	256	19	9
502	18	9	502	19	9
1	18	10	1	19	10
2	18	10	2	19	10
3	18	10	3	19	10
4	18	10	4	19	10
5	18	10	5	19	10

RelB-linker (SEQ ID NO: 18)-RelA			RelB-linker (SEQ ID NO: 19)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
6	18	10	6	19	10
249	18	10	249	19	10
255	18	10	255	19	10
256	18	10	256	19	10
502	18	10	502	19	10
1	18	11	1	19	11
2	18	11	2	19	11
3	18	11	3	19	11
4	18	11	4	19	11
5	18	11	5	19	11
6	18	11	6	19	11
249	18	11	249	19	11
255	18	11	255	19	11
256	18	11	256	19	11
502	18	11	502	19	11
1	18	12	1	19	12
2	18	12	2	19	12
3	18	12	3	19	12
4	18	12	4	19	12
5	18	12	5	19	12
6	18	12	6	19	12
249	18	12	249	19	12
255	18	12	255	19	12
256	18	12	256	19	12
502	18	12	502	19	12
1	18	13	1	19	13
2	18	13	2	19	13
3	18	13	3	19	13
4	18	13	4	19	13
5	18	13	5	19	13
6	18	13	6	19	13
249	18	13	249	19	13
255	18	13	255	19	13
256	18	13	256	19	13
502	18	13	502	19	13
1	18	14	1	19	14
2	18	14	2	19	14
3	18	14	3	19	14
4	18	14	4	19	14
5	18	14	5	19	14
6	18	14	6	19	14
249	18	14	249	19	14
255	18	14	255	19	14
256	18	14	256	19	14

RelB-linker (SEQ ID NO: 18)-RelA			RelB-linker (SEQ ID NO: 19)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
502	18	14	502	19	14
1	18	15	1	19	15
2	18	15	2	19	15
3	18	15	3	19	15
4	18	15	4	19	15
5	18	15	5	19	15
6	18	15	6	19	15
249	18	15	249	19	15
255	18	15	255	19	15
256	18	15	256	19	15
502	18	15	502	19	15
1	18	257	1	19	257
2	18	257	2	19	257
3	18	257	3	19	257
4	18	257	4	19	257
5	18	257	5	19	257
6	18	257	6	19	257
249	18	257	249	19	257
255	18	257	255	19	257
256	18	257	256	19	257
502	18	257	502	19	257
1	18	259	1	19	259
2	18	259	2	19	259
3	18	259	3	19	259
4	18	259	4	19	259
5	18	259	5	19	259
6	18	259	6	19	259
249	18	259	249	19	259
255	18	259	255	19	259
256	18	259	256	19	259
502	18	259	502	19	259
1	18	260	1	19	260
2	18	260	2	19	260
3	18	260	3	19	260
4	18	260	4	19	260
5	18	260	5	19	260
6	18	260	6	19	260
249	18	260	249	19	260
255	18	260	255	19	260
256	18	260	256	19	260
502	18	260	502	19	260
1	18	261	1	19	261
2	18	261	2	19	261
3	18	261	3	19	261

RelB-linker (SEQ ID NO: 18)-RelA			RelB-linker (SEQ ID NO: 19)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
4	18	261	4	19	261
5	18	261	5	19	261
6	18	261	6	19	261
249	18	261	249	19	261
255	18	261	255	19	261
256	18	261	256	19	261
502	18	261	502	19	261
1	18	503	1	19	503
2	18	503	2	19	503
3	18	503	3	19	503
4	18	503	4	19	503
5	18	503	5	19	503
6	18	503	6	19	503
249	18	503	249	19	503
255	18	503	255	19	503
256	18	503	256	19	503
502	18	503	502	19	503
1	18	504	1	19	504
2	18	504	2	19	504
3	18	504	3	19	504
4	18	504	4	19	504
5	18	504	5	19	504
6	18	504	6	19	504
249	18	504	249	19	504
255	18	504	255	19	504
256	18	504	256	19	504
502	18	504	502	19	504
1	18	507	1	19	507
2	18	507	2	19	507
3	18	507	3	19	507
4	18	507	4	19	507
5	18	507	5	19	507
6	18	507	6	19	507
249	18	507	249	19	507
255	18	507	255	19	507
256	18	507	256	19	507
502	18	507	502	19	507
1	18	550	1	19	550
2	18	550	2	19	550
3	18	550	3	19	550
4	18	550	4	19	550
5	18	550	5	19	550
6	18	550	6	19	550
249	18	550	249	19	550

RelB-linker (SEQ ID NO: 18)-RelA			RelB-linker (SEQ ID NO: 19)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
255	18	550	255	19	550
256	18	550	256	19	550
502	18	550	502	19	550
1	18	551	1	19	551
2	18	551	2	19	551
3	18	551	3	19	551
4	18	551	4	19	551
5	18	551	5	19	551
6	18	551	6	19	551
249	18	551	249	19	551
255	18	551	255	19	551
256	18	551	256	19	551
502	18	551	502	19	551
1	18	552	1	19	552
2	18	552	2	19	552
3	18	552	3	19	552
4	18	552	4	19	552
5	18	552	5	19	552
6	18	552	6	19	552
249	18	552	249	19	552
255	18	552	255	19	552
256	18	552	256	19	552
502	18	552	502	19	552
1	18	553	1	19	553
2	18	553	2	19	553
3	18	553	3	19	553
4	18	553	4	19	553
5	18	553	5	19	553
6	18	553	6	19	553
249	18	553	249	19	553
255	18	553	255	19	553
256	18	553	256	19	553
502	18	553	502	19	553
1	18	554	1	19	554
2	18	554	2	19	554
3	18	554	3	19	554
4	18	554	4	19	554
5	18	554	5	19	554
6	18	554	6	19	554
249	18	554	249	19	554
255	18	554	255	19	554
256	18	554	256	19	554
502	18	554	502	19	554
1	18	555	1	19	555

RelB-linker (SEQ ID NO: 18)-RelA			RelB-linker (SEQ ID NO: 19)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
2	18	555	2	19	555
3	18	555	3	19	555
4	18	555	4	19	555
5	18	555	5	19	555
6	18	555	6	19	555
249	18	555	249	19	555
255	18	555	255	19	555
256	18	555	256	19	555
502	18	555	502	19	555
1	18	556	1	19	556
2	18	556	2	19	556
3	18	556	3	19	556
4	18	556	4	19	556
5	18	556	5	19	556
6	18	556	6	19	556
249	18	556	249	19	556
255	18	556	255	19	556
256	18	556	256	19	556
502	18	556	502	19	556
1	18	557	1	19	557
2	18	557	2	19	557
3	18	557	3	19	557
4	18	557	4	19	557
5	18	557	5	19	557
6	18	557	6	19	557
249	18	557	249	19	557
255	18	557	255	19	557
256	18	557	256	19	557
502	18	557	502	19	557
1	18	558	1	19	558
2	18	558	2	19	558
3	18	558	3	19	558
4	18	558	4	19	558
5	18	558	5	19	558
6	18	558	6	19	558
249	18	558	249	19	558
255	18	558	255	19	558
256	18	558	256	19	558
502	18	558	502	19	558

Table 4. continued

RelB-linker (SEQ ID NO: 20)-RelA			RelB-linker (SEQ ID NO: 21)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	20	8	1	21	8
2	20	8	2	21	8
3	20	8	3	21	8
4	20	8	4	21	8
5	20	8	5	21	8
6	20	8	6	21	8
249	20	8	249	21	8
255	20	8	255	21	8
256	20	8	256	21	8
502	20	8	502	21	8
1	20	9	1	21	9
2	20	9	2	21	9
3	20	9	3	21	9
4	20	9	4	21	9
5	20	9	5	21	9
6	20	9	6	21	9
249	20	9	249	21	9
255	20	9	255	21	9
256	20	9	256	21	9
502	20	9	502	21	9
1	20	10	1	21	10
2	20	10	2	21	10
3	20	10	3	21	10
4	20	10	4	21	10
5	20	10	5	21	10
6	20	10	6	21	10
249	20	10	249	21	10
255	20	10	255	21	10
256	20	10	256	21	10
502	20	10	502	21	10
1	20	11	1	21	11
2	20	11	2	21	11
3	20	11	3	21	11
4	20	11	4	21	11
5	20	11	5	21	11
6	20	11	6	21	11
249	20	11	249	21	11
255	20	11	255	21	11
256	20	11	256	21	11
502	20	11	502	21	11
1	20	12	1	21	12
2	20	12	2	21	12

RelB-linker (SEQ ID NO: 20)-RelA			RelB-linker (SEQ ID NO: 21)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
3	20	12	3	21	12
4	20	12	4	21	12
5	20	12	5	21	12
6	20	12	6	21	12
249	20	12	249	21	12
255	20	12	255	21	12
256	20	12	256	21	12
502	20	12	502	21	12
1	20	13	1	21	13
2	20	13	2	21	13
3	20	13	3	21	13
4	20	13	4	21	13
5	20	13	5	21	13
6	20	13	6	21	13
249	20	13	249	21	13
255	20	13	255	21	13
256	20	13	256	21	13
502	20	13	502	21	13
1	20	14	1	21	14
2	20	14	2	21	14
3	20	14	3	21	14
4	20	14	4	21	14
5	20	14	5	21	14
6	20	14	6	21	14
249	20	14	249	21	14
255	20	14	255	21	14
256	20	14	256	21	14
502	20	14	502	21	14
1	20	15	1	21	15
2	20	15	2	21	15
3	20	15	3	21	15
4	20	15	4	21	15
5	20	15	5	21	15
6	20	15	6	21	15
249	20	15	249	21	15
255	20	15	255	21	15
256	20	15	256	21	15
502	20	15	502	21	15
1	20	257	1	21	257
2	20	257	2	21	257
3	20	257	3	21	257
4	20	257	4	21	257
5	20	257	5	21	257
6	20	257	6	21	257

RelB-linker (SEQ ID NO: 20)-RelA			RelB-linker (SEQ ID NO: 21)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
249	20	257	249	21	257
255	20	257	255	21	257
256	20	257	256	21	257
502	20	257	502	21	257
1	20	259	1	21	259
2	20	259	2	21	259
3	20	259	3	21	259
4	20	259	4	21	259
5	20	259	5	21	259
6	20	259	6	21	259
249	20	259	249	21	259
255	20	259	255	21	259
256	20	259	256	21	259
502	20	259	502	21	259
1	20	260	1	21	260
2	20	260	2	21	260
3	20	260	3	21	260
4	20	260	4	21	260
5	20	260	5	21	260
6	20	260	6	21	260
249	20	260	249	21	260
255	20	260	255	21	260
256	20	260	256	21	260
502	20	260	502	21	260
1	20	261	1	21	261
2	20	261	2	21	261
3	20	261	3	21	261
4	20	261	4	21	261
5	20	261	5	21	261
6	20	261	6	21	261
249	20	261	249	21	261
255	20	261	255	21	261
256	20	261	256	21	261
502	20	261	502	21	261
1	20	503	1	21	503
2	20	503	2	21	503
3	20	503	3	21	503
4	20	503	4	21	503
5	20	503	5	21	503
6	20	503	6	21	503
249	20	503	249	21	503
255	20	503	255	21	503
256	20	503	256	21	503
502	20	503	502	21	503

RelB-linker (SEQ ID NO: 20)-RelA			RelB-linker (SEQ ID NO: 21)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	20	504	1	21	504
2	20	504	2	21	504
3	20	504	3	21	504
4	20	504	4	21	504
5	20	504	5	21	504
6	20	504	6	21	504
249	20	504	249	21	504
255	20	504	255	21	504
256	20	504	256	21	504
502	20	504	502	21	504
1	20	507	1	21	507
2	20	507	2	21	507
3	20	507	3	21	507
4	20	507	4	21	507
5	20	507	5	21	507
6	20	507	6	21	507
249	20	507	249	21	507
255	20	507	255	21	507
256	20	507	256	21	507
502	20	507	502	21	507
1	20	550	1	21	550
2	20	550	2	21	550
3	20	550	3	21	550
4	20	550	4	21	550
5	20	550	5	21	550
6	20	550	6	21	550
249	20	550	249	21	550
255	20	550	255	21	550
256	20	550	256	21	550
502	20	550	502	21	550
1	20	551	1	21	551
2	20	551	2	21	551
3	20	551	3	21	551
4	20	551	4	21	551
5	20	551	5	21	551
6	20	551	6	21	551
249	20	551	249	21	551
255	20	551	255	21	551
256	20	551	256	21	551
502	20	551	502	21	551
1	20	552	1	21	552
2	20	552	2	21	552
3	20	552	3	21	552
4	20	552	4	21	552

RelB-linker (SEQ ID NO: 20)-RelA			RelB-linker (SEQ ID NO: 21)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
5	20	552	5	21	552
6	20	552	6	21	552
249	20	552	249	21	552
255	20	552	255	21	552
256	20	552	256	21	552
502	20	552	502	21	552
1	20	553	1	21	553
2	20	553	2	21	553
3	20	553	3	21	553
4	20	553	4	21	553
5	20	553	5	21	553
6	20	553	6	21	553
249	20	553	249	21	553
255	20	553	255	21	553
256	20	553	256	21	553
502	20	553	502	21	553
1	20	554	1	21	554
2	20	554	2	21	554
3	20	554	3	21	554
4	20	554	4	21	554
5	20	554	5	21	554
6	20	554	6	21	554
249	20	554	249	21	554
255	20	554	255	21	554
256	20	554	256	21	554
502	20	554	502	21	554
1	20	555	1	21	555
2	20	555	2	21	555
3	20	555	3	21	555
4	20	555	4	21	555
5	20	555	5	21	555
6	20	555	6	21	555
249	20	555	249	21	555
255	20	555	255	21	555
256	20	555	256	21	555
502	20	555	502	21	555
1	20	556	1	21	556
2	20	556	2	21	556
3	20	556	3	21	556
4	20	556	4	21	556
5	20	556	5	21	556
6	20	556	6	21	556
249	20	556	249	21	556
255	20	556	255	21	556

RelB-linker (SEQ ID NO: 20)-RelA			RelB-linker (SEQ ID NO: 21)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
256	20	556	256	21	556
502	20	556	502	21	556
1	20	557	1	21	557
2	20	557	2	21	557
3	20	557	3	21	557
4	20	557	4	21	557
5	20	557	5	21	557
6	20	557	6	21	557
249	20	557	249	21	557
255	20	557	255	21	557
256	20	557	256	21	557
502	20	557	502	21	557
1	20	558	1	21	558
2	20	558	2	21	558
3	20	558	3	21	558
4	20	558	4	21	558
5	20	558	5	21	558
6	20	558	6	21	558
249	20	558	249	21	558
255	20	558	255	21	558
256	20	558	256	21	558
502	20	558	502	21	558

Table 4. continued

RelB-linker (SEQ ID NO: 22)-RelA			RelB-linker (SEQ ID NO: 23)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	22	8	1	23	8
2	22	8	2	23	8
3	22	8	3	23	8
4	22	8	4	23	8
5	22	8	5	23	8
6	22	8	6	23	8
249	22	8	249	23	8
255	22	8	255	23	8
256	22	8	256	23	8
502	22	8	502	23	8
1	22	9	1	23	9
2	22	9	2	23	9
3	22	9	3	23	9
4	22	9	4	23	9
5	22	9	5	23	9

RelB-linker (SEQ ID NO: 22)-RelA			RelB-linker (SEQ ID NO: 23)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
6	22	9	6	23	9
249	22	9	249	23	9
255	22	9	255	23	9
256	22	9	256	23	9
502	22	9	502	23	9
1	22	10	1	23	10
2	22	10	2	23	10
3	22	10	3	23	10
4	22	10	4	23	10
5	22	10	5	23	10
6	22	10	6	23	10
249	22	10	249	23	10
255	22	10	255	23	10
256	22	10	256	23	10
502	22	10	502	23	10
1	22	11	1	23	11
2	22	11	2	23	11
3	22	11	3	23	11
4	22	11	4	23	11
5	22	11	5	23	11
6	22	11	6	23	11
249	22	11	249	23	11
255	22	11	255	23	11
256	22	11	256	23	11
502	22	11	502	23	11
1	22	12	1	23	12
2	22	12	2	23	12
3	22	12	3	23	12
4	22	12	4	23	12
5	22	12	5	23	12
6	22	12	6	23	12
249	22	12	249	23	12
255	22	12	255	23	12
256	22	12	256	23	12
502	22	12	502	23	12
1	22	13	1	23	13
2	22	13	2	23	13
3	22	13	3	23	13
4	22	13	4	23	13
5	22	13	5	23	13
6	22	13	6	23	13
249	22	13	249	23	13
255	22	13	255	23	13
256	22	13	256	23	13

RelB-linker (SEQ ID NO: 22)-RelA			RelB-linker (SEQ ID NO: 23)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
502	22	13	502	23	13
1	22	14	1	23	14
2	22	14	2	23	14
3	22	14	3	23	14
4	22	14	4	23	14
5	22	14	5	23	14
6	22	14	6	23	14
249	22	14	249	23	14
255	22	14	255	23	14
256	22	14	256	23	14
502	22	14	502	23	14
1	22	15	1	23	15
2	22	15	2	23	15
3	22	15	3	23	15
4	22	15	4	23	15
5	22	15	5	23	15
6	22	15	6	23	15
249	22	15	249	23	15
255	22	15	255	23	15
256	22	15	256	23	15
502	22	15	502	23	15
1	22	257	1	23	257
2	22	257	2	23	257
3	22	257	3	23	257
4	22	257	4	23	257
5	22	257	5	23	257
6	22	257	6	23	257
249	22	257	249	23	257
255	22	257	255	23	257
256	22	257	256	23	257
502	22	257	502	23	257
1	22	259	1	23	259
2	22	259	2	23	259
3	22	259	3	23	259
4	22	259	4	23	259
5	22	259	5	23	259
6	22	259	6	23	259
249	22	259	249	23	259
255	22	259	255	23	259
256	22	259	256	23	259
502	22	259	502	23	259
1	22	260	1	23	260
2	22	260	2	23	260
3	22	260	3	23	260

RelB-linker (SEQ ID NO: 22)-RelA			RelB-linker (SEQ ID NO: 23)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
4	22	260	4	23	260
5	22	260	5	23	260
6	22	260	6	23	260
249	22	260	249	23	260
255	22	260	255	23	260
256	22	260	256	23	260
502	22	260	502	23	260
1	22	261	1	23	261
2	22	261	2	23	261
3	22	261	3	23	261
4	22	261	4	23	261
5	22	261	5	23	261
6	22	261	6	23	261
249	22	261	249	23	261
255	22	261	255	23	261
256	22	261	256	23	261
502	22	261	502	23	261
1	22	503	1	23	503
2	22	503	2	23	503
3	22	503	3	23	503
4	22	503	4	23	503
5	22	503	5	23	503
6	22	503	6	23	503
249	22	503	249	23	503
255	22	503	255	23	503
256	22	503	256	23	503
502	22	503	502	23	503
1	22	504	1	23	504
2	22	504	2	23	504
3	22	504	3	23	504
4	22	504	4	23	504
5	22	504	5	23	504
6	22	504	6	23	504
249	22	504	249	23	504
255	22	504	255	23	504
256	22	504	256	23	504
502	22	504	502	23	504
1	22	507	1	23	507
2	22	507	2	23	507
3	22	507	3	23	507
4	22	507	4	23	507
5	22	507	5	23	507
6	22	507	6	23	507
249	22	507	249	23	507

RelB-linker (SEQ ID NO: 22)-RelA			RelB-linker (SEQ ID NO: 23)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
255	22	507	255	23	507
256	22	507	256	23	507
502	22	507	502	23	507
1	22	550	1	23	550
2	22	550	2	23	550
3	22	550	3	23	550
4	22	550	4	23	550
5	22	550	5	23	550
6	22	550	6	23	550
249	22	550	249	23	550
255	22	550	255	23	550
256	22	550	256	23	550
502	22	550	502	23	550
1	22	551	1	23	551
2	22	551	2	23	551
3	22	551	3	23	551
4	22	551	4	23	551
5	22	551	5	23	551
6	22	551	6	23	551
249	22	551	249	23	551
255	22	551	255	23	551
256	22	551	256	23	551
502	22	551	502	23	551
1	22	552	1	23	552
2	22	552	2	23	552
3	22	552	3	23	552
4	22	552	4	23	552
5	22	552	5	23	552
6	22	552	6	23	552
249	22	552	249	23	552
255	22	552	255	23	552
256	22	552	256	23	552
502	22	552	502	23	552
1	22	553	1	23	553
2	22	553	2	23	553
3	22	553	3	23	553
4	22	553	4	23	553
5	22	553	5	23	553
6	22	553	6	23	553
249	22	553	249	23	553
255	22	553	255	23	553
256	22	553	256	23	553
502	22	553	502	23	553
1	22	554	1	23	554

RelB-linker (SEQ ID NO: 22)-RelA			RelB-linker (SEQ ID NO: 23)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
2	22	554	2	23	554
3	22	554	3	23	554
4	22	554	4	23	554
5	22	554	5	23	554
6	22	554	6	23	554
249	22	554	249	23	554
255	22	554	255	23	554
256	22	554	256	23	554
502	22	554	502	23	554
1	22	555	1	23	555
2	22	555	2	23	555
3	22	555	3	23	555
4	22	555	4	23	555
5	22	555	5	23	555
6	22	555	6	23	555
249	22	555	249	23	555
255	22	555	255	23	555
256	22	555	256	23	555
502	22	555	502	23	555
1	22	556	1	23	556
2	22	556	2	23	556
3	22	556	3	23	556
4	22	556	4	23	556
5	22	556	5	23	556
6	22	556	6	23	556
249	22	556	249	23	556
255	22	556	255	23	556
256	22	556	256	23	556
502	22	556	502	23	556
1	22	557	1	23	557
2	22	557	2	23	557
3	22	557	3	23	557
4	22	557	4	23	557
5	22	557	5	23	557
6	22	557	6	23	557
249	22	557	249	23	557
255	22	557	255	23	557
256	22	557	256	23	557
502	22	557	502	23	557
1	22	558	1	23	558
2	22	558	2	23	558
3	22	558	3	23	558
4	22	558	4	23	558
5	22	558	5	23	558

RelB-linker (SEQ ID NO: 22)-RelA			RelB-linker (SEQ ID NO: 23)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
6	22	558	6	23	558
249	22	558	249	23	558
255	22	558	255	23	558
256	22	558	256	23	558
502	22	558	502	23	558

Table 4. continued

RelB-linker (SEQ ID NO: 24)-RelA			RelB-linker (SEQ ID NO: 26)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	24	8	1	26	8
2	24	8	2	26	8
3	24	8	3	26	8
4	24	8	4	26	8
5	24	8	5	26	8
6	24	8	6	26	8
249	24	8	249	26	8
255	24	8	255	26	8
256	24	8	256	26	8
502	24	8	502	26	8
1	24	9	1	26	9
2	24	9	2	26	9
3	24	9	3	26	9
4	24	9	4	26	9
5	24	9	5	26	9
6	24	9	6	26	9
249	24	9	249	26	9
255	24	9	255	26	9
256	24	9	256	26	9
502	24	9	502	26	9
1	24	10	1	26	10
2	24	10	2	26	10
3	24	10	3	26	10
4	24	10	4	26	10
5	24	10	5	26	10
6	24	10	6	26	10
249	24	10	249	26	10
255	24	10	255	26	10
256	24	10	256	26	10
502	24	10	502	26	10
1	24	11	1	26	11
2	24	11	2	26	11

RelB-linker (SEQ ID NO: 24)-RelA			RelB-linker (SEQ ID NO: 26)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
3	24	11	3	26	11
4	24	11	4	26	11
5	24	11	5	26	11
6	24	11	6	26	11
249	24	11	249	26	11
255	24	11	255	26	11
256	24	11	256	26	11
502	24	11	502	26	11
1	24	12	1	26	12
2	24	12	2	26	12
3	24	12	3	26	12
4	24	12	4	26	12
5	24	12	5	26	12
6	24	12	6	26	12
249	24	12	249	26	12
255	24	12	255	26	12
256	24	12	256	26	12
502	24	12	502	26	12
1	24	13	1	26	13
2	24	13	2	26	13
3	24	13	3	26	13
4	24	13	4	26	13
5	24	13	5	26	13
6	24	13	6	26	13
249	24	13	249	26	13
255	24	13	255	26	13
256	24	13	256	26	13
502	24	13	502	26	13
1	24	14	1	26	14
2	24	14	2	26	14
3	24	14	3	26	14
4	24	14	4	26	14
5	24	14	5	26	14
6	24	14	6	26	14
249	24	14	249	26	14
255	24	14	255	26	14
256	24	14	256	26	14
502	24	14	502	26	14
1	24	15	1	26	15
2	24	15	2	26	15
3	24	15	3	26	15
4	24	15	4	26	15
5	24	15	5	26	15
6	24	15	6	26	15

RelB-linker (SEQ ID NO: 24)-RelA			RelB-linker (SEQ ID NO: 26)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
249	24	15	249	26	15
255	24	15	255	26	15
256	24	15	256	26	15
502	24	15	502	26	15
1	24	257	1	26	257
2	24	257	2	26	257
3	24	257	3	26	257
4	24	257	4	26	257
5	24	257	5	26	257
6	24	257	6	26	257
249	24	257	249	26	257
255	24	257	255	26	257
256	24	257	256	26	257
502	24	257	502	26	257
1	24	259	1	26	259
2	24	259	2	26	259
3	24	259	3	26	259
4	24	259	4	26	259
5	24	259	5	26	259
6	24	259	6	26	259
249	24	259	249	26	259
255	24	259	255	26	259
256	24	259	256	26	259
502	24	259	502	26	259
1	24	260	1	26	260
2	24	260	2	26	260
3	24	260	3	26	260
4	24	260	4	26	260
5	24	260	5	26	260
6	24	260	6	26	260
249	24	260	249	26	260
255	24	260	255	26	260
256	24	260	256	26	260
502	24	260	502	26	260
1	24	261	1	26	261
2	24	261	2	26	261
3	24	261	3	26	261
4	24	261	4	26	261
5	24	261	5	26	261
6	24	261	6	26	261
249	24	261	249	26	261
255	24	261	255	26	261
256	24	261	256	26	261
502	24	261	502	26	261

RelB-linker (SEQ ID NO: 24)-RelA			RelB-linker (SEQ ID NO: 26)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	24	503	1	26	503
2	24	503	2	26	503
3	24	503	3	26	503
4	24	503	4	26	503
5	24	503	5	26	503
6	24	503	6	26	503
249	24	503	249	26	503
255	24	503	255	26	503
256	24	503	256	26	503
502	24	503	502	26	503
1	24	504	1	26	504
2	24	504	2	26	504
3	24	504	3	26	504
4	24	504	4	26	504
5	24	504	5	26	504
6	24	504	6	26	504
249	24	504	249	26	504
255	24	504	255	26	504
256	24	504	256	26	504
502	24	504	502	26	504
1	24	507	1	26	507
2	24	507	2	26	507
3	24	507	3	26	507
4	24	507	4	26	507
5	24	507	5	26	507
6	24	507	6	26	507
249	24	507	249	26	507
255	24	507	255	26	507
256	24	507	256	26	507
502	24	507	502	26	507
1	24	550	1	26	550
2	24	550	2	26	550
3	24	550	3	26	550
4	24	550	4	26	550
5	24	550	5	26	550
6	24	550	6	26	550
249	24	550	249	26	550
255	24	550	255	26	550
256	24	550	256	26	550
502	24	550	502	26	550
1	24	551	1	26	551
2	24	551	2	26	551
3	24	551	3	26	551
4	24	551	4	26	551

RelB-linker (SEQ ID NO: 24)-RelA			RelB-linker (SEQ ID NO: 26)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
5	24	551	5	26	551
6	24	551	6	26	551
249	24	551	249	26	551
255	24	551	255	26	551
256	24	551	256	26	551
502	24	551	502	26	551
1	24	552	1	26	552
2	24	552	2	26	552
3	24	552	3	26	552
4	24	552	4	26	552
5	24	552	5	26	552
6	24	552	6	26	552
249	24	552	249	26	552
255	24	552	255	26	552
256	24	552	256	26	552
502	24	552	502	26	552
1	24	553	1	26	553
2	24	553	2	26	553
3	24	553	3	26	553
4	24	553	4	26	553
5	24	553	5	26	553
6	24	553	6	26	553
249	24	553	249	26	553
255	24	553	255	26	553
256	24	553	256	26	553
502	24	553	502	26	553
1	24	554	1	26	554
2	24	554	2	26	554
3	24	554	3	26	554
4	24	554	4	26	554
5	24	554	5	26	554
6	24	554	6	26	554
249	24	554	249	26	554
255	24	554	255	26	554
256	24	554	256	26	554
502	24	554	502	26	554
1	24	555	1	26	555
2	24	555	2	26	555
3	24	555	3	26	555
4	24	555	4	26	555
5	24	555	5	26	555
6	24	555	6	26	555
249	24	555	249	26	555
255	24	555	255	26	555

RelB-linker (SEQ ID NO: 24)-RelA			RelB-linker (SEQ ID NO: 26)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
256	24	555	256	26	555
502	24	555	502	26	555
1	24	556	1	26	556
2	24	556	2	26	556
3	24	556	3	26	556
4	24	556	4	26	556
5	24	556	5	26	556
6	24	556	6	26	556
249	24	556	249	26	556
255	24	556	255	26	556
256	24	556	256	26	556
502	24	556	502	26	556
1	24	557	1	26	557
2	24	557	2	26	557
3	24	557	3	26	557
4	24	557	4	26	557
5	24	557	5	26	557
6	24	557	6	26	557
249	24	557	249	26	557
255	24	557	255	26	557
256	24	557	256	26	557
502	24	557	502	26	557
1	24	558	1	26	558
2	24	558	2	26	558
3	24	558	3	26	558
4	24	558	4	26	558
5	24	558	5	26	558
6	24	558	6	26	558
249	24	558	249	26	558
255	24	558	255	26	558
256	24	558	256	26	558
502	24	558	502	26	558

Table 4. continued

RelB-linker (SEQ ID NO: 27)-RelA			RelB-linker (SEQ ID NO: 272)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	27	8	1	272	8
2	27	8	2	272	8
3	27	8	3	272	8
4	27	8	4	272	8
5	27	8	5	272	8

RelB-linker (SEQ ID NO: 27)-RelA			RelB-linker (SEQ ID NO: 272)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
6	27	8	6	272	8
249	27	8	249	272	8
255	27	8	255	272	8
256	27	8	256	272	8
502	27	8	502	272	8
1	27	9	1	272	9
2	27	9	2	272	9
3	27	9	3	272	9
4	27	9	4	272	9
5	27	9	5	272	9
6	27	9	6	272	9
249	27	9	249	272	9
255	27	9	255	272	9
256	27	9	256	272	9
502	27	9	502	272	9
1	27	10	1	272	10
2	27	10	2	272	10
3	27	10	3	272	10
4	27	10	4	272	10
5	27	10	5	272	10
6	27	10	6	272	10
249	27	10	249	272	10
255	27	10	255	272	10
256	27	10	256	272	10
502	27	10	502	272	10
1	27	11	1	272	11
2	27	11	2	272	11
3	27	11	3	272	11
4	27	11	4	272	11
5	27	11	5	272	11
6	27	11	6	272	11
249	27	11	249	272	11
255	27	11	255	272	11
256	27	11	256	272	11
502	27	11	502	272	11
1	27	12	1	272	12
2	27	12	2	272	12
3	27	12	3	272	12
4	27	12	4	272	12
5	27	12	5	272	12
6	27	12	6	272	12
249	27	12	249	272	12
255	27	12	255	272	12
256	27	12	256	272	12

RelB-linker (SEQ ID NO: 27)-RelA			RelB-linker (SEQ ID NO: 272)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
502	27	12	502	272	12
1	27	13	1	272	13
2	27	13	2	272	13
3	27	13	3	272	13
4	27	13	4	272	13
5	27	13	5	272	13
6	27	13	6	272	13
249	27	13	249	272	13
255	27	13	255	272	13
256	27	13	256	272	13
502	27	13	502	272	13
1	27	14	1	272	14
2	27	14	2	272	14
3	27	14	3	272	14
4	27	14	4	272	14
5	27	14	5	272	14
6	27	14	6	272	14
249	27	14	249	272	14
255	27	14	255	272	14
256	27	14	256	272	14
502	27	14	502	272	14
1	27	15	1	272	15
2	27	15	2	272	15
3	27	15	3	272	15
4	27	15	4	272	15
5	27	15	5	272	15
6	27	15	6	272	15
249	27	15	249	272	15
255	27	15	255	272	15
256	27	15	256	272	15
502	27	15	502	272	15
1	27	257	1	272	257
2	27	257	2	272	257
3	27	257	3	272	257
4	27	257	4	272	257
5	27	257	5	272	257
6	27	257	6	272	257
249	27	257	249	272	257
255	27	257	255	272	257
256	27	257	256	272	257
502	27	257	502	272	257
1	27	259	1	272	259
2	27	259	2	272	259
3	27	259	3	272	259

RelB-linker (SEQ ID NO: 27)-RelA			RelB-linker (SEQ ID NO: 272)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
4	27	259	4	272	259
5	27	259	5	272	259
6	27	259	6	272	259
249	27	259	249	272	259
255	27	259	255	272	259
256	27	259	256	272	259
502	27	259	502	272	259
1	27	260	1	272	260
2	27	260	2	272	260
3	27	260	3	272	260
4	27	260	4	272	260
5	27	260	5	272	260
6	27	260	6	272	260
249	27	260	249	272	260
255	27	260	255	272	260
256	27	260	256	272	260
502	27	260	502	272	260
1	27	261	1	272	261
2	27	261	2	272	261
3	27	261	3	272	261
4	27	261	4	272	261
5	27	261	5	272	261
6	27	261	6	272	261
249	27	261	249	272	261
255	27	261	255	272	261
256	27	261	256	272	261
502	27	261	502	272	261
1	27	503	1	272	503
2	27	503	2	272	503
3	27	503	3	272	503
4	27	503	4	272	503
5	27	503	5	272	503
6	27	503	6	272	503
249	27	503	249	272	503
255	27	503	255	272	503
256	27	503	256	272	503
502	27	503	502	272	503
1	27	504	1	272	504
2	27	504	2	272	504
3	27	504	3	272	504
4	27	504	4	272	504
5	27	504	5	272	504
6	27	504	6	272	504
249	27	504	249	272	504

RelB-linker (SEQ ID NO: 27)-RelA			RelB-linker (SEQ ID NO: 272)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
255	27	504	255	272	504
256	27	504	256	272	504
502	27	504	502	272	504
1	27	507	1	272	507
2	27	507	2	272	507
3	27	507	3	272	507
4	27	507	4	272	507
5	27	507	5	272	507
6	27	507	6	272	507
249	27	507	249	272	507
255	27	507	255	272	507
256	27	507	256	272	507
502	27	507	502	272	507
1	27	550	1	272	550
2	27	550	2	272	550
3	27	550	3	272	550
4	27	550	4	272	550
5	27	550	5	272	550
6	27	550	6	272	550
249	27	550	249	272	550
255	27	550	255	272	550
256	27	550	256	272	550
502	27	550	502	272	550
1	27	551	1	272	551
2	27	551	2	272	551
3	27	551	3	272	551
4	27	551	4	272	551
5	27	551	5	272	551
6	27	551	6	272	551
249	27	551	249	272	551
255	27	551	255	272	551
256	27	551	256	272	551
502	27	551	502	272	551
1	27	552	1	272	552
2	27	552	2	272	552
3	27	552	3	272	552
4	27	552	4	272	552
5	27	552	5	272	552
6	27	552	6	272	552
249	27	552	249	272	552
255	27	552	255	272	552
256	27	552	256	272	552
502	27	552	502	272	552
1	27	553	1	272	553

RelB-linker (SEQ ID NO: 27)-RelA			RelB-linker (SEQ ID NO: 272)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
2	27	553	2	272	553
3	27	553	3	272	553
4	27	553	4	272	553
5	27	553	5	272	553
6	27	553	6	272	553
249	27	553	249	272	553
255	27	553	255	272	553
256	27	553	256	272	553
502	27	553	502	272	553
1	27	554	1	272	554
2	27	554	2	272	554
3	27	554	3	272	554
4	27	554	4	272	554
5	27	554	5	272	554
6	27	554	6	272	554
249	27	554	249	272	554
255	27	554	255	272	554
256	27	554	256	272	554
502	27	554	502	272	554
1	27	555	1	272	555
2	27	555	2	272	555
3	27	555	3	272	555
4	27	555	4	272	555
5	27	555	5	272	555
6	27	555	6	272	555
249	27	555	249	272	555
255	27	555	255	272	555
256	27	555	256	272	555
502	27	555	502	272	555
1	27	556	1	272	556
2	27	556	2	272	556
3	27	556	3	272	556
4	27	556	4	272	556
5	27	556	5	272	556
6	27	556	6	272	556
249	27	556	249	272	556
255	27	556	255	272	556
256	27	556	256	272	556
502	27	556	502	272	556
1	27	557	1	272	557
2	27	557	2	272	557
3	27	557	3	272	557
4	27	557	4	272	557
5	27	557	5	272	557

RelB-linker (SEQ ID NO: 27)-RelA			RelB-linker (SEQ ID NO: 272)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
6	27	557	6	272	557
249	27	557	249	272	557
255	27	557	255	272	557
256	27	557	256	272	557
502	27	557	502	272	557
1	27	558	1	272	558
2	27	558	2	272	558
3	27	558	3	272	558
4	27	558	4	272	558
5	27	558	5	272	558
6	27	558	6	272	558
249	27	558	249	272	558
255	27	558	255	272	558
256	27	558	256	272	558
502	27	558	502	272	558

Table 4. continued

RelB-linker (SEQ ID NO: 273)-RelA			RelB-linker (SEQ ID NO: 274)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	273	8	1	274	8
2	273	8	2	274	8
3	273	8	3	274	8
4	273	8	4	274	8
5	273	8	5	274	8
6	273	8	6	274	8
249	273	8	249	274	8
255	273	8	255	274	8
256	273	8	256	274	8
502	273	8	502	274	8
1	273	9	1	274	9
2	273	9	2	274	9
3	273	9	3	274	9
4	273	9	4	274	9
5	273	9	5	274	9
6	273	9	6	274	9
249	273	9	249	274	9
255	273	9	255	274	9
256	273	9	256	274	9
502	273	9	502	274	9
1	273	10	1	274	10
2	273	10	2	274	10

RelB-linker (SEQ ID NO: 273)-RelA			RelB-linker (SEQ ID NO: 274)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
3	273	10	3	274	10
4	273	10	4	274	10
5	273	10	5	274	10
6	273	10	6	274	10
249	273	10	249	274	10
255	273	10	255	274	10
256	273	10	256	274	10
502	273	10	502	274	10
1	273	11	1	274	11
2	273	11	2	274	11
3	273	11	3	274	11
4	273	11	4	274	11
5	273	11	5	274	11
6	273	11	6	274	11
249	273	11	249	274	11
255	273	11	255	274	11
256	273	11	256	274	11
502	273	11	502	274	11
1	273	12	1	274	12
2	273	12	2	274	12
3	273	12	3	274	12
4	273	12	4	274	12
5	273	12	5	274	12
6	273	12	6	274	12
249	273	12	249	274	12
255	273	12	255	274	12
256	273	12	256	274	12
502	273	12	502	274	12
1	273	13	1	274	13
2	273	13	2	274	13
3	273	13	3	274	13
4	273	13	4	274	13
5	273	13	5	274	13
6	273	13	6	274	13
249	273	13	249	274	13
255	273	13	255	274	13
256	273	13	256	274	13
502	273	13	502	274	13
1	273	14	1	274	14
2	273	14	2	274	14
3	273	14	3	274	14
4	273	14	4	274	14
5	273	14	5	274	14
6	273	14	6	274	14

RelB-linker (SEQ ID NO: 273)-RelA			RelB-linker (SEQ ID NO: 274)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
249	273	14	249	274	14
255	273	14	255	274	14
256	273	14	256	274	14
502	273	14	502	274	14
1	273	15	1	274	15
2	273	15	2	274	15
3	273	15	3	274	15
4	273	15	4	274	15
5	273	15	5	274	15
6	273	15	6	274	15
249	273	15	249	274	15
255	273	15	255	274	15
256	273	15	256	274	15
502	273	15	502	274	15
1	273	257	1	274	257
2	273	257	2	274	257
3	273	257	3	274	257
4	273	257	4	274	257
5	273	257	5	274	257
6	273	257	6	274	257
249	273	257	249	274	257
255	273	257	255	274	257
256	273	257	256	274	257
502	273	257	502	274	257
1	273	259	1	274	259
2	273	259	2	274	259
3	273	259	3	274	259
4	273	259	4	274	259
5	273	259	5	274	259
6	273	259	6	274	259
249	273	259	249	274	259
255	273	259	255	274	259
256	273	259	256	274	259
502	273	259	502	274	259
1	273	260	1	274	260
2	273	260	2	274	260
3	273	260	3	274	260
4	273	260	4	274	260
5	273	260	5	274	260
6	273	260	6	274	260
249	273	260	249	274	260
255	273	260	255	274	260
256	273	260	256	274	260
502	273	260	502	274	260

RelB-linker (SEQ ID NO: 273)-RelA			RelB-linker (SEQ ID NO: 274)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	273	261	1	274	261
2	273	261	2	274	261
3	273	261	3	274	261
4	273	261	4	274	261
5	273	261	5	274	261
6	273	261	6	274	261
249	273	261	249	274	261
255	273	261	255	274	261
256	273	261	256	274	261
502	273	261	502	274	261
1	273	503	1	274	503
2	273	503	2	274	503
3	273	503	3	274	503
4	273	503	4	274	503
5	273	503	5	274	503
6	273	503	6	274	503
249	273	503	249	274	503
255	273	503	255	274	503
256	273	503	256	274	503
502	273	503	502	274	503
1	273	504	1	274	504
2	273	504	2	274	504
3	273	504	3	274	504
4	273	504	4	274	504
5	273	504	5	274	504
6	273	504	6	274	504
249	273	504	249	274	504
255	273	504	255	274	504
256	273	504	256	274	504
502	273	504	502	274	504
1	273	507	1	274	507
2	273	507	2	274	507
3	273	507	3	274	507
4	273	507	4	274	507
5	273	507	5	274	507
6	273	507	6	274	507
249	273	507	249	274	507
255	273	507	255	274	507
256	273	507	256	274	507
502	273	507	502	274	507
1	273	550	1	274	550
2	273	550	2	274	550
3	273	550	3	274	550
4	273	550	4	274	550

RelB-linker (SEQ ID NO: 273)-RelA			RelB-linker (SEQ ID NO: 274)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
5	273	550	5	274	550
6	273	550	6	274	550
249	273	550	249	274	550
255	273	550	255	274	550
256	273	550	256	274	550
502	273	550	502	274	550
1	273	551	1	274	551
2	273	551	2	274	551
3	273	551	3	274	551
4	273	551	4	274	551
5	273	551	5	274	551
6	273	551	6	274	551
249	273	551	249	274	551
255	273	551	255	274	551
256	273	551	256	274	551
502	273	551	502	274	551
1	273	552	1	274	552
2	273	552	2	274	552
3	273	552	3	274	552
4	273	552	4	274	552
5	273	552	5	274	552
6	273	552	6	274	552
249	273	552	249	274	552
255	273	552	255	274	552
256	273	552	256	274	552
502	273	552	502	274	552
1	273	553	1	274	553
2	273	553	2	274	553
3	273	553	3	274	553
4	273	553	4	274	553
5	273	553	5	274	553
6	273	553	6	274	553
249	273	553	249	274	553
255	273	553	255	274	553
256	273	553	256	274	553
502	273	553	502	274	553
1	273	554	1	274	554
2	273	554	2	274	554
3	273	554	3	274	554
4	273	554	4	274	554
5	273	554	5	274	554
6	273	554	6	274	554
249	273	554	249	274	554
255	273	554	255	274	554

RelB-linker (SEQ ID NO: 273)-RelA			RelB-linker (SEQ ID NO: 274)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
256	273	554	256	274	554
502	273	554	502	274	554
1	273	555	1	274	555
2	273	555	2	274	555
3	273	555	3	274	555
4	273	555	4	274	555
5	273	555	5	274	555
6	273	555	6	274	555
249	273	555	249	274	555
255	273	555	255	274	555
256	273	555	256	274	555
502	273	555	502	274	555
1	273	556	1	274	556
2	273	556	2	274	556
3	273	556	3	274	556
4	273	556	4	274	556
5	273	556	5	274	556
6	273	556	6	274	556
249	273	556	249	274	556
255	273	556	255	274	556
256	273	556	256	274	556
502	273	556	502	274	556
1	273	557	1	274	557
2	273	557	2	274	557
3	273	557	3	274	557
4	273	557	4	274	557
5	273	557	5	274	557
6	273	557	6	274	557
249	273	557	249	274	557
255	273	557	255	274	557
256	273	557	256	274	557
502	273	557	502	274	557
1	273	558	1	274	558
2	273	558	2	274	558
3	273	558	3	274	558
4	273	558	4	274	558
5	273	558	5	274	558
6	273	558	6	274	558
249	273	558	249	274	558
255	273	558	255	274	558
256	273	558	256	274	558
502	273	558	502	274	558

Table 4. continued

RelB-linker (SEQ ID NO: 275)-RelA			RelB-linker (SEQ ID NO: 276)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	275	8	1	276	8
2	275	8	2	276	8
3	275	8	3	276	8
4	275	8	4	276	8
5	275	8	5	276	8
6	275	8	6	276	8
249	275	8	249	276	8
255	275	8	255	276	8
256	275	8	256	276	8
502	275	8	502	276	8
1	275	9	1	276	9
2	275	9	2	276	9
3	275	9	3	276	9
4	275	9	4	276	9
5	275	9	5	276	9
6	275	9	6	276	9
249	275	9	249	276	9
255	275	9	255	276	9
256	275	9	256	276	9
502	275	9	502	276	9
1	275	10	1	276	10
2	275	10	2	276	10
3	275	10	3	276	10
4	275	10	4	276	10
5	275	10	5	276	10
6	275	10	6	276	10
249	275	10	249	276	10
255	275	10	255	276	10
256	275	10	256	276	10
502	275	10	502	276	10
1	275	11	1	276	11
2	275	11	2	276	11
3	275	11	3	276	11
4	275	11	4	276	11
5	275	11	5	276	11
6	275	11	6	276	11
249	275	11	249	276	11
255	275	11	255	276	11
256	275	11	256	276	11
502	275	11	502	276	11
1	275	12	1	276	12
2	275	12	2	276	12

RelB-linker (SEQ ID NO: 275)-RelA			RelB-linker (SEQ ID NO: 276)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
3	275	12	3	276	12
4	275	12	4	276	12
5	275	12	5	276	12
6	275	12	6	276	12
249	275	12	249	276	12
255	275	12	255	276	12
256	275	12	256	276	12
502	275	12	502	276	12
1	275	13	1	276	13
2	275	13	2	276	13
3	275	13	3	276	13
4	275	13	4	276	13
5	275	13	5	276	13
6	275	13	6	276	13
249	275	13	249	276	13
255	275	13	255	276	13
256	275	13	256	276	13
502	275	13	502	276	13
1	275	14	1	276	14
2	275	14	2	276	14
3	275	14	3	276	14
4	275	14	4	276	14
5	275	14	5	276	14
6	275	14	6	276	14
249	275	14	249	276	14
255	275	14	255	276	14
256	275	14	256	276	14
502	275	14	502	276	14
1	275	15	1	276	15
2	275	15	2	276	15
3	275	15	3	276	15
4	275	15	4	276	15
5	275	15	5	276	15
6	275	15	6	276	15
249	275	15	249	276	15
255	275	15	255	276	15
256	275	15	256	276	15
502	275	15	502	276	15
1	275	257	1	276	257
2	275	257	2	276	257
3	275	257	3	276	257
4	275	257	4	276	257
5	275	257	5	276	257
6	275	257	6	276	257

RelB-linker (SEQ ID NO: 275)-RelA			RelB-linker (SEQ ID NO: 276)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
249	275	257	249	276	257
255	275	257	255	276	257
256	275	257	256	276	257
502	275	257	502	276	257
1	275	259	1	276	259
2	275	259	2	276	259
3	275	259	3	276	259
4	275	259	4	276	259
5	275	259	5	276	259
6	275	259	6	276	259
249	275	259	249	276	259
255	275	259	255	276	259
256	275	259	256	276	259
502	275	259	502	276	259
1	275	260	1	276	260
2	275	260	2	276	260
3	275	260	3	276	260
4	275	260	4	276	260
5	275	260	5	276	260
6	275	260	6	276	260
249	275	260	249	276	260
255	275	260	255	276	260
256	275	260	256	276	260
502	275	260	502	276	260
1	275	261	1	276	261
2	275	261	2	276	261
3	275	261	3	276	261
4	275	261	4	276	261
5	275	261	5	276	261
6	275	261	6	276	261
249	275	261	249	276	261
255	275	261	255	276	261
256	275	261	256	276	261
502	275	261	502	276	261
1	275	503	1	276	503
2	275	503	2	276	503
3	275	503	3	276	503
4	275	503	4	276	503
5	275	503	5	276	503
6	275	503	6	276	503
249	275	503	249	276	503
255	275	503	255	276	503
256	275	503	256	276	503
502	275	503	502	276	503

RelB-linker (SEQ ID NO: 275)-RelA			RelB-linker (SEQ ID NO: 276)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
1	275	504	1	276	504
2	275	504	2	276	504
3	275	504	3	276	504
4	275	504	4	276	504
5	275	504	5	276	504
6	275	504	6	276	504
249	275	504	249	276	504
255	275	504	255	276	504
256	275	504	256	276	504
502	275	504	502	276	504
1	275	507	1	276	507
2	275	507	2	276	507
3	275	507	3	276	507
4	275	507	4	276	507
5	275	507	5	276	507
6	275	507	6	276	507
249	275	507	249	276	507
255	275	507	255	276	507
256	275	507	256	276	507
502	275	507	502	276	507
1	275	550	1	276	550
2	275	550	2	276	550
3	275	550	3	276	550
4	275	550	4	276	550
5	275	550	5	276	550
6	275	550	6	276	550
249	275	550	249	276	550
255	275	550	255	276	550
256	275	550	256	276	550
502	275	550	502	276	550
1	275	551	1	276	551
2	275	551	2	276	551
3	275	551	3	276	551
4	275	551	4	276	551
5	275	551	5	276	551
6	275	551	6	276	551
249	275	551	249	276	551
255	275	551	255	276	551
256	275	551	256	276	551
502	275	551	502	276	551
1	275	552	1	276	552
2	275	552	2	276	552
3	275	552	3	276	552
4	275	552	4	276	552

RelB-linker (SEQ ID NO: 275)-RelA			RelB-linker (SEQ ID NO: 276)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
5	275	552	5	276	552
6	275	552	6	276	552
249	275	552	249	276	552
255	275	552	255	276	552
256	275	552	256	276	552
502	275	552	502	276	552
1	275	553	1	276	553
2	275	553	2	276	553
3	275	553	3	276	553
4	275	553	4	276	553
5	275	553	5	276	553
6	275	553	6	276	553
249	275	553	249	276	553
255	275	553	255	276	553
256	275	553	256	276	553
502	275	553	502	276	553
1	275	554	1	276	554
2	275	554	2	276	554
3	275	554	3	276	554
4	275	554	4	276	554
5	275	554	5	276	554
6	275	554	6	276	554
249	275	554	249	276	554
255	275	554	255	276	554
256	275	554	256	276	554
502	275	554	502	276	554
1	275	555	1	276	555
2	275	555	2	276	555
3	275	555	3	276	555
4	275	555	4	276	555
5	275	555	5	276	555
6	275	555	6	276	555
249	275	555	249	276	555
255	275	555	255	276	555
256	275	555	256	276	555
502	275	555	502	276	555
1	275	556	1	276	556
2	275	556	2	276	556
3	275	556	3	276	556
4	275	556	4	276	556
5	275	556	5	276	556
6	275	556	6	276	556
249	275	556	249	276	556
255	275	556	255	276	556

RelB-linker (SEQ ID NO: 275)-RelA			RelB-linker (SEQ ID NO: 276)-RelA		
N-terminal Peptide	Linker peptide	C-terminal Peptide	N-terminal Peptide	Linker peptide	C-terminal Peptide
SEQ ID NO:			SEQ ID NO:		
256	275	556	256	276	556
502	275	556	502	276	556
1	275	557	1	276	557
2	275	557	2	276	557
3	275	557	3	276	557
4	275	557	4	276	557
5	275	557	5	276	557
6	275	557	6	276	557
249	275	557	249	276	557
255	275	557	255	276	557
256	275	557	256	276	557
502	275	557	502	276	557
1	275	558	1	276	558
2	275	558	2	276	558
3	275	558	3	276	558
4	275	558	4	276	558
5	275	558	5	276	558
6	275	558	6	276	558
249	275	558	249	276	558
255	275	558	255	276	558
256	275	558	256	276	558
502	275	558	502	276	558

[0132] In some embodiments, there are additional amino acids between the N-terminal peptide and the linker peptide. In some embodiments, there are additional amino acids between the C-terminal peptide and the linker peptide. In some embodiments, there are no additional amino acids between the N-terminal peptide and the linker peptide. In some embodiments, there are no additional amino acids between the C-terminal peptide and the linker peptide.

[0133] In some embodiments, the portion of the fusion protein comprising the N-terminal peptide, the linker peptide, and the C-terminal peptide comprises or consists of the amino acid sequences shown in Table 5, below.

Table 5. Peptide Combinations for the Fusion Protein

SEQ ID NO:	Amino Acid Sequence
28	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGADANAGARQLYSALANK CCHVGCTKRSLAQFC
29	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGANADAGARQLYSALANK CCHVGCTKRSLAQFC

SEQ ID NO:	Amino Acid Sequence
30	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGADADAGARQLYSALANK CCHVGCTKRSLAQFC
31	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCHVGCTKRSLAQFC
32	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAQADAGARQLYSALANK CCHVGCTKRSLAQFC
33	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGADAQAGARQLYSALANK CCHVGCTKRSLAQFC
34	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAAQAGARQLYSALANK CCHVGCTKRSLAQFC
35	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGADANAGARQLYSALANK CCHVGCTKRSLAQFC
36	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGANADAGARQLYSALANK CCHVGCTKRSLAQFC
37	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGADADAGARQLYSALANK CCHVGCTKRSLAQFC
38	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGAEAEAGARQLYSALANK CCHVGCTKRSLAQFC
39	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGAQADAGARQLYSALANK CCHVGCTKRSLAQFC
40	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGADAQAGARQLYSALANK CCHVGCTKRSLAQFC
41	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGAAQAGARQLYSALANK CCHVGCTKRSLAQFC
42	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGADANAGARQLYSALANK CCHVGCTKQSLAQFC
43	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGANADAGARQLYSALANK CCHVGCTKQSLAQFC
44	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGADADAGARQLYSALANK CCHVGCTKQSLAQFC
45	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCHVGCTKQSLAQFC
46	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAQADAGARQLYSALANK CCHVGCTKQSLAQFC
47	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGADAQAGARQLYSALANK CCHVGCTKQSLAQFC
48	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAAQAGARQLYSALANK CCHVGCTKQSLAQFC
49	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGADANAGARQLYSALANK CCHVGCTKQSLAQFC
50	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGANADAGARQLYSALANK CCHVGCTKQSLAQFC
51	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGADADAGARQLYSALANK CCHVGCTKQSLAQFC
52	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGAEAEAGARQLYSALANK CCHVGCTKQSLAQFC
53	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGAQADAGARQLYSALANK CCHVGCTKQSLAQFC

SEQ ID NO:	Amino Acid Sequence
54	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGADAQAGARQLYSALANK CCHVGCTKQSLAQFC
55	DSWQEEVIKLCGRELVRAQIAICGQSTASDAAGAQAQAGARQLYSALANK CCHVGCTKQSLAQFC
56	DSYQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCHVGCTKRSLAQFC
57	DSFQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCHVGCTKRSLAQFC
58	DSLQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCHVGCTKRSLAQFC
59	DSIQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCHVGCTKRSLAQFC
60	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCYVGCTKRSLAQFC
61	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCLVGCTKRSLAQFC
62	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCQVGCTKRSLAQFC
63	DSWQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCKVGCTKRSLAQFC
64	DSYQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCYVGCTKRSLAQFC
65	DSYQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCKVGCTKRSLAQFC
66	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGEGGGGRQLYSALANK CCYVGCTKRSLAQFC
67	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGEGGGGRQLYSALANK CCKVGCTKRSLAQFC
68	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGSGGGGRQLYSALANK CCYVGCTKRSLAQFC
69	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGSGGGGRQLYSALANK CCKVGCTKRSLAQFC
70	DSYQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCYVGCTKQSLAQFC
71	DSYQEEVIKLCGRELVRAQIAICGKSTASDAAGAEAEAGARQLYSALANK CCKVGCTKQSLAQFC
72	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGEGGGGRQLYSALANK CCYVGCTKQSLAQFC
73	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGEGGGGRQLYSALANK CCKVGCTKQSLAQFC
74	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGSGGGGRQLYSALANK CCYVGCTKQSLAQFC
75	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGSGGGGRQLYSALANK CCKVGCTKQSLAQFC
278	DSWKEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLARFC
279	DSWKEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGGQLYSALAN KCCHVGCTKRSLARFC

SEQ ID NO:	Amino Acid Sequence
280	DSWMEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLARFC
281	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLARFC
282	DSWMEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGGQLYSALAN KCCHVGCTKRSLARFC
283	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGGQLYSALAN KCCHVGCTKRSLARFC
284	DSWMEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGGQLYSALANK CCHVGCTKRSLARFC
285	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGGQLYSALANK CCHVGCTKRSLARFC
286	DSWMEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGGQLYSALANK CCHVGCTKRSLARFC
287	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGGQLYSALANK CCHVGCTKRSLARFC
288	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLAQFC
289	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLARFC
290	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLAQFC
291	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLARFC
292	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLAQFC
293	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLARFC
294	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLAQFC
295	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLAQFC
296	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLARFC
297	DSWQEEVIKLCGRELVRAQIAICGKSTGGGEGGGEGGGEGGRQLYSALANK CCHVGCTKRSLAQFC
508	DSYQEEVIKLCGRELVRAQIAICGKSTGGGEGSGGEGGGGRQLYSALANK CCHVGCTKRSLAQFC
509	DSYQEEVIKLCGRELVRAQIAICGKSTGGGEGSGGEGGGGRQLYSALANK CCQVGCTKRSLAQFC
510	DSYQEEVIKLCGRELVRAQIAICGKSTGGGEGSGGEGGGGRQLYSALANK CCHVGCTKQSLAQFC
511	DSYQEEVIKLCGRELVRAQIAICGKSTGGGEGSGGEGGGGRQLYSALANK CCQVGCTKQSLAQFC
512	DSYQEEVIKLCGRELVRAQIAICGKSTGGGEGSGGEGSGGGRQLYSALANK CCHVGCTKRSLAQFC
513	DSYQEEVIKLCGRELVRAQIAICGKSTGGGEGSGGEGSGGGRQLYSALANK CCQVGCTKRSLAQFC

SEQ ID NO:	Amino Acid Sequence
514	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGSGGGRQLYSALANK CCHVGCTKQSLAQFC
515	DSYQEEVIKLCGRELVRAQIAICGKSTGGEGSGGEGSGGGRQLYSALANK CCQVGCTKQSLAQFC

IgG Fc

[0134] In some embodiments, the fusion proteins provided herein further comprise an IgG Fc (or Fc region). As used herein, the term “IgG Fc” or “Fc region” refers to the portion of an immunoglobulin formed by the Fc domains of its two heavy chains. The Fc region can be a wild-type Fc region (native Fc region) or a variant Fc region. A native Fc region is homodimeric. In some embodiments, the fusion proteins provided herein form dimers (*e.g.*, homodimers via interaction between Fc regions. In some embodiments, two fusion proteins are linked into a dimer (*e.g.*, a homodimer) via 2 hinge region interchain disulfide bonds between the Fc regions of each fusion protein (*e.g.*, at the N-terminus). In some embodiments, the Fc region comprises one intrachain disulfide bond in the CH2 domain and one intrachain disulfide bond in the CH3 domain.

[0135] The Fc region of the fusion proteins provided herein can be derived from any native immunoglobulin. In some embodiments, the Fc region is formed from an IgA, IgD, IgE, or IgG heavy chain constant region. In some embodiments, the Fc region is formed from an IgG heavy chain constant region. In some embodiments, the IgG heavy chain is an IgG1, IgG2, IgG3 or IgG4 heavy chain constant region. In some embodiments, the Fc region is formed from an IgG1 heavy chain constant region. In some embodiments, the IgG1 heavy chain constant region comprises a G1m1(a), G1m2(x), G1m3(f), or G1m17(z) allotype. *See, e.g.*, Jefferis and Lefranc (2009) mAbs 1(4): 332-338, and de Taeye *et al.* (2020) Front Immunol. 11:740, incorporated herein by reference in their entirety. The IgG Fc can be linked to the N-terminal end of the N-terminal peptide or the C-terminal end of the C-terminal peptide. The IgG Fc can be linked directly to the N-terminal peptide or the C-terminal peptide or they can be linked to the N-terminal peptide or the C-terminal peptide through an IgG Fc linker. In some embodiments, the IgG Fc linker comprises or consists of 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids. In some embodiments, the IgG Fc linker comprises or consists of 1, 2, 3, 4, or 5 amino acids. In some embodiments, the IgG Fc linker comprises or consists of 3 or 4 amino acids. In some embodiments, the IgG Fc linker comprises or consists of the amino acid sequence of GGS. In some embodiments, the IgG Fc linker comprises or consists of the amino acid sequence of EGGS (SEQ ID NO: 299).

[0136] In some embodiments, the IgG Fc comprises a C-terminal lysine (K). It is known in the art that the C-terminal lysine (K) in many monoclonal antibodies is flexible, and is often clipped off during expression and purification with no known impairment in activity. In some embodiments, the C-terminal lysine (K) is replaced with a C-terminal glutamic acid (E). As such, in some embodiments, the IgG Fc comprises a C-terminal glutamic acid (E).

[0137] In some embodiments, the IgG Fc comprises the amino acid sequence of one of SEQ ID NOs: 76-83 with GGS as the IgG Fc linker at the C-terminal end of the IgG Fc. In some embodiments, the IgG Fc comprises the amino acid sequence of one of SEQ ID NOs: 76-83 with SEQ ID NO: 299 as the IgG Fc linker at the C-terminal end of the IgG Fc.

[0138] In some embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into the Fc region of an antibody described herein (*e.g.*, CH2 domain (residues 231-340 of human IgG1) and/or CH3 domain (residues 341-447 of human IgG1)) and/or the hinge region, numbered according to the EU numbering system, to alter one or more functional properties of the antibody, such as serum half-life, complement fixation, Fc receptor binding, and/or antigen-dependent cellular cytotoxicity.

[0139] In certain embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into the hinge region of the Fc region (CH1 domain) such that the number of cysteine residues in the hinge region are altered (*e.g.*, increased or decreased) as described in, *e.g.*, U.S. Pat. No. 5,677,425, herein incorporated by reference in its entirety. The number of cysteine residues in the hinge region of the CH1 domain may be altered to, *e.g.*, facilitate assembly of the light and heavy chains, or to alter (*e.g.*, increase or decrease) the stability of the antibody.

[0140] In a specific embodiment, one, two, or more amino acid mutations (*e.g.*, substitutions, insertions or deletions) are introduced into an IgG constant domain, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc domain fragment) to alter (*e.g.*, decrease or increase) half-life of the antibody *in vivo*. *See, e.g.*, International Publication Nos. WO 02/060919; WO 98/23289; and WO 97/34631; and U.S. Pat. Nos. 5,869,046, 6,121,022, 6,277,375, and 6,165,745, all of which are herein incorporated by reference in their entireties, for examples of mutations that will alter (*e.g.*, decrease or increase) the half-life of an antibody *in vivo*. In certain embodiments, one, two, or more amino acid mutations (*e.g.*, substitutions, insertions, or deletions) are introduced into an IgG constant domain, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc domain fragment) to decrease the half-life of the antibody *in vivo*. In other embodiments, one, two, or more amino acid mutations (*e.g.*, substitutions,

insertions, or deletions) are introduced into an IgG constant domain, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc domain fragment) to increase the half-life of the antibody *in vivo*. In a specific embodiment, the antibodies may have one or more amino acid mutations (*e.g.*, substitutions) in the second constant (CH2) domain (residues 231-340 of human IgG1) and/or the third constant (CH3) domain (residues 341-447 of human IgG1), numbered according to the EU numbering system. In a specific embodiment, the constant region of the IgG1 of an antibody described herein comprises a methionine (M) to tyrosine (Y) substitution in position 252, a serine (S) to threonine (T) substitution in position 254, and a threonine (T) to glutamic acid (E) substitution in position 256, numbered according to the EU numbering system. *See*, U.S. Pat. No. 7,658,921, which is herein incorporated by reference in its entirety. This type of mutant IgG, referred to as “YTE mutant” has been shown to display fourfold increased half-life as compared to wild-type versions of the same antibody (*see*, Dall’Acqua W F *et al.*, (2006) *J Biol Chem* 281: 23514-24, which is herein incorporated by reference in its entirety). In certain embodiments, an antibody comprises an IgG constant domain comprising one, two, three or more amino acid substitutions of amino acid residues at positions 251-257, 285-290, 308-314, 385-389, and 428-436, numbered according to the EU numbering system.

[0141] In certain embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into the Fc region of an antibody described herein (*e.g.*, CH2 domain (residues 231-340 of human IgG1) and/or CH3 domain (residues 341-447 of human IgG1)) and/or the hinge region, numbered according to the EU numbering system, to increase or decrease the affinity of the antibody for an Fc receptor (*e.g.*, an activated Fc receptor) on the surface of an effector cell. Mutations in the Fc region of an antibody that decrease or increase the affinity of an antibody for an Fc receptor and techniques for introducing such mutations into the Fc receptor or fragment thereof are known to one of skill in the art. Examples of mutations in the Fc receptor of an antibody that can be made to alter the affinity of the antibody for an Fc receptor are described in, *e.g.*, Smith P *et al.*, (2012) *PNAS* 109: 6181-6186, U.S. Pat. No. 6,737,056, and International Publication Nos. WO 02/060919; WO 98/23289; and WO 97/34631, all of which are herein incorporated by reference in their entireties.

[0142] In certain embodiments, the antibody comprises a heavy chain constant region that is a variant of a wild-type heavy chain constant region, wherein the variant heavy chain constant region binds to FcγRIIB with higher affinity than the wild-type heavy chain constant region binds to FcγRIIB. In certain embodiments, the variant heavy chain constant region is a variant human heavy chain constant region, *e.g.*, a variant human IgG1, a variant human IgG2, or a

variant human IgG4 heavy chain constant region. In certain embodiments, the variant human IgG heavy chain constant region comprises one or more of the following amino acid mutations, according to the EU numbering system: G236D, P238D, S239D, S267E, L328F, and L328E. In certain embodiments, the variant human IgG heavy chain constant region comprises a set of amino acid mutations selected from the group consisting of: S267E and L328F; P238D and L328E; P238D and one or more substitutions selected from the group consisting of E233D, G237D, H268D, P271G, and A330R; P238D, E233D, G237D, H268D, P271G, and A330R; G236D and S267E; S239D and S267E; V262E, S267E, and L328F; and V264E, S267E, and L328F, according to the EU numbering system. In certain embodiments, the FcγRIIB is expressed on a cell selected from the group consisting of macrophages, monocytes, B cells, dendritic cells, endothelial cells, and activated T cells.

[0143] In a further embodiment, one, two, or more amino acid substitutions are introduced into an IgG constant domain Fc region to alter the effector function(s) of the antibody. For example, one or more amino acids selected from amino acid residues 234, 235, 236, 237, 239, 243, 267, 292, 297, 300, 318, 320, 322, 328, 330, 332, and 396, numbered according to the EU numbering system, can be replaced with a different amino acid residue such that the antibody has an altered affinity for an effector ligand but retains the antigen-binding ability of the parent antibody. The effector ligand to which affinity is altered can be, for example, an Fc receptor or the C1 component of complement. This approach is described in further detail in U.S. Patent Nos. 5,624,821 and 5,648,260, each of which is herein incorporated by reference in its entirety. In certain embodiments, the deletion or inactivation (through point mutations or other means) of a constant region domain may reduce Fc receptor binding of the circulating antibody thereby increasing tumor localization. *See, e.g.*, U.S. Pat. Nos. 5,585,097 and 8,591,886, each of which is herein incorporated by reference in its entirety, for a description of mutations that delete or inactivate the constant domain and thereby increase tumor localization. In certain embodiments, one or more amino acid substitutions may be introduced into the Fc region of an antibody described herein to remove potential glycosylation sites on the Fc region, which may reduce Fc receptor binding (*see, e.g.*, Shields R L *et al.*, (2001) *J Biol Chem* 276: 6591-604, which is herein incorporated by reference in its entirety). In various embodiments, one or more of the following mutations in the constant region of an antibody described herein may be made: an N297A substitution; an N297Q substitution; an L234A substitution; an L234F substitution; an L235A substitution; an L235F substitution; an L235V substitution; an L237A substitution; an S239D substitution; an E233P substitution; an L234V substitution; an L235A substitution;

a C236 deletion; a P238A substitution; an S239D substitution; an F243L substitution; a D265A substitution; an S267E substitution; an L328F substitution; an R292P substitution; a Y300L substitution; an A327Q substitution; a P329A substitution (PA); an A332L substitution; an I332E substitution; or a P396L substitution, numbered according to the EU numbering system.

5 **[0144]** In certain embodiments, a mutation selected from the group consisting of D265A, P329A, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of L235A, L237A, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of S267E, L328F, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of S239D, I332E, optionally A330L, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of L235V, F243L, R292P, Y300L, P396L, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of S267E, L328F, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein.

15 **[0145]** In a specific embodiment, an antibody described herein comprises the constant domain of an IgG1 with an N297Q or N297A amino acid substitution, numbered according to the EU numbering system. In one embodiment, an antibody described herein comprises the constant domain of an IgG1 with a mutation selected from the group consisting of D265A, P329A, and a combination thereof, numbered according to the EU numbering system. In another embodiment, an antibody described herein comprises the constant domain of an IgG1 with a mutation selected from the group consisting of L234A, L235A (LALA), and a combination thereof, numbered according to the EU numbering system. In another embodiment, an antibody described herein comprises the constant domain of an IgG1 with a mutation selected from the group consisting of L234F, L235F, N297A, and a combination thereof, numbered according to the EU numbering system. In certain embodiments, amino acid residues in the constant region of an antibody described herein in the positions corresponding to positions

L234, L235, and D265 in a human IgG1 heavy chain, numbered according to the EU numbering system, are not L, L, and D, respectively. This approach is described in detail in International Publication No. WO 14/108483, which is herein incorporated by reference in its entirety. In a particular embodiment, the amino acids corresponding to positions L234, L235, and D265 in a human IgG1 heavy chain are F, E, and A; or A, A, and A, respectively, numbered according to the EU numbering system.

[0146] In certain embodiments, one or more amino acids selected from amino acid residues 329, 331, and 322 in the constant region of an antibody described herein, numbered according to the EU numbering system, can be replaced with a different amino acid residue such that the antibody has altered C1q binding and/or reduced or abolished complement dependent cytotoxicity (CDC). This approach is described in further detail in U.S. Pat. No. 6,194,551 (Idusogie *et al.*), which is herein incorporated by reference in its entirety. In certain embodiments, one or more amino acid residues within amino acid positions 231 to 238 in the N-terminal region of the CH2 domain of an antibody described herein are altered to thereby alter the ability of the antibody to fix complement, numbered according to the EU numbering system. This approach is described further in International Publication No. WO 94/29351, which is herein incorporated by reference in its entirety. In certain embodiments, the Fc region of an antibody described herein is modified to increase the ability of the antibody to mediate antibody dependent cellular cytotoxicity (ADCC) and/or to increase the affinity of the antibody for an Fcγ receptor by mutating one or more amino acids (*e.g.*, introducing amino acid substitutions) at the following positions: 238, 239, 248, 249, 252, 254, 255, 256, 258, 265, 267, 268, 269, 270, 272, 276, 278, 280, 283, 285, 286, 289, 290, 292, 293, 294, 295, 296, 298, 301, 303, 305, 307, 309, 312, 315, 320, 322, 324, 326, 327, 328, 329, 330, 331, 333, 334, 335, 337, 338, 340, 360, 373, 376, 378, 382, 388, 389, 398, 414, 416, 419, 430, 434, 435, 437, 438, or 439, numbered according to the EU numbering system. This approach is described further in International Publication No. WO 00/42072, which is herein incorporated by reference in its entirety.

[0147] In some embodiments, the IgG Fc is an IgG1 Fc, or a derivative thereof. In some embodiments, the IgG Fc or IgG1 Fc comprises an amino acid sequence at least 85, 90, 95, 96, 97, 98, or 99% identical to the amino acid sequence of IgG1 Fc. In some embodiments, the IgG Fc or IgG1 Fc comprises an amino acid sequence at least 85, 90, 95, 96, 97, 98, 99, or 100% identical to an amino acid sequence provided below in Table 6.

Table 6. IgG Fc Amino Acid Sequences

SEQ ID NO:	Description	Sequence
76	IgG1 Fc	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
77	IgG1 Fc LALA	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
78	IgG1 Fc LALA PA	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK
79	IgG1 Fc LALA PA LS	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCSVLHEALHSHYTQKSLSLSPGK
80	IgG1 Fc without C-terminal lysine	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPG
81	IgG1 Fc LALA without C-terminal lysine	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPG
82	IgG1 Fc LALA PA without C-terminal lysine	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPG
83	IgG1 Fc LALA PA LS without C-terminal lysine	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCSVLHEALHSHYTQKSLSLSPG

[0148] In some embodiments, any IgG Fc, or derivative thereof, can be linked to the N-terminus or C-terminus of any of the embodiments described in Table 4 or 5 above with or without an IgG Fc linker. In some embodiments, human IgG1 Fc, or a derivative thereof, can

be linked to the N-terminus or C-terminus of any of the embodiments described in Table 4 or 5 above with or without an IgG Fc linker. In some embodiments, the amino acid sequence of the human IgG1 Fc comprises or consists of the amino acid sequence of SEQ ID NO: 76 or 80. In some embodiments, the derivative if human IgG1 Fc comprises an amino acid sequence at
5 least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 76 or 80.

[0149] In some embodiments, a human IgG1 Fc comprising a LALA mutation, or a derivative thereof, can be linked to the N-terminus or C-terminus of any of the embodiments described in Table 4 or 5 above with or without an IgG Fc linker. In some embodiments, the amino acid sequence of the human IgG1 Fc comprising a LALA mutation comprises or consists of the amino acid sequence of SEQ ID NO: 77 or 81. In some embodiments, the derivative if human IgG1 Fc comprising a LALA mutation comprises an amino acid sequence at least 85, 90, 95,
10 96, 97, 98, or 99% identical to the amino acid sequence of SEQ ID NO: 77 or 81.

[0150] In some embodiments, a human IgG1 Fc comprising a LALA PA mutation, or a derivative thereof, can be linked to the N-terminus or C-terminus of any of the embodiments described in Table 4 or 5 above with or without an IgG Fc linker. In some embodiments, the amino acid sequence of the human IgG1 Fc comprising a LALA PA mutation comprises or
20 consists of the amino acid sequence of SEQ ID NO: 78 or 82. In some embodiments, the derivative if human IgG1 Fc comprising a LALA PA mutation comprises an amino acid sequence at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% identical
25 to the amino acid sequence of SEQ ID NO: 78 or 82.

[0151] In some embodiments, a human IgG1 Fc comprising a LALA PA LS mutation, or a derivative thereof, can be linked to the N-terminus or C-terminus of any of the embodiments described in Table 4 or 5 above with or without an IgG Fc linker. In some embodiments, the amino acid sequence of the human IgG1 Fc comprising a LALA PA LS mutation comprises or
30 consists of the amino acid sequence of SEQ ID NO: 79 or 83. In some embodiments, the derivative if human IgG1 Fc comprising a LALA PA LS mutation comprises an amino acid sequence at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at

least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 79 or 83.

[0152] In some embodiments, the fusion protein comprises an amino acid sequence at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% identical to the amino acid sequences shown in Table 7. In some embodiments, the fusion protein comprises or consists of the amino acid sequences shown in Table 7.

10 Table 7. Fusion Protein Amino Acid Sequences

SEQ ID NO:	Sequence
84	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADANAGARQLYS ALANKCCHVGCTKRS LAQFC
85	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGANADAGARQLYS ALANKCCHVGCTKRS LAQFC
86	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADADAGARQLYS ALANKCCHVGCTKRS LAQFC
87	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKRS LAQFC
88	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAQADAGARQLYS ALANKCCHVGCTKRS LAQFC

SEQ ID NO:	Sequence
89	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADAQAGARQLYS ALANKCCHVGCTKRSLAQFC
90	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAQAQAGARQLYS ALANKCCHVGCTKRSLAQFC
91	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADANAGARQLYS ALANKCCHVGCTKRSLAQFC
92	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGANADAGARQLYS ALANKCCHVGCTKRSLAQFC
93	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADADAGARQLYS ALANKCCHVGCTKRSLAQFC
94	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKRSLAQFC
95	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAQAQADAGARQLYS ALANKCCHVGCTKRSLAQFC
96	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS

SEQ ID NO:	Sequence
	LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADAQAGARQLYS ALANKCCHVGCTKRSLAQFC
97	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAQAQAGARQLYS ALANKCCHVGCTKRSLAQFC
98	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGADANAGARQLYS ALANKCCHVGCTKRSLAQFC
99	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGANADAGARQLYS ALANKCCHVGCTKRSLAQFC
100	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGADADAGARQLYS ALANKCCHVGCTKRSLAQFC
101	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKRSLAQFC
102	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGAQAADAGARQLYS ALANKCCHVGCTKRSLAQFC
103	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGADAQAGARQLYS ALANKCCHVGCTKRSLAQFC
104	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG

SEQ ID NO:	Sequence
	QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGAQAQAGARQLYS ALANKCCHVGCTKRS LAQFC
105	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADANAGARQLYS ALANKCCHVGCTKQSLAQFC
106	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGANADAGARQLYS ALANKCCHVGCTKQSLAQFC
107	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADADAGARQLYS ALANKCCHVGCTKQSLAQFC
108	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKQSLAQFC
109	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAQAQAGARQLYS ALANKCCHVGCTKQSLAQFC
110	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADAQAGARQLYS ALANKCCHVGCTKQSLAQFC
111	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAQAQAGARQLYS ALANKCCHVGCTKQSLAQFC
112	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA

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	PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGADANAGARQLYS ALANKCCHVGCTKQSLAQFC
113	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGANADAGARQLYS ALANKCCHVGCTKQSLAQFC
114	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGADADAGARQLYS ALANKCCHVGCTKQSLAQFC
115	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKQSLAQFC
116	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGAQADAGARQLYS ALANKCCHVGCTKQSLAQFC
117	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGADAQAGARQLYS ALANKCCHVGCTKQSLAQFC
118	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQSTASDAAGAQQAQAGARQLYS ALANKCCHVGCTKQSLAQFC
119	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKRSLAQFC

SEQ ID NO:	Sequence
120	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSFQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKRSLAQFC
121	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSLQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKRSLAQFC
122	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSIQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCHVGCTKRSLAQFC
123	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCYVGCTKRSLAQFC
124	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCLVGCTKRSLAQFC
125	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCQVGCTKRSLAQFC
126	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCKVGCTKRSLAQFC
127	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFCSVLHEALHSHYTQKS

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	LSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCYVGCTKRSLAQFC
128	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCYVGCTKRSLAQFC
129	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGEGGGGRQLYS ALANKCCYVGCTKRSLAQFC
130	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGEGGGGRQLYS ALANKCCYVGCTKRSLAQFC
131	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGGRQLYS ALANKCCYVGCTKRSLAQFC
132	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGGRQLYS ALANKCCYVGCTKRSLAQFC
133	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCYVGCTKQSLAQFC
134	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYS ALANKCCYVGCTKQSLAQFC
135	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG

SEQ ID NO:	Sequence
	QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGEGGGGRQLYS ALANKCCYVGCTKQSLAQFC
136	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGEGGGGRQLYS ALANKCCYVGCTKQSLAQFC
137	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGGRQLYS ALANKCCYVGCTKQSLAQFC
138	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGGRQLYS ALANKCCYVGCTKQSLAQFC
300	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKS LSLSPGKGGSDSWKEEVIKLCGRELVRQAIAICGKSTGGEGGGEGGGEGGRQLYS ALANKCCHVGCTKRSLARFC
301	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKS LSLSPGKGGSDSWKEEVIKLCGRELVRQAIAICGKSTGGEGGGEGGGEGGGGQLY SALANKCCHVGCTKRSLARFC
302	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKS LSLSPGKGGSDSWMEEVIKLCGRELVRQAIAICGKSTGGEGGGEGGGEGGRQLYS ALANKCCHVGCTKRSLARFC
303	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGEGGGEGGGEGGRQLYS ALANKCCHVGCTKRSLARFC
304	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA

SEQ ID NO:	Sequence
	PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGGEGGRQLYS ALANKCCHVGCTKRSLARFC
305	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKS LSLSPGKGGSDSWMEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGGEGGGGQLY SALANKCCHVGCTKRSLARFC
306	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGGEGGGGQLY SALANKCCHVGCTKRSLARFC
307	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGGEGGGGQLY SALANKCCHVGCTKRSLARFC
308	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKS LSLSPGKGGSDSWMEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGGEGGGGQLYS ALANKCCHVGCTKRSLARFC
309	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGGEGGGGQLYS ALANKCCHVGCTKRSLARFC
310	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKS LSLSPGGGSDSWMEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGGEGGGGQLYSA LANKCCHVGCTKRSLARFC
311	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKS LSLSPGGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGGEGGGGQLYSA LANKCCHVGCTKRSLARFC

SEQ ID NO:	Sequence
312	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGEGGEGGRQLYS ALANKCCHVGCTKRSLAQFC
313	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGEGGEGGRQLYS ALANKCCHVGCTKRSLAQFC
314	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGEGGEGGRQLYSA LANKCCHVGCTKRSLARFC
315	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGEGGEGGRQLYSA LANKCCHVGCTKRSLARFC
316	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGEGGEGGRQLYSA LANKCCHVGCTKRSLAQFC
317	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGEGGEGGRQLYSA LANKCCHVGCTKRSLAQFC
318	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGEGGEGGRQLYS ALANKCCHVGCTKRSLARFC
319	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQKS

SEQ ID NO:	Sequence
	LSLS PGKGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGGEEGGGEEGGGRQLYS ALANKCCHVGCTKRSLARFC
320	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNYHTQKS LSLS PGKGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGGEEGGGEEGGGRQLYS ALANKCCHVGCTKRSLAQFC
321	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVLHEALHSHYTQKS LSLS PGKGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGGEEGGGEEGGGRQLYS ALANKCCHVGCTKRSLAQFC
322	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNYHTQKS LSLS PGKGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGGEEGGGEEGGGRQLYSA LANKCCHVGCTKRSLARFC
323	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVLHEALHSHYTQKS LSLS PGKGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGGEEGGGEEGGGRQLYSA LANKCCHVGCTKRSLARFC
324	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNYHTQKS LSLS PGKGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGGEEGGGEEGGGRQLYSA LANKCCHVGCTKRSLAQFC
325	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVLHEALHSHYTQKS LSLS PGKGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGGEEGGGEEGGGRQLYSA LANKCCHVGCTKRSLAQFC
326	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVLHEALHSHYTQKS LSLS PGKGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGEGEGEGEGEGGRQLYS ALANKCCHVGCTKRSLAQFC
327	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG

SEQ ID NO:	Sequence
	QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGEGEGGEGGSGRQLYSA LANKCCHVGCTKRSLARFC
328	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGGGSDSWQEEVIKLCGRELVRAQIAICGKSTGGEGEGGEGGSGRQLYSA LANKCCHVGCTKRSLAQFC
359	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSWKEEVIKLCGRELVRAQIAICGKSTASDAAGANANAGARQLYS ALANKCCHVGCTKRSLAQFC
360	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSWKEEVIKLCGRELVRAQIAICGKSTASDAAGANANAGARQLYS ALANKCCHVGCTKRSLAEFC
361	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSWKEEVIKLCGRELVRAQIAICGKSTGGEGEGGEGGEGGRQLYS ALANKCCHVGCTKRSLARFC
362	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSWKEEVIKLCGRELVRAQIAICGKSTGGEGEGGEGGEGGGGQLY SALANKCCHVGCTKRSLARFC
363	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSWMEEVIKLCGRELVRAQIAICGKSTGGEGEGGEGGEGGEGGRQLYS ALANKCCHVGCTKRSLARFC
364	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGKGGSDSWMEEVIKLCGRELVRAQIAICGKSTGGEGEGGEGGEGGEGGGQLY SALANKCCHVGCTKRSLARFC
365	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA

SEQ ID NO:	Sequence
	PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWMEEVIKLCGRELVRQAIAICGKSTGGEGGGEGGGEGGQLYS ALANKCCHVGCTKRSLARFC
366	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGEGGGEGGGEGGQLYS ALANKCCHVGCTKRSLARFC
367	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWMEEVIKLCGRELVRQAIAICGKSTGGEGGGEGGGEGGQLYSA LANKCCHVGCTKRSLARFC
368	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGEGGGEGGGEGGQLYSA LANKCCHVGCTKRSLARFC
369	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWKEEVIKLCGRELVRQAIAICGKSTASDAAGANANAGARQLYS ALANKCCHVGCTKRSLAQFC
370	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSWKEEVIKLCGRELVRQAIAICGKSTASDAAGANANAGARQLYS ALANKCCHVGCTKRSLAEFC
516	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGEGGGRQLYS ALANKCCHVGCTKRSLAQFC
517	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTQKS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGEGGGRQLYS ALANKCCQVGCTKRSLAQFC

SEQ ID NO:	Sequence
518	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFVLSHESLHSHYTSQS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGGGGRQLYS ALANKCCHVGCTKQSLAQFC
519	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFVLSHESLHSHYTSQS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGGGGRQLYS ALANKCCQVGCTKQSLAQFC
520	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFVLSHESLHSHYTSQS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGGRQLYS ALANKCCHVGCTKRS LAQFC
521	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFVLSHESLHSHYTSQS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGGRQLYS ALANKCCQVGCTKRS LAQFC
522	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFVLSHESLHSHYTSQS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGGRQLYS ALANKCCHVGCTKQSLAQFC
523	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWKYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFVLSHESLHSHYTSQS LSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGGRQLYS ALANKCCQVGCTKQSLAQFC

[0153] In some embodiments, the IgG Fc comprises a mouse IgG kappa signal sequence comprising the amino acid sequence of METDTLLLVVLLLVPGSTG (SEQ ID NO: 329). In some embodiments, the IgG Fc comprises a mouse IgG heavy chain signal sequence. In some

5 embodiments, the IgG Fc comprises a signal sequence comprising the amino acid sequence of MGWSCIILFLVATATGVHS (SEQ ID NO: 548). In some embodiments a different signal

sequence is used. In some embodiments, no signal sequence is present on the fusion protein as produced.

[0154] In some embodiments, the fusion protein comprises an amino acid sequence at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% identical to the amino acid sequences shown in Table 8. In some embodiments, the fusion protein comprises or consists of the amino acid sequences shown in Table 8.

10 **Table 8. Fusion Protein Amino Acid Sequences**

SEQ ID NO:	Sequence
139	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGADANAGARQLYSALANKCCHVGCTKRSLAQFC
140	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGANADAGARQLYSALANKCCHVGCTKRSLAQFC
141	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGADADAGARQLYSALANKCCHVGCTKRSLAQFC
142	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCHVGCTKRSLAQFC
143	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGAQADAGARQLYSALANKCCHVGCTKRSLAQFC
144	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH

SEQ ID NO:	Sequence
	QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGSAFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTKQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADAQAGARQLYSALANKCCHVGCTKRSLAQFC
145	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGSAFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTKQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAAQAGARQLYSALANKCCHVGCTKRSLAQFC
146	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGSAFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTKQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADANAGARQLYSALANKCCHVGCTKRSLAQFC
147	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGSAFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTKQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGANADAGARQLYSALANKCCHVGCTKRSLAQFC
148	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGSAFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTKQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADADAGARQLYSALANKCCHVGCTKRSLAQFC
149	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGSAFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTKQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYSALANKCCHVGCTKRSLAQFC
150	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGSAFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTKQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAAQADAGARQLYSALANKCCHVGCTKRSLAQFC
151	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGSAFFLYSKLTVDKSRWQQGNVFSQSVLHEALHSHYTKQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGADAQAGARQLYSALANKCCHVGCTKRSLAQFC

SEQ ID NO:	Sequence
152	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTKQSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGAAQAAGARQLYSALANKCCHVGCTKRSLAQFC
153	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTKQSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGADANAGARQLYSALANKCCHVGCTKRSLAQFC
154	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTKQSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGANADAGARQLYSALANKCCHVGCTKRSLAQFC
155	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTKQSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGADADAGARQLYSALANKCCHVGCTKRSLAQFC
156	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTKQSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGAEAEAGARQLYSALANKCCHVGCTKRSLAQFC
157	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTKQSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGAQAADAGARQLYSALANKCCHVGCTKRSLAQFC
158	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTKQSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGADAQAAGARQLYSALANKCCHVGCTKRSLAQFC
159	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG

SEQ ID NO:	Sequence
	NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRAQIAICGQ STASDAAGAAQAGARQLYSALANKCCHVGCTKRS LAQFC
160	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTT PPVLDS DGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRAQIAICGK STASDAAGADANAGARQLYSALANKCCHVGCTKQSLAQFC
161	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTT PPVLDS DGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRAQIAICGK STASDAAGANADAGARQLYSALANKCCHVGCTKQSLAQFC
162	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTT PPVLDS DGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRAQIAICGK STASDAAGADADAGARQLYSALANKCCHVGCTKQSLAQFC
163	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTT PPVLDS DGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRAQIAICGK STASDAAGAEAEAGARQLYSALANKCCHVGCTKQSLAQFC
164	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTT PPVLDS DGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRAQIAICGK STASDAAGAQADAGARQLYSALANKCCHVGCTKQSLAQFC
165	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTT PPVLDS DGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRAQIAICGK STASDAAGADAQAGARQLYSALANKCCHVGCTKQSLAQFC
166	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTT PPVLDS DGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRAQIAICGK STASDAAGAAQAGARQLYSALANKCCHVGCTKQSLAQFC
167	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL

SEQ ID NO:	Sequence
	TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGADANAGARQLYSALANKCCHVGCTKQSLAQFC
168	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGANADAGARQLYSALANKCCHVGCTKQSLAQFC
169	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGADADAGARQLYSALANKCCHVGCTKQSLAQFC
170	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGAEAEAGARQLYSALANKCCHVGCTKQSLAQFC
171	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGAQADAGARQLYSALANKCCHVGCTKQSLAQFC
172	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGADAQAGARQLYSALANKCCHVGCTKQSLAQFC
173	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSWQEEVIKLCGRELVRQAIAICGQ STASDAAGAQAGARQLYSALANKCCHVGCTKQSLAQFC
174	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGSDSYQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCHVGCTKRS LAQFC
175	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH

SEQ ID NO:	Sequence
	QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSFQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCHVGCTKRSLAQFC
176	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSLQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCHVGCTKRSLAQFC
177	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSIQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCHVGCTKRSLAQFC
178	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCYVGCTKRSLAQFC
179	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCLVGCTKRSLAQFC
180	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCQVGCTKRSLAQFC
181	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCKVGCTKRSLAQFC
182	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGK STASDAAGAEAEAGARQLYSALANKCCYVGCTKRSLAQFC

SEQ ID NO:	Sequence
183	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGK STASDAAGAAEAEAGARQLYSALANKCKKVGCTKRS LAQFC
184	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGK STGGEGSGGEGEGGGRQLYSALANKCCYVGCTKRS LAQFC
185	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGK STGGEGSGGEGEGGGRQLYSALANKCKKVGCTKRS LAQFC
186	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGK STGGEGSGGEGSGGGRQLYSALANKCCYVGCTKRS LAQFC
187	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGEGGSDSYQEEVIKLCGRELVRQAIAICGK STGGEGSGGEGSGGGRQLYSALANKCKKVGCTKRS LAQFC
188	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGK STASDAAGAAEAEAGARQLYSALANKCCYVGCTKQSLAQFC
189	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGK STASDAAGAAEAEAGARQLYSALANKCKKVGCTKQSLAQFC
190	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG

SEQ ID NO:	Sequence
	NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSYQEEVIKLCGRELVRAQIAICGK STGGEGSGGEGEGGGGRQLYSALANKCCYVGCTKQSLAQFC
191	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSYQEEVIKLCGRELVRAQIAICGK STGGEGSGGEGEGGGGRQLYSALANKCCKVGCTKQSLAQFC
192	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSYQEEVIKLCGRELVRAQIAICGK STGGEGSGGEGSGGGGRQLYSALANKCCYVGCTKQSLAQFC
193	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSYQEEVIKLCGRELVRAQIAICGK STGGEGSGGEGSGGGGRQLYSALANKCCKVGCTKQSLAQFC
330	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSMHEALHNHYTQKSLSLSPGKGGSDSWKEEVIKLCGRELVRAQIAICGK STGGEGGGEGGGEGGRQLYSALANKCCHVGCTKRSLARFC
331	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSMHEALHNHYTQKSLSLSPGKGGSDSWKEEVIKLCGRELVRAQIAICGK STGGEGGGEGGGEGGGQLYSALANKCCHVGCTKRSLARFC
332	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSMHEALHNHYTQKSLSLSPGKGGSDSWMEEVIKLCGRELVRAQIAICGK STGGEGGGEGGGEGGRQLYSALANKCCHVGCTKRSLARFC
333	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQG NVFSCSMHEALHNHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRAQIAICGK STGGEGGGEGGGEGGRQLYSALANKCCHVGCTKRSLARFC
334	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL

SEQ ID NO:	Sequence
	TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGEGGGEGGGEGGRQLYSALANKCCHVGCTKRSLARFC
335	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGEGGGEGGGEGGGQLYSALANKCCHVGCTKRSLARFC
336	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGEGGGEGGGEGGGQLYSALANKCCHVGCTKRSLARFC
337	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGEGGGEGGGEGGGQLYSALANKCCHVGCTKRSLARFC
338	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGEGGGEGGGEGGGQLYSALANKCCHVGCTKRSLARFC
339	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGEGGGEGGGEGGGQLYSALANKCCHVGCTKRSLARFC
340	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGGGSDSWQEEVIKLCGRELVRQAIAICGKS TGEGGGEGGGEGGGQLYSALANKCCHVGCTKRSLARFC
341	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGGGSDSWQEEVIKLCGRELVRQAIAICGKS TGEGGGEGGGEGGGQLYSALANKCCHVGCTKRSLARFC
342	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH

SEQ ID NO:	Sequence
	QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMEALHNHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGEGGRQLYSALANKCCHVGCTKRSLAQFC
343	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGEGGRQLYSALANKCCHVGCTKRSLAQFC
344	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMEALHNHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGEGGRQLYSALANKCCHVGCTKRSLARFC
345	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGEGGRQLYSALANKCCHVGCTKRSLARFC
346	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMEALHNHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGEGGRQLYSALANKCCHVGCTKRSLAQFC
347	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGEGGRQLYSALANKCCHVGCTKRSLAQFC
348	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMEALHNHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGEGGRQLYSALANKCCHVGCTKRSLARFC
349	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTGGGEGGGEGGEGGRQLYSALANKCCHVGCTKRSLARFC

SEQ ID NO:	Sequence
350	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGGEEGGGEEGGGRQLYSALANKCCHVGCTKRSLAQFC
351	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGGEEGGGEEGGGRQLYSALANKCCHVGCTKRSLAQFC
352	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKS TGGGEEGGGEEGGGRQLYSALANKCCHVGCTKRSLARFC
353	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKS TGGGEEGGGEEGGGRQLYSALANKCCHVGCTKRSLARFC
354	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKS TGGGEEGGGEEGGGRQLYSALANKCCHVGCTKRSLAQFC
355	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKS TGGGEEGGGEEGGGRQLYSALANKCCHVGCTKRSLAQFC
356	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGK STGGEGEGEGEGGGRQLYSALANKCCHVGCTKRSLAQFC
357	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG

SEQ ID NO:	Sequence
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SEQ ID NO:	Sequence
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524	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGGGSDSYQEEVIKLCGRELVRAQIAICGK STGGEGSGGEGEGGGRQLYSALANKCCHVGCTKRSLAQFC
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526	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVLHEALHSHYTQKSLSLSPGGGSDSYQEEVIKLCGRELVRAQIAICGK STGGEGSGGEGEGGGRQLYSALANKCCHVGCTKQSLAQFC
527	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH

SEQ ID NO:	Sequence
	QDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTKQSLSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGRQLYSALANKCCQVGCTKQSLAQFC
528	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTKQSLSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGRQLYSALANKCCCHVGCTKRSLAQFC
529	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTKQSLSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGRQLYSALANKCCQVGCTKRSLAQFC
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531	METDTLLLWVLLLWVPGSTGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTKQSLSLSPGKGGSDSYQEEVIKLCGRELVRQAIAICGKSTGGEGSGGEGSGGGRQLYSALANKCCQVGCTKQSLAQFC
549	MGWSCIIILFLVATATGVHSDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTKQSLSLSPGKGGSDSWQEEVIKLCGRELVRQAIAICGKSTASDAAGAEAEAGARQLYSALANKCCCHVGCTKRSLAQFC

Other Half-Life Extending Moieties

[0155] As used herein, the term “half-life extending moiety” includes non-proteinaceous, half-life extending moieties, such as PEG or HES, and proteinaceous half-life extending moieties such as Fc domain. In some embodiments, non-proteinaceous half-life extending moieties are linked to the fusion proteins described herein. In some embodiments, the non-proteinaceous half-life extending moieties are linked to the fusion proteins instead of IgG Fc. In some

embodiments, the non-proteinaceous half-life extending moieties are linked to the fusion proteins in addition to IgG Fc.

[0156] Examples of suitable polymer molecules that act as non-proteinaceous half-life extending moieties include polymer molecules selected from the group consisting of polyalkylene oxide (PAO), including polyalkylene glycol (PAG), such as polyethylene glycol (PEG) and polypropylene glycol (PPG), branched PEGs, hydroxyalkyl starch (HAS), such as hydroxyethyl starch (HES), polysialic acid (PSA), poly-vinyl alcohol (PVA), poly-carboxylate, poly-(vinylpyrrolidone), polyethylene-co-maleic acid anhydride, polystyrene-co-maleic acid anhydride, dextran, including carboxymethyl-dextran, or any other biopolymer suitable for reducing immunogenicity and/or increasing functional *in vivo* half-life and/or serum half-life. Another example of a polymer molecule is human albumin or another abundant plasma protein. Generally, polyalkylene glycol-derived polymers are biocompatible, non-toxic, non-antigenic, non-immunogenic, have various water solubility properties, and are easily excreted from living organisms.

[0157] PEG has the advantage of having only few reactive groups capable of cross-linking compared to, *e.g.*, polysaccharides such as dextran. In particular, monofunctional PEG, *e.g.*, methoxypolyethylene glycol (mPEG), is of interest since its coupling chemistry is relatively simple (only one reactive group is available for conjugating with attachment groups on the polypeptide). Consequently, as the risk of cross-linking is eliminated, the resulting conjugated fusion proteins described herein are more homogeneous, and the reaction of the polymer molecules with the variant polypeptide is easier to control.

[0158] To effect covalent attachment of the polymer molecule(s) to the fusion proteins described herein, the hydroxyl end groups of the polymer molecule must be provided in activated form, *i.e.*, with reactive functional groups (examples of which include primary amino groups, hydrazide (HZ), thiol, succinate (SUC), succinimidyl succinate (SS), succinimidyl succinamide (SSA), succinimidyl propionate (SPA), succinimidyl butyrate (SBA), succinimidyl carboxymethylate (SCM), benzotriazole carbonate (BTC), N-hydroxysuccinimide (NHS), aldehyde, nitrophenylcarbonate (NPC), and tresylate (TRES)). Suitable activated polymer molecules are commercially available, *e.g.*, from Shearwater Polymers, Inc., Huntsville, Ala., USA, or from PolyMASC Pharmaceuticals plc, UK.

[0159] Alternatively, the polymer molecules can be activated by conventional methods known in the art, *e.g.*, as disclosed in WO 90/13540. Specific examples of activated linear or branched polymer molecules for use herein are described in the Shearwater Polymers, Inc. 1997 and

2000 Catalogs (Functionalized Biocompatible Polymers for Research and pharmaceuticals, Polyethylene Glycol and Derivatives, incorporated herein by reference). Specific examples of activated PEG polymers include the following linear PEGs: NHS-PEG (*e.g.*, SPA-PEG, SSPA-PEG, SBA-PEG, SS-PEG, SSA-PEG, SC-PEG, SG-PEG, and SCM-PEG), and NOR-PEG, 5 BTC-PEG, EPOXPEG, NCO-PEG, NPC-PEG, CDI-PEG, ALD-PEG, TRES-PEG, VS-PEG, IODO-PEG, and MAL-PEG, and branched PEGs such as PEG2-NHS and those disclosed in U.S. Pat. No. 5,932,462 and U.S. Pat. No. 5,643,575, both of which are incorporated herein by reference. Furthermore, the following publications disclose useful polymer molecules and/or PEGylation chemistries: U.S. Pat. No. 5,824,778, U.S. Pat. No. 5,476,653, WO 97/32607, EP 10 229,108, EP 402,378, U.S. Pat. No. 4,902,502, U.S. Pat. No. 5,281,698, U.S. Pat. No. 5,122,614, U.S. Pat. No. 5,219,564, WO 92/16555, WO 94/04193, WO 94/14758, WO 94/17039, WO 94/18247, WO 94/28024, WO 95/00162, WO 95/11924, WO 95/13090, WO 95/33490, WO 96/00080, WO 97/18832, WO 98/41562, WO 98/48837, WO 99/32134, WO 99/32139, WO 99/32140, WO 96/40791, WO 98/32466, WO 95/06058, EP 439 508, WO 15 97/03106, WO 96/21469, WO 95/13312, EP 921 131, U.S. Pat. No. 5,736,625, WO 98/05363, EP 809 996, U.S. Pat. No. 5,629,384, WO 96/41813, WO 96/07670, U.S. Pat. No. 5,473,034, U.S. Pat. No. 5,516,673, EP 605 963, U.S. Pat. No. 5,382,657, EP 510 356, EP 400 472, EP 183 503, and EP 154 316.

[0160] Specific examples of activated PEG polymers particularly preferred for coupling to 20 cysteine residues, include the following linear PEGs: vinylsulfone-PEG (VS-PEG), preferably vinylsulfone-mPEG (VS-mPEG); maleimide-PEG (MAL-PEG), preferably maleimide-mPEG (MAL-mPEG) and orthopyridyl-disulfide-PEG (OPSS-PEG), preferably orthopyridyl-disulfide-mPEG (OPSS-mPEG). Typically, such PEG or mPEG polymers will have a size of about 5 kDa, about 10 kDa, about 12 kDa or about 20 kDa.

25 [0161] The conjugation of the fusion proteins described herein and the activated polymer molecules is conducted by use of any conventional method, *e.g.*, as described in the following references (which also describe suitable methods for activation of polymer molecules): Harris and Zalipsky, eds., *Poly(ethylene glycol) Chemistry and Biological Applications*, AZC Washington; R. F. Taylor, (1991), "Protein immobilisation. Fundamental and applications," 30 Marcel Dekker, N.Y.; S. S. Wong, (1992), "Chemistry of Protein Conjugation and Crosslinking," CRC Press, Boca Raton; G. T. Hermanson *et al.*, (1993), "Immobilized Affinity Ligand Techniques", Academic Press, N.Y.

[0162] The skilled person will be aware that the activation method and/or conjugation chemistry to be used depends on the attachment group(s) of the fusion protein (examples of which are given further above), as well as the functional groups of the polymer (*e.g.*, being amine, hydroxyl, carboxyl, aldehyde, sulfhydryl, succinimidyl, maleimide, vinylsulfone or haloacetate). The PEGylation may be directed towards conjugation to all available attachment groups on the fusion protein (*i.e.*, such attachment groups that are exposed at the surface of the polypeptide) or may be directed towards one or more specific attachment groups, *e.g.*, the N-terminal amino group as described in U.S. Pat. No. 5,985,265 or to cysteine residues. Furthermore, the conjugation may be achieved in one step or in a stepwise manner (*e.g.*, as described in WO 99/55377).

[0163] For PEGylation to cysteine residues (see above) the fusion protein is usually treated with a reducing agent, such as dithiothreitol (DDT) prior to PEGylation. The reducing agent is subsequently removed by any conventional method, such as by desalting. Conjugation of PEG to a cysteine residue typically takes place in a suitable buffer at pH 6-9 at temperatures varying from 4° C to 25° C for periods up to 16 hours.

[0164] It will be understood that the PEGylation is designed so as to produce the optimal molecule with respect to the number of PEG molecules attached, the size and form of such molecules (*e.g.*, whether they are linear or branched), and the attachment site(s) in the fusion protein. The molecular weight of the polymer to be used may *e.g.*, be chosen on the basis of the desired effect to be achieved.

[0165] In connection with conjugation to only a single attachment group on the fusion protein (*e.g.*, the N-terminal amino group), it may be advantageous that the polymer molecule, which may be linear or branched, has a high molecular weight, preferably about 10-25 kDa, such as about 15-25 kDa, *e.g.*, about 20 kDa.

[0166] Normally, the polymer conjugation is performed under conditions aimed at reacting as many of the available polymer attachment groups with polymer molecules. This is achieved by means of a suitable molar excess of the polymer relative to the polypeptide. Typically, the molar ratios of activated polymer molecules to polypeptide are up to about 1000-1, such as up to about 200-1, or up to about 100-1. In some cases, the ratio may be somewhat lower, however, such as up to about 50-1, 10-1, 5-1, 2-1 or 1-1 in order to obtain optimal reaction.

[0167] It is also contemplated to couple the polymer molecules to the fusion protein through a linker. Suitable linkers are well known to the skilled person. A preferred example is cyanuric

chloride (Abuchowski *et al.*, (1977), *J. Biol. Chem.*, 252, 3578-3581; U.S. Pat. No. 4,179,337; Shafer *et al.*, (1986), *J. Polym. Sci. Polym. Chem. Ed.*, 24, 375-378).

[0168] Subsequent to the conjugation, residual activated polymer molecules are blocked according to methods known in the art, *e.g.*, by addition of primary amine to the reaction mixture, and the resulting inactivated polymer molecules are removed by a suitable method.

[0169] It will be understood that depending on the circumstances, *e.g.*, the amino acid sequence of the fusion protein, the nature of the activated PEG compound being used and the specific PEGylation conditions, including the molar ratio of PEG to polypeptide, varying degrees of PEGylation may be obtained, with a higher degree of PEGylation generally being obtained with a higher ratio of PEG to fusion protein. The PEGylated fusion proteins resulting from any given PEGylation process will, however, normally comprise a stochastic distribution of conjugated fusion protein having slightly different degrees of PEGylation.

[0170] For improvement of the biological half-life of the fusion proteins described herein, chemical modification such as PEGylation, or HESylation are applicable.

[0171] HAS and HES non-proteinaceous polymers, as well as methods of producing HAS or HES conjugates are disclosed for example in WO 02/080979, WO 03/070772, WO 057092391 and WO 057092390.

[0172] Polysialylation is another technology, which uses the natural polymer polysialic acid (PSA) to prolong the half-life and improve the stability of therapeutic peptides and proteins. PSA is a polymer of sialic acid (a sugar). When used for protein and therapeutic peptide drug delivery, polysialic acid provides a protective microenvironment on conjugation. This increases the active life of the fusion protein in the circulation and prevents it from being recognized by the immune system. The PSA polymer is naturally found in the human body. It was adopted by certain bacteria which evolved over millions of years to coat their walls with it. These naturally polysialylated bacteria were then able, by virtue of molecular mimicry, to foil the body's defense system. PSA, nature's ultimate stealth technology, can be easily produced from such bacteria in large quantities and with predetermined physical characteristics. Bacterial PSA is completely non-immunogenic, even when coupled to proteins, as it is chemically identical to PSA in the human body.

30 Biological Activity of the Relaxin-2 Fusion Proteins

[0173] In some embodiments, the relaxin-2 fusion proteins described herein have high levels of biological activity as compared to native relaxin-2. In some embodiments, any of the relaxin-2 fusion proteins described herein have from about 1% to about 200% of a biological

- activity as compared to native relaxin-2. In some embodiments, the relaxin-2 fusion protein has at least about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 100%, about 125% about 150%, about 175%, or about 200% of a biological activity as compared to native relaxin-2.
- 5 **[0174]** In some embodiments, any of the relaxin-2 fusion proteins described herein have from about 1% to about 200% of maximal biological activity as compared to native relaxin-2. In some embodiments, maximal biological activity is the maximum response ($E_{\max}$) of relaxin-2 or relaxin-2 fusion protein. In some embodiments, the relaxin-2 fusion protein has at least
- 10 about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 100%, about 125% about 150%, about 175%, or about 200% of a maximal biological activity as compared to native relaxin-2.
- 15 **[0175]** In some embodiments, any of the relaxin-2 fusion proteins described herein have about at least about 0.001-fold to about at least 1,000-fold enhanced potency as compared to native relaxin-2. In some embodiments, potency is the concentration of relaxin-2 or relaxin-2 fusion protein to elicit a half-maximal response (EC_{50}). In some embodiments, the relaxin-2 fusion protein has at least about 0.001-fold, about 0.01-fold, about 0.1-fold, about 1-fold, about 10-fold, about 100-fold, or about 1,000-fold of the potency as compared to native relaxin-2.
- 20 **[0176]** The biological activity can be any biological activity of native relaxin-2. For example, the biological activity can be the capacity to bind the receptor of native relaxin-2, RXFP1. The binding of relaxin-2 to RXFP1 can be measured by any well-known methods in the art, such as radioligand binding. In some embodiments, the fusion proteins described herein bind to RXFP1 when it is expressed on a cell surface.
- 25 **[0177]** In some embodiments, the biological activity can be the capacity to activate RXFP1 on a cell surface. The activation of RXFP1 by the relaxin-2 fusion proteins described herein can be determined by the increase of cAMP using any methods well known in the art, such as measuring the activity of a cAMP-driven reporter gene, *e.g.*, β -galactosidase. The activation of RXFP1 by the relaxin-2 fusion proteins described herein in a cell may also be determined
- 30 by using a biosensor such as the GloSensor biosensor. The activation of RXFP1 by the relaxin-2 fusion proteins described herein in a cell may also be determined by measuring the expression of certain genes, such as angiogenic factors, *e.g.*, VEGF, or the expression of MMPs using well-known methods in the art. In some embodiments, the biological activity is a

physiological, biochemical activity or any other effect-inducing activity of the relaxin-2. Exemplary biological activities include, but are not limited to, vasodilation, collagen degradation, angiogenesis, decreasing arterial blood pressure, increasing renal artery blood flow, increasing renal plasma flow, increasing cardiac filling at diastole, resolving established
5 fibrosis, and suppressing new fibrosis development.

[0178] In some embodiments, the fusion proteins described herein have improved pharmacokinetics profiles. Without wishing to be bound by any theory, the structure of the fusion proteins described herein is based upon, at least in part, the surprising discovery that reducing the pI of relaxin-2 fusion protein analogs increases their circulating half-life. In some
10 embodiments, the fusion proteins described herein have high bioavailability. In some embodiments, the fusion proteins described herein have high and/or stable serum levels. In some embodiments, the circulating half-life, bioavailability, high serum level, and/or stable serum level is in a mammal. In some embodiments, the mammal is a rodent or a primate. In some embodiments, the rodent is a rat or a mouse. In some embodiments, the primate is a
15 human or a monkey. In some embodiments, the monkey is a cynomolgus monkey. In some embodiments, the mammal is a human.

[0179] In some embodiments, the fusion proteins described herein may have a circulating half-life of greater than about 5 hours, 10 hours, 20 hours, 50 hours, 75 hours, 100 hours, 125 hours, 150 hours, or more. In some embodiments, the fusion proteins described herein may have a
20 circulating half-life of 5-10 hours, 10-20 hours, 20-50 hours, 50-75 hours, 75-100 hours, 100-125 hours, or 125-150 hours. In some embodiments, the fusion proteins described herein may have a circulating half-life of about 10 days, about 11 days, about 12 days, about 13 days, about 14 days, about 15 days, about 16 days, about 17 days, about 18 days, about 19 days, about 20 days, about 21 days, about 22 days, or about 23 days. In some embodiments, the fusion proteins
25 described herein may have a circulating half-life of 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 16 days, 17 days, 18 days, 19 days, 20 days, 21 days, 22 days, or 23 days. In some embodiments, the fusion proteins described herein may have a circulating half-life of at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21
30 days, at least 22 days, or at least 23 days. In some embodiments, the fusion proteins described herein may have a circulating half-life of greater than about 5 hours, 10 hours, 20 hours, 50 hours, 75 hours, 100 hours, 125 hours, 150 hours, or more, when administered to a human. In some embodiments, the fusion proteins described herein may have a circulating half-life of 5-

10 hours, 10-20 hours, 20-50 hours, 50-75 hours, 75-100 hours, 100-125 hours, or 125-150 hours, when administered to a human. In some embodiments, the fusion proteins described herein may have a circulating half-life of about 10 days, about 11 days, about 12 days, about 13 days, about 14 days, about 15 days, about 16 days, about 17 days, about 18 days, about 19 days, about 20 days, about 21 days, about 22 days, or about 23 days, when administered to a human. In some embodiments, the fusion proteins described herein may have a circulating half-life of 10 days, 11 days, 12 days, 13 days, 14 days, 15 days, 16 days, 17 days, 18 days, 19 days, 20 days, 21 days, 22 days, or 23 days, when administered to a human. In some embodiments, the fusion proteins described herein may have a circulating half-life of at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21 days, at least 22 days, or at least 23 days, when administered to a human. Values and ranges intermediate to the recited values are also intended to be part of this disclosure. In some embodiments, the fusion proteins described herein have a longer circulating half-life than a native two chain relaxin-2. For example, the circulating half-life of a native two chain relaxin-2 may be less than about 5 hours. (*See, e.g., Chen et al., The Pharmacokinetics of Recombinant Human Relaxin in Non-Pregnant Women after Intravenous, Intravaginal, and Intracervical Administration, Pharm. Res. 10: 834038 (1993), incorporated herein by reference.*)

[0180] This increased half-life can be, at least in part, attributed to the reduced pI of the fusion proteins described herein. In some embodiments, the fusion protein has a pI that is less than about 9.4. As used herein, the term “about” when referring to pI encompasses variations of $\pm 1\%$ of a given value or range, as is appropriate to perform the methods disclosed herein. In some embodiments, the fusion protein has a pI that is less than 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, or 6.1, or is less than about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, or 6.1. In some embodiments, the fusion protein has a pI that is less than 9.0. In some embodiments, the fusion protein has a pI that is less than about 8.2. In some embodiments, the fusion protein has a pI from about 6.0 to about 9.4. In some embodiments, the fusion protein has a pI from about 6.5 to about 8.5, about 6.6 to about 8.4, about 6.7 to about 8.3, about 6.8 to about 8.2, about 6.8 to about 8.1, about 6.8 to about 8.0, about 6.8 to about 7.9, about 6.0 to about 8.2, about 6.0 to about 8.1, about 6.0 to about 8.0, about 6.0 to about 7.9, about 6.0 to about 7.8, about 6.0 to about 7.7, about 6.0 to about 7.6, about 6.0 to about 7.5, about 6.0 to about 7.4, about 6.0 to about 7.3,

about 6.0 to about 7.2, about 6.0 to about 7.1, about 6.0 to about 7.0, about 6.0 to about 6.9, about 6.0 to about 6.8, about 6.0 to about 6.7, about 6.0 to about 6.6, about 6.0 to about 6.5, about 6.0 to about 6.4, about 6.0 to about 6.3, about 6.0 to about 6.2, or about 6.0 to about 6.1.

In some embodiments, the fusion protein has a pI from about 6.0 to about 8.2. In some
5 embodiments, the fusion protein has a pI of 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0,
7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8, 7.9, 8.0, 8.1, or 8.2, or is about 6.0, 6.1, 6.2, 6.3, 6.4, 6.5,
6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8, 7.9, 8.0, 8.1, or 8.2, or is between any
two such values. In some embodiments, the fusion protein has a pI of about 6.8. In some
embodiments, the fusion protein has a pI of about 7.0. In some embodiments, the fusion protein
10 has a pI of about 7.1. In some embodiments, the fusion protein has a pI of about 7.4. In some
embodiments, the fusion protein has a pI of about 7.5. In some embodiments, the fusion protein
has a pI of about 7.9. In some embodiments, the fusion protein has a pI of about 8.0. In some
embodiments, the fusion protein has a pI of about 8.4. In some embodiments, the fusion protein
has a pI of about 8.5. In some embodiments, the fusion protein has a pI of about 8.8. In some
15 embodiments, the fusion protein has a pI of about 8.9. In some embodiments, any of the pIs
referred to above is the calculated or theoretical pI. In some embodiments, any of the pIs
referred to above is the experimentally measured pI.

[0181] As used herein, the term “about” when referring to dosages encompasses variations of
±10% of a given value or range, as is appropriate to perform the methods disclosed herein.

20 [0182] “Circulating half-life,” as used herein, refers to the time it takes for the blood plasma
concentration of a drug to halve its steady-state when circulating in the full blood of an
organism. Circulating half-life of a particular agent may vary depending on a multitude of
factors including, but not limited to, dosage, formulation, and/or administration route of the
agent. One of ordinary skill in the art is able to determine the circulating half-life of an agent
25 using well known methods in the art, such as the method described Chen *supra*.

[0183] In some embodiments, the fusion proteins described herein have high bioavailability.
In some embodiments, the fusion proteins have high bioavailability when administered, *e.g.*,
intravenously or subcutaneously. In some embodiments, the fusion proteins have high
bioavailability when administered subcutaneously. In some embodiments, the fusion proteins
30 have high subcutaneous bioavailability. In some embodiments, the fusion proteins have
bioavailability of at least about 40%, at least about 45%, at least about 50%, at least about 55%,
at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about
80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least

- about 99%, or more. In some embodiments, the fusion proteins have bioavailability of about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 98%, about 99%, or about 100%. In some embodiments, the fusion proteins have bioavailability of 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98%, 99%, or 100%. In some embodiments, the fusion proteins have bioavailability of about 40% to about 80%, about 40% to about 75%, about 40% to about 70%, about 40% to about 60%, about 50% to about 80%, about 50% to about 70%, about 50% to about 60%, about 60% to about 80%, or about 70% to about 80. In some embodiments, the fusion proteins have bioavailability of about 50% to about 60% (*e.g.*, 50% to 60%). In some embodiments, the fusion proteins have bioavailability, when administered subcutaneously, of at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or more. In some embodiments, the fusion proteins have bioavailability, when administered subcutaneously, of about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 98%, about 99%, or about 100%. In some embodiments, the fusion proteins have bioavailability, when administered subcutaneously, of 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98%, 99%, or 100%. In some embodiments, the fusion proteins have bioavailability, when administered subcutaneously, of about 40% to about 80%, about 40% to about 75%, about 40% to about 70%, about 40% to about 60%, about 50% to about 80%, about 50% to about 70%, about 50% to about 60%, about 60% to about 80%, or about 70% to about 80. In some embodiments, the fusion proteins have bioavailability, when administered subcutaneously, of about 50% to about 60% (*e.g.*, 50% to 60%).
- 25 **[0184]** “Bioavailability,” as used herein, refers to the fraction of administered drug that arrives in systemic circulation. Bioavailability of a particular agent may vary depending on a multitude of factors including, but not limited to, dosage, formulation, administration route, and/or properties of the agent. One of ordinary skill in the art is able to determine the bioavailability of an agent using well known methods in the art.
- 30 **[0185]** In some embodiments, the fusion proteins have high and/or stable serum levels when administered to a subject, *e.g.*, intravenously, subcutaneously, and/or according to any of the methods described herein. In some embodiments the fusion proteins are present in subject serum at a level of at least about 0.5 µg/mL, at least about 1 µg/mL, at least about 2 µg/mL, at

least about 3 µg/mL, at least about 4 µg/mL, at least about 5 µg/mL, at least about 6 µg/mL, at least about 7 µg/mL, at least about 8 µg/mL, or at least about 9 µg/mL 0.5 days, 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, or more after administration. In some embodiments the fusion proteins are present in subject serum at a level of at least about 0.5 µg/mL (*e.g.*, at least about 1 µg/mL, at least about 2 µg/mL, at least about 3 µg/mL, at least about 4 µg/mL, at least about 5 µg/mL, at least about 6 µg/mL, at least about 7 µg/mL, at least about 8 µg/mL, or at least about 9 µg/mL) for at least 0.5 days, at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, or more after administration. In some embodiments the fusion proteins are present in subject serum at a level of at least about 0.5 µg/mL (*e.g.*, at least about 1 µg/mL, at least about 2 µg/mL, at least about 3 µg/mL, at least about 4 µg/mL, at least about 5 µg/mL, at least about 6 µg/mL, at least about 7 µg/mL, at least about 8 µg/mL, or at least about 9 µg/mL) for at least 0.5 days, at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, or more after intravenous administration. In some embodiments the fusion proteins are present in subject serum at a level of at least about 0.5 µg/mL (*e.g.*, at least about 1 µg/mL, at least about 2 µg/mL, at least about 3 µg/mL, at least about 4 µg/mL, at least about 5 µg/mL, at least about 6 µg/mL, at least about 7 µg/mL, at least about 8 µg/mL, or at least about 9 µg/mL) for at least 0.5 days, at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, or more after subcutaneous administration.

Vectors and Host Cells

[0186] The disclosure also provides nucleic acid molecules that encode any of the fusion proteins or peptides described herein. In some embodiments, the nucleic acid molecules described herein are DNA molecules. In some embodiments, the nucleic acid molecules described herein are RNA molecules.

[0187] The nucleic acid molecules described herein can be transcribed from a promoter in an expression vector. In some embodiments, the vector is a non-viral vector. Exemplary non-viral vectors include, but are not limited to, plasmid DNA, transposons, episomal plasmids, minicircles, ministrings, and oligonucleotides (*e.g.*, mRNA, naked DNA). In some embodiments, the vector is a DNA plasmid vector.

[0188] In some embodiments, the vector is a viral vector. Viral vectors can be replication competent or replication incompetent. Viral vectors can be integrating or non-integrating. A number of viral based systems have been developed for gene transfer into mammalian cells, and a suitable viral vector can be selected by a person of ordinary skill in the art. Exemplary viral vectors include, but are not limited to, adenovirus vectors (*e.g.*, adenovirus 5), adeno-associated virus (AAV) vectors (*e.g.*, AAV2, 3, 5, 6, 8, 9), retrovirus vectors (MMSV, MSCV), lentivirus vectors (*e.g.*, HIV-1, HIV-2), gammaretrovirus vectors, herpes virus vectors (*e.g.*, HSV1, HSV2), alphavirus vectors (*e.g.*, SFV, SIN, VEE, M1), flavivirus (*e.g.*, Kunjin, West Nile, Dengue virus), rhabdovirus vectors (*e.g.*, rabies virus, VSV), measles virus vector (*e.g.*, MV-Edm), Newcastle disease virus vectors, poxvirus vectors (*e.g.*, VV), measles virus, and picornavirus vectors (*e.g.*, Cocksackievirus).

[0189] In some embodiments, the vector or expression cassette comprises one or more additional elements. Additional elements include, but are not limited to, promoters, enhancers, polyadenylation (polyA) sequences, and selection genes.

[0190] In some embodiments, the vector comprises a polynucleotide sequence that encodes an amino acid sequence at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% identical to an amino acid sequence recited in any of Tables 1-8. In some embodiments, the vector comprises a polynucleotide sequence that encodes an amino acid sequence that comprises or consists of an amino acid sequence recited in any of Tables 1-8. In some embodiments, the vector comprises a polynucleotide sequence that is at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% identical to a sequence recited in Table 9, below. In some embodiments, the vector comprises a polynucleotide sequence that comprises or consists of a sequence recited in Table 9, below.

Table 9. Nucleotide Sequences Encoding Fusion Proteins and Peptide Components

SEQ ID NO:	Sequence
410	GACAAGACCCATACATGTCCGCCTTGTCTGCGCCTGAGGCAGCAGGCG GACCATCAGTCTTCTTGTTCCTCCCAAGCCGAAGGACACCCTTATGATC TCACGCACCCCGAAGTAACTTGTGTAGTCGTTGATGTCTCACACGAAG

SEQ ID NO:	Sequence
	ACCCGGAAGTAAAGTTTAATTGGTATGTCGATGGTGTGAGGTCCACAA CGCTAAAACGAAACCGCGGGAAGAACAATACAACCTCCACATATCGAGT AGTCTCCGTCCTGACTGTTCTTCACCAGGACTGGCTGAATGGTAAAGAAT ACAAATGTAAAGTGAGTAACAAGGCCCTTGACAGCACCCATCGAGAAGAC GATATCCAAAGCCAAGGGGCAACCGCGCGAGCCACAAGTTTACACGCTC CCACCCTCAAGAGACGAACTCACCAAAAAATCAAGTGTCCCTGACATGTC TGGTGAAAGGATTCTATCCCAGCGACATAGCTGTAGAATGGGAGAGTAA TGGCCAACCCGAAAACAATTACAAAACCTACCCCCCGGTTTTGGATAGT GATGGTTCATTCTTCTCTATAGTAAACTTACCGTGGATAAGTCTCGGTG GCAGCAGGGGAACGTGTTTAGCTGTTCAGTCTCCATGAGGCACTCCAT AGTCACTATACGCAAAAGTCATTGTCCCTTTCTCCGGGCAAGGGCGGGT CAGACTCCTGGCAGGAAGAGGTAATTAAGCTTTGTGGGCGAGAAGCTCGT TAGGGCACAGATAGCAATCTGCGGGAAAAGTACAGCTTCCGATGCTGCC GGGGCTGACGCCAATGCGGGAGCACGCCAGCTCTACTCAGCCCTCGCCA ACAAGTGTGTGCATGTAGGTTGCACCAAAAGAAGTCTGGCACAGTTTTG C
411	GACAAGACGCATACTTGTCTCCCTGCCCAGCTCCCGAAGCGGCTGGGG GGGCCTCTGTCTTTCTGTTTCCGCCTAAGCCCAAGGACACGCTCATGATA AGTCGCACTCCGGAAGTCACCTGTGTTGTCGTCGATGTTAGCCATGAAG ATCCAGAGGTGAAATTTAACTGGTACGTCGACGGAGTGGAGGTTCAAA TGCTAAAACCAAACCGCGAGAAGAGCAATACAATTCCACGTATAGGGTC GTCTCCGTCCTGACAGTACTCCATCAGGATTGGCTGAATGGAAAAGAAT ACAAGTGCAAGGTTTCCAATAAAGCCTTGGCCGCACCTATTGAGAAAAC GATATCAAAAGCTAAGGGACAACCTCGGGAGCCGCAAGTATATACACTC CCCCCCTCTAGGGACGAAGTACAAAAAACCAAGTTAGTCTGACTTGTC TTGTGAAAGGTTTTTACCCGAGTGATATAGCCGTAGAATGGGAGAGCAA TGGCCAGCCCCGAAAACAATTACAAAACAACCTCCCCAGTATTGGACAGT GACGGGTCATTTTTTTTGTATTCTAAATTGACCGTAGACAAGTCACGCTG GCAACAAGGGAATGTATTTAGCTGTTCCGTCCTTCATGAGGCGCTCCATA GCCATTACACTCAGAAGTCTTTGTCACTGTACCGGGCAAGGGTGGTTCT GATTCATGGCAAGAGGAAGTGATTAAGCTGTGCGGTCGGGAGTTGGTAA GAGCTCAAATTGCGATTTGTGGCAAGAGCACTGCGTCCGATGCCGCAGG TGCTAATGCCGACGCCGGTGCGAGACAGCTTTATTCTGCGCTGGCCAAC AAGTGCTGCCACGTCGGATGCACCAAAACGGAGCCTTGCTCAGTTTTGC
412	GACAAAACCTCATACTTGTCCACCATGCCCAGCCCCGAGGCGGCTGGCG GCCCCAGCGTATTCTTTTCCCCC AAAACCTAAGGACACGCTTATGATA TCTAGAACCCCGGAGGTCACATGTGTCTGTCGTAGACGTAAGTCACGAAG ATCCTGAAGTCAAGTTTAACTGGTACGTCGATGGAGTCGAGGTCCATAA TGCTAAAACGAAGCCTCGCGAAGAACAGTATAATTCTACCTATCGCGTA GTCTCTGTCTCACCGTCTTGTCATCAAGACTGGTTGAACGGCAAGGAGTA CAAGTGTAAGGTTTCAAACAAAGCCCTTGCCGCGCCGATAGAGAAAACA ATTAGCAAAGCGAAGGGGAGCCGAGAGAGCCGCAAGTGTATACCTTTC CTCCTAGTAGAGACGAGTTGACCAAAAACAGGTGTCACTTACATGCCT CGTGAAAGGCTTCTACCCGAGTGATATTGCAGTCGAGTGGAATCCAAC GGCCAGCCCGAGAATAACTACAAAACGACGCCGCCCGTACTGGACAGTG ATGGAAGTTTTTTTTTGTACTCAAACTCACGGTTGACAAAAGTCGGTGG

SEQ ID NO:	Sequence
	CAGCAAGGGAACGTTTTAGCTGCTCTGTCCTCCATGAAGCACTCCATTC TCATTATACCCAGAAGTCTCTGTCTCTCTCCCTGGTAAGGGAGGTTCTG ACAGTTGGCAGGAAGAGGTAATAAACTCTGCGGTCGAGAGCTTGTTTCG AGCACAAATTGCTATATGTGGAAAATCTACCGCTTCAGACGCCGCCGGA GCTGATGCGGATGCCGGGGCTCGCCAGCTCTATAGCGCCTTGGCCAACA AATGTTGTCACGTTGGCTGCACGAAGCGCTCCCTGGCTCAGTTTTGC
413	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAACCTGTGTCTGTTGTGGATGTGTACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGTCCTTTTTCTTTATTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCTTTTCTTGACGCTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCATTGTCCCCAGGTAAGGGCGGAAGCG ACTCATGGCAAGAAGAAGTCATTAACCTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTGTCACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
414	GATAAACTCATACTTGCCCCCCTGCCCCGCGCCTGAAGCTGCAGGGG GGCCATCAGTCTTCTTGTTTCCACCAAAACCTAAGGATACTCTCATGATT AGCCGGACCCCTGAGGTGACATGTGTTGTGGTCGATGTATCTCATGAAG ATCCCGAAGTAAAATTTAAGTGGTACGTAGACGGGGTTGAAGTTCATAA CGCGAAAACGAAACCTCGGGAGGAGCAATATAATAGCACGTATAGAGT TGTTTCAGTCCTTACAGTTCTCCACCAAGACTGGCTGAATGGCAAGGAGT ATAAGTGTAAAGTATCCAATAAAGCCTTGGCTGCGCCAATCGAGAAGAC GATCAGCAAAAGCCAAAGGTCAGCCTCGCGAACCGCAGGTCTATACATTG CCCCCTTCACGCGACGAACCTACGAAAAATCAAGTCTCTTTGACTTGCCT TGTGAAAGGCTTCTACCCCTCCGATATTGCCGTCGAATGGGAAAGCAAT GGACAGCCGGAATAATTACAAAACGACACCCCCCGTGTGGATTCCG ATGGGTCTTCTTCTCTATTCCAAGCTGACGGTCGATAAGTCTCGATGG CAGCAGGGAAATGTCTTCTCTTGCTCCGTCCTTCATGAGGCATTGCACAG CCATTATACTCAAAGAGTCTCTCTCTGTCTCCAGGCAAAGGGGGTTCCG ACTCTTGGCAAGAAGAGGTCATAAACTGTGCGGCCGGGAGCTCGTCAG AGCGCAGATCGCTATATGTGGAAAATCCACCGCGAGTGACGCAGCAGGT GCACAAGCCGACGCAGGAGCTAGGCAACTGTACTCAGCCCTTGCCAATA AGTGTGTCACGTAGGTTGTACTAAACGCTCCCTGGCACAATTTGT
415	GATAAGACACACAGTGCCACCCCTGCCCTGCCCCAGAGGCAGCCGGAG GTCCTAGTGTGTTTCTGTTCCCCCAAGCCCAAGGACACCCCTTATGATA TCTAGGACACCAGAAGTTACGTGCGTCGTTGTGGACGTTAGCCACGAAG ACCCAGAAGTGAAGTTTAATTGGTACGTTGATGGAGTCGAAGTGCACAA

SEQ ID NO:	Sequence
	TGCAAAAACAAAACCACGAGAAGAGCAGTATAACAGTACTTATAGAGT AGTCAGCGTCCTTACTGTATTGCATCAGGATTGGCTGAATGGGAAGGAA TATAAATGTAAGGTTAGCAATAAAGCCCTTGCGGCTCCTATCGAGAAAA CTATTAGCAAAGCAAAGGGCCAACCCCGAGAGCCCCAAGTTTATACACT GCCACCCAGTCGAGATGAGCTGACTAAAAATCAAGTATCCCTGACCTGC TTGGTTAAGGGGTTTTATCCTAGTGACATCGCGGTTGAGTGGGAATCCAA CGGCCAACCGGAGAATAATTACAAAACCACGCCACCTGTATTGGATTCC GATGGTAGCTTCTTTCTCTATAGTAACTTACAGTCGATAAGTCAAGATG GCAGCAGGGAACGTATTTTCATGCTCAGTTCTGCATGAGGCCCTGCACT CCCATTACACTCAAAAATCACTGAGCCTCAGTCCTGGTAAGGGTGGCTCT GACTCATGGCAGGAGGAAGTAATCAAGCTGTGTGGGAGGGAATTGGTA AGGGCTCAGATTGCAATTTGTGGAAAGAGCACAGCGTCTGACGCTGCAG GTGCCGACGCACAGGCGGGCGCGAGGCAGCTCTACAGTGCTCTTGCGAA CAAGTGTTGTCATGTAGGTTGCACGAAACGAAGTTTGCGCAATTCTGT
416	GATAAAACACACACCTGCCCCCTTGCCCAGCACCTGAAGCAGCGGGTG GTCCCAGCGTTTTTCTTTTCCCCCTAAGCCAAAGGACACGCTCATGATA AGTCGCACCCCGGAGGTCACCTGCGTCGTTGTTGACGTATCACATGAAG ATCTGAGGTGAAGTTTAATTGGTACGTAGATGGTGTGAGGTCCACAA CGCAAAGACGAAACCGAGGGAAGAACAGTACAACAGTACTTATCGCGT AGTCTCCGTTCTGACTGTCCTGCATCAAGATTGGTTGAACGGGAAGGAG TACAAGTGCAAAGTTAGTAACAAGGCTCTCGCGGCCCCAATTGAGAAGA CGATATCCAAAGCGAAAGGACAGCCGAGAGAGCCCCAAGTCTACACTCT GCCCCCTTCCAGGGATGAGCTCACCAAAAATCAGGTCAGTCTCACGTGC CTGGTTAAGGGATTCTACCCAAGTGATATAGCAGTTGAATGGGAGAGTA ACGGCCAGCCCGAGAACAACATAAACTACACCGCCCGTTCTTGATTC CGATGGGTCTTTCTTCTTTATAGTAAGCTCACCGTTGATAAGTCCCGAT GGCAGCAAGGTAATGTCTTCTCATGTTTCAGTTCTTCATGAAGCCCTGCAT TCCATTATACACAAAAGAGCTTGTCTTGTACCCGGGCAAAGGCGGTA GCGATTCTTGGCAAGAAGAAGTTATAAAGTTGTGCGGTAGGGAACCTGGT ACGCGCTCAAATAGCTATATGCGGTAAGTCTACTGCTTCAGATGCGGCT GGCGCACAGGCACAGGCCGGTGCTAGACAACCTCTATAGTGCGCTGGCCA ACAAGTGCTGCCATGTGGGGTGTACAAAACGGAGTCTTGCCCAGTTTGT
417	GACAAAACATCATACATGCCCCCATGCCCAGCACCCGAAGCGGCCGGAG GTCCGCTGTCTTTCTGTTTCCGCCGAAACCTAAAGATACGTTGATGATT AGCAGAACCCCTGAGGTAACATGTGTGGTAGTCGATGTCTCCCATGAGG ACCCCGAGGTAAAGTTCAATTGGTATGTTGACGGCGTCGAAGTCCATAA CGCAAAAACGAAGCCCCGAGAGGAGCAATATAACTCTACCTATCGCGTT GTTTCTGTTTTGACTGTGTTGCACCAGGATTGGCTCAACGGCAAGGAATA CAAATGTAAAGTGTCCAACAAGGCCCTTGCTGCACCTATCGAAAAAACG ATTAGTAAGGCAAAGGGACAACCGCGCGAACCACAGGTATATACTTTGC CGCCTAGCAGAGATGAACTACCAAGAATCAAGTTTCCCTTACCTGTTTG GTTAAAGGATTTTACCCGCTCTGACATAGCTGTTGAATGGGAGAGCAATG GTCAGCCGGAAAAATAATTATAAAACACCCCGCCAGTATTGGATTACAG TGGGTCTTTTCTTGTATTCTAAACTTACCGTGGATAAGTCTAGGTGGC AACAGGGAAACGTCTTTTCATGTAGTGTACTTCATGAAGCCCTCCATAGT

SEQ ID NO:	Sequence
	CACTACACGCAGAAATCCTTGTCTCTTAGTCCGGGTGAAGGTGGGTCTG ATTCTTGGCAGGAAGAGGTGATAAAGCTCTGTGGTCGGGAACCTTGTTAG GGCGCAGATCGCTATTTGCGGCAAATCTACAGCATCAGATGCCGCCGGA GCTGATGCGAACGCAGGAGCGAGGCAGCTGTACTCCGCACCTTGCTAACA AGTGTGTCATGTCGGCTGCACCAAGAGGAGTCTTGCTCAATTCTGC
418	GATAAGACCCATACATGCCCGCCATGTCCCGCACCCGAGGCAGCGGGTG GACCCCTCTGTCTTTCTGTTCCCTCCAAAGCCAAAAGATACCCTGATGATT AGCCGAACCCCGGAGGTGACTTGTGTCGTAGTAGATGTCAGTCACGAGG ATCCCGAAGTAAAGTTTAATTGGTATGTGGACGGTGTGGAGGTACATAA CGCTAAGACGAAACCCCGAGAGGAACAATACTACTACGTACAGGGTCT GTCTCAGTGCTCACGGTCCCTGCACCAGGACTGGCTTAATGGGAAGGAAT ATAAATGCAAAGTCTCTAATAAGGCGCTTGCTGCACCTATTGAAAAAC GATTTCTAAGGCGAAGGGACAACCCCGGAGCCACAAGTCTACACCCTT CCTCCAAGCAGAGATGAGCTTACGAAAAATCAAGTGTCTCTTACGTGCC TCGTAAAGGGCTTTTACCCATCCGACATTGCGGTGGAGTGGGAATCAAA CGGGCAGCCGGAATAAATACTACAAAACAACGCCGCCTGTATTGGATTCC GACGGCTCTTTCTTCTTTACAGCAAACTGACAGTCGATAAATCCAGATG GCAACAAGGGAACGTTTTTTCATGTTCCGTTCTGCATGAAGCCCTTCACA GTCATTACACCCAAAAGTCACTTTCATTTTACCAGGCGAGGGGGGGT AGACTCCTGGCAAGAGGAAGTTATAAAGTTGTGCGGCAGGGAAGTGGTT AGAGCGCAGATAGCGATTTGCGGAAAATCTACTGCGAGTGATGCTGCGG GAGCGAATGCGGACGCCGGGGCCCCGACAGCTCTATTCCGCACTCGCCAA TAAGTGCTGCCATGTTGGTTGTACGAAGAGAAGTCTTGACACAATTTTGC
419	GATAAGACACATACATGCCCCCCTGCCCGGCTCCCGAAGCTGCCGGGG GACCGTCAGTGTTTTTGTTCGCCCCAAGCCGAAGGATACTTTGATGATT AGTCGGACACCAGAAGTGACATGTGTTGTCGTTGACGTGAGTCACGAGG ATCCCGAGGTCAAGTTCAACTGGTACGTTGATGGGGTTGAAGTTCAACA CGCTAAAACGAAACCCCGCAAGAGCAGTATAACTCCACTTACCGGGTCT GTCAGTGTCCTGACGGTCTTGCACCAGGACTGGCTGAATGGAAAGGAAT ACAAGTGTAAGTTTCCAATAAAGCACTGGCCGCCCCGATCGAAAAAAC AATTTCCAAAGCTAAGGGACAGCCAGGGAACCGCAAGTTTATACTCTT CCACCCTCCCGGGATGAAGTACCAAAAAACCAAGTGTCTTTGACGTGCC TCGTAAAGGGCTTCTACCCGTCAGACATAGCTGTGCAATGGGAGTCTAA TGGACAGCCGGAACAATTATAAGACTACACCGCCGGTGCTTGATAGT GATGGAAGTTTCTTTTGTACTCCAACTTACGGTCGATAAAGCCGGTG GCAGCAGGGAAACGTATTCAGTTGTAGCGTTCTGCATGAAGCTCTTCATT CTCACTACACCCAGAAGTCTCTGTCTCTGAGCCCCGAGAGGGTGGATC TGATTCTTGGCAGGAAGAAGTGATAAAGTTGTGCGGCCGGGAATTGGTA CGCGCCCAGATAGCCATTTGCGGGAAGTCTACGGCGAGTGACGCAGCAG GTGCTGACGCGGACGCTGGTGCTAGACAGCTGTATTCTGCCCTGGCTAAT AAGTGTTGCCACGTTGGCTGCACCAAGAGATCCCTGGCCCAATTCTGT
420	GACAAGACACATACTTGTCCCCCTGCCAGCTCCAGAAGCTGCCGGAG GGCCGTCAGTCTTCTTTTCCCTCCAAAACCTAAGGATACGCTTATGATT TCTCGAACGCCAGAGGTTACGTGTGTAGTCGTGGACGTTTCCACGAGG ATCTGAGGTCAAGTTTAACTGGTATGTAGACGGGGTTGAGGTCCATAA TGCCAAGACAAAGCCGCGCGAGGAACAATAACAGTACATATAGGGT

SEQ ID NO:	Sequence
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421	GATAAAACCCATACATGTCTCCGTGTCCCGCTCCAGAAGCCGCTGGCG GGCCATCTGTGTTTTTGTTCACCCCAAGCCTAAGGATACGTTGATGATC AGCAGGACCCCGGAGGTACATGCGTAGTAGTTGACGTTTCTCATGAAG ACCCAGAAGTAAAATTTAACTGGTATGTGATGGCGTCGAAGTACATAA TGCTAAACTAAGCCAGGGAAGAGCAATACAATTCAACGTACCGAGTT GTGAGTGTCTTACGGTCCTGCACCAAGACTGGTTGAACGGCAAAGAGT ACAAATGCAAAGTGTCTAACAAGGCATTGGCCGCGCCTATAGAAAAGAC CATTAGCAAAGCAAAGGGCAGCCTCGGGAACCCAGGTCTACACGCTG CCACCTTCCCGAGATGAATTGACGAAAACCAGGTCTCTTTGACCTGCTT GGTTAAAGGCTTCTACCCAAGCGACATTGCAGTGGAGTGGGAGTCTAAC GGGCAACCCGAAAACAACATAAGACGACTCCCCCTGTTCTTGATTCTG ATGGGAGTTTTTTTCTGTACAGTAAGTTGACAGTGGATAAATCAAGATG GCAGCAAGGTAATGTCTTCTTGTTCAGTGCTTCACGAAGCATTGCATT CTCACTACACACAAAAGTCTTTGTCTTGTCTCCAGGTGAAGGCGGTAGC GATTCATGGCAAGAAGAAGTCATTAAGCTGTGTGGAAGGGAAGTGGTTA GGGCCCCAATTGCGATATGTGGAAAGTCTACGGCGAGTGATGCGGCCGG TGCTCAAGCGGATGCGGGTGCTAGACAGTTGTACTCAGCCCTTGCGAAC AAATGTTGTACGTTGGCTGTACGAAACGCAGCCTTGCTCAATTCTGC
422	GATAAACTCACACATGCCCCCATGCCCAGCACCGGAAGCTGCCGGAG GACCGTCTGTATTCTCTTTCCGCCCAAACCGAAAGACACGTTGATGATT TCTCGGACTCCCGAGGTAACCTTGTGTCGTGGTTCGACGTCTCACACGAGG ACCCGGAGGTCAAATTTAACTGGTATGTGATGGGGTGGAGGTCCATAA TGCTAAGACGAAGCCAGAGAAGAACAGTATAACTCTACTTATAGAGTT GTAAGCGTGCTCACTGTATTGCACCAGGACTGGCTCAACGGGAAAGAAT ATAAGTGTAAGGTCTCAAACAAAGCTCTCGCAGCCCCGATAGAGAAAAC AATATCTAAGGCCAAGGGCCAACCGCGCGAGCCGAGGTTTATACACTT CCACCCTCCCGCGATGAGCTGACCAAGAACCAGGTCTCTCTCACCTGTCT CGTAAAGGGCTTTTATCCCTCCGACATTGCAGTGGAGTGGGAATCAAAC GGCCAGCCGGAATAATTACAAGACCCTCTCCCGTCTCGACTCCG ATGGGTCAATTTTCTGTACAGTAAGCTCACCCTTGATAAGTCAAGGTGG CAGCAGGGCAACGTGTTTAGCTGTAGTGTCTGCATGAGGCGCTCCACA GTCCTACACCCAGAAAAGTCTGAGCCTTTCCCAGGTGAGGGTGGTAG CGATAGCTGGCAGGAGGAAGTAATTAACCTCTGCGGTAGAGAATTGGTA

SEQ ID NO:	Sequence
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423	GACAAAACACATACATGCCCCCCTTGCCCGGCTCCCGAGGCCGCCGGTG GTCCTAGCGTCTTTCTTTTCCCTCCCAAACCCAAAGACACACTTATGATT AGCAGAACTCCCGAGGTAACATGTGTGGTCGTAGACGTAAGTCACGAAG ATCCCGAAGTTAAATTCAACTGGTACGTTGATGGTGTGGAAGTTCATAAT GCAAAAACCAAACCGCGAGAGGAACAGTATAACTCTACCTACCGCGTGG TCTCAGTGCTGACTGTCTGCATCAGGACTGGCTCAACGGGAAGGAATA TAAGTGCAAAGTGAGTAATAAGGCCCTTGACGCTCCCATAGAAAAGACG ATATCAAAGGCTAAAGGACAGCCGAGGGAGCCACAGGTGTACACTTTGC CTCCGAGTAGAGATGAACTCACTAAAAACCAAGTAAGTTTGACATGCCT GGTCAAAGGTTTTTACCCCACTGATATAGCGGTTGAGTGGGAGTCCAAT GGGCAACCGGAGAACAACACTATAAGACTACTCCACCTGTCTGGATAGCG ATGGAAGTTTTTTTCTTTACTCAAAGCTGACGGTGGATAAGAGTCGATGG CAGCAGGGCAATGTGTTTAGCTGTTCTGTGCTTCACGAAGCACTTCACTC TCATTATACCCAGAAGTCATTGAGCCTTTCCCTTGGTGAAGGAGGGTCA GATTCTGGCAGGAGGAGGTTATAAAGCTGTGTGGCCGGGAACCTCGTGC GAGTCTCAAATTGCGATCTGTGGAAAATCCACCGCTAGTGATGCGGCGGG AGCACAAGCTCAAGCGGGCGCTCGACAACCTTTATAGCGCTTTGGCTAAT AAGTGCTGCCATGTGGGTTGTACAAAGCGCAGCCTCGCTCAATTTTGC
424	GATAAGACGCACACTTGCCCTCCTTGCCCGGCACCCGAAGCCGCTGGTG GGCCTAGTGTATTCTGTTCCTCCCGGAAGCCGAAGGATACTCTTATGATT TCACGCACGCCCCGAGGTTACATGCGTAGTAGTGGACGTATCTCACGAAG ATCCCGAAGTCAAGTTCAATTGGTATGTCGACGGAGTAGAAGTTCACAA CGCAAAGACAAAACCGCGGGAAGAGCAATACAACCTCCACGTACCGCGT CGTTTCTGTCTTACGGTCTTGCACCAGGACTGGCTCAATGGCAAGGAGT ATAAGTGCAAGGTATCCAACAAGGCCCTTGCCGCACCTATTGAAAAGAC TATCAGCAAGGCCAAGGGACAGCCAAGGGAGCCTCAAGTCTACACGCTC CCGCTAGTAGAGACGAGTTGACAAAGAATCAAGTGAGTTTGACTTGTC TGGTTAAAGGTTTTTACCCGTCAGATATTGCAGTAGAATGGGAATCTAAC GGACAACCCGAAAACAACATAAAAACGACGCCTCCTGTGTTGGATTGAG ATGGGTCAATTTTTCTCTACTCAAAGCTCACGGTAGATAAATCAAGATGG CAACAAGGCAATGTATTTTCTGCTCCGTGCTCCACGAGGCTCTGCACAG CCATTATACGCAAAAGAGTCTGTCTTTGAGCCAGGTGAGGGTGGCTCC GATTCTGGCAGGAGGAAGTAATTAAGTTGTGCGGCAGGGAACCTTGTTG GCGCACAAATAGCCATTTGTGGTCAGAGCACAGCATCAGATGCCGCCGG AGCCGACGCCAACGCAGGTGCCCCGCAACTTTATTCTGCCCTCGCAAAC AAATGCTGCCACGTGCGGCTGCACGAAGAGGAGCCTCGCCCAATTTTGC
425	GATAAGACCCATACGTGCCCGCCATGTCCAGCCCCCGAGGCAGCCGGAG GTCTTCCGTTTTCTTTTCCCCCCTAAGCCCAAGGACACTCTGATGATCT CCCGGACGCCTGAAGTCACTTGCGTAGTCGTAGACGTTTCACATGAGGA TCCAGAAGTTAAATTTAACTGGTACGTCGATGGCGTCGAGGTCCATAAC GCGAAAACCAAGCCCAGGGAGGAACAATATAACTCCACCTATAGGGTC GTGAGTGTGCTCACCCTTTTGCACCAAGACTGGCTCAACGGGAAAGAGT ACAAATGTAAAGTTTCAAATAAGGCTTTGGCCGCCCAATAGAGAAGAC

SEQ ID NO:	Sequence
	TATATCCAAGGCTAAGGGACAGCCTCGAGAACCGCAGGTATATACGCTT CCTCCGTCTAGGGATGAACCTACAAAAAACCAGGTTTCTTTGACCTGCTT GGTAAGGGATTTTATCCCTCCGACATTGCGGTCGAATGGGAGAGCAAC GGACAGCCGGAACAATTACAAAACGACACCCCGGTTTTGGACTCTG ATGGAAGCTTCTTCTCTATAGTAAGTTGACCGTAGACAAGTCTCGCTGG CAGCAGGGAAACGTCTTCAGTTGCTCAGTTCTCCATGAGGCGTTGCATA GTCCTATACACAGAAGAGTCTTAGTTTGTCTCCAGGAGAAGGAGGTTT TGATTCTTGGCAAGAGGAGGTAATCAAATTGTGTGGCCGAGAAGTTGTT AGAGCTCAGATAGCCATCTGCGGACAGTCTACGGCGTCCGATGCGGCCG GAGCTAATGCTGACGCAGGTGCGCGACAGCTGTACTCCGCACTGGCGAA TAAGTGCTGCCACGTGGGATGCACTAAGCGGTCTCTCGCGCAATTCTGT
426	GATAAAACCCACACCTGTCCACCATGCCCGGCGCCGGAAGCCGCCGGG GACCCAGCGTATTTCTTTCCCCCCCCAAGCCCAAAGACACGCTGATGATT TCACGAACGCCGGAGGTGACTTGCCTGGTAGTGGACGCTCTCCATGAGG ATCCCGAAGTTAAATTTAATTGGTATGTAGATGGTGTGAGGTCCATAAT GCTAAACAAAGCCGCGGGAAGAGCAATATAACTCCACCTATAGAGTG GTCTCTGTACTCACTGTCTGCACACAGGATTGGCTGAATGGGAAAGAGT ACAAGTGTAAGTTAGCAACAAGCGCTCGCCGCGCTATCGAAAAAAC GATTTCCAAAGCAAAGGGCCAAACCAGAGAACCCAGGTTTACACCTG CCACCCAGTCGAGATGAACCTACTAAGAATCAGGTGTCCCTTACATGCC TCGTCAAGGGATTCTATCCGAGCGATATAGCGGTGGAATGGGAGAGTAA CGGTCAACCCGAAAATAACTATAAAACCACTCCGCCGGTACTCGATTCT GACGGTTCCTTCTTTCTTTATTCCAAACTGACTGTAGACAAATCACGGTG GCAGCAGGGCAACGTGTTTAGCTGCTCTGTACTCCATGAGGCCCTGCATT CTCATTATACTCAAAAGAGTCTGAGTCTGAGTCCAGGTGAAGGGGGTTC CGATTCTATGGCAAGAGGAAGTCATTAAACTCTGCGGAAGGGAACTTGTA AGAGCACAAATCGCGATTTGTGGGCAATCTACCGCATCCGACGCGGCTG GAGCAGATGCAGATGCCGAGCGAGGCAGCTGTATTACGATTGGCTAA CAAATGTTGCCATGTTGGATGTACGAAGAGATCACTTGCACAGTTCTGT
427	GATAAGACTCATACCTGCCCGCCCTGTCCCGCACCCGAGGCTGCCGGAG GGCCATCAGTGTTCTTTTCCCACCAAGCCGAAGGATACACTTATGATC AGCAGGACACCCGAAGTGACCTGTGTAGTCGTAGACGTGTCCACGAAG ACCCCGAAGTAAAATTTAATTGGTATGTCGATGGCGTAGAGGTCCACAA CGCGAAAACGAAACCCCGCGAAGAACAATATAATTCCACATACCGAGTT GTCAGCGTCTCACTGTTCTCCATCAGGACTGGCTGAATGGGAAGGAAT ATAAGTGCAAGGTCTCAAACAAGGCGCTGGCGGCCCCCATAGAGAAAA CGATTTCTAAGGCCAAAGGACAGCCACGGGAACCGCAGGTCTATACGCT CCCACCTAGTAGGGATGAGTTGACCAAGAATCAGGTATCCCTCACATGT CTCGTCAAGGGATTCTATCCCAGCGACATAGCCGTGGAGTGGGAATCTA ACGGTCAACCTGAGAATAACTATAAAACAACCCCCCGGTCCTCGACTC CGATGGTAGCTTCTTTCTGTATTCCAAACTGACGGTAGATAAAAGCCGAT GGCAACAGGGTAACGTCTTTAGTTGTTCTGTATTGCACGAGGCGCTCCAT AGTCACTACACACAGAAGTCTTTGAGCCTCTCACCTGGGGAGGGGGTA GCGATTCTTGGCAGGAGGAAGTGATCAAACCTGTGCGGCAGGGAAGTGT CAGAGCACAGATAGCAATATGCGGTACAGGTACGGCCTCTGACGCCGCC GGTGCGGAGGCTGAGGCAGGGGCGAGACAGCTCTACAGCGCTCTTGCAA

SEQ ID NO:	Sequence
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428	GATAAGACCCACACATGTCCGCCATGTCCAGCCCCAGAGGCAGCAGGGG GCCCCGTCCGTATTCTTGTTCCTCCCGAAACCCAAAGATACCCCTTATGATT AGTCGAATCCAGAAGTCACGTGTGTGGTGGTGGACGTATCCCACGAGG ACCCCGAAGTGAAATTCAATTGGTATGTGGACGGGGTGGAAGTCCATAA CGCTAAGACGAAGCCCAGAGAGGAGCAGTACAATTCTACCTATCGGGTT GTATCTGTGCTTACTGTTCTCCATCAAGATTGGCTGAACGGGAAGGAATA CAAATGTAAAGTTAGTAACAAAGCATTGGCAGCTCCTATCGAAAAGACG ATAAGCAAGGCTAAAGGTCAACCCCGAGAGCCTCAGGTCTACACTTTGC CGCCCTCCAGGGATGAGCTTACCAAGAACCAAGTGAGCTTGACGTGTCT CGTGAAGGGATTCTACCCATCAGATATAGCGGTAGAATGGGAGTCTAAT GGGCAGCCCGAGAACAACCTATAAGACCACCCCTCCCGTTCTTGACTCCG ACGGTTCCTTTTTCTTGTACTCCAAACTCACGGTCGACAAGTCTAGGTGG CAGCAAGGCAATGTTTTTCAGTTGTTCCGTGCTGCACGAAGCTCTTCATTC TCACTATACGCAAAAAAGCCTGAGTCTTTCACCTGGAGAGGGGGGTTC GATTCTTGGCAGGAAGAAGTCATTAAGCTGTGCGGCAGAGAAGCTTGTGC GCGCACAAATTGCTATTTGTGGACAGTCAACTGCATCTGACGCCGCTGG AGCCCAAGCGGACGCAGGGGCAAGGCAGCTTTATTACGCGCTTGCGAAT AAGTGTGCCATGTGGGTGTCACGAAACGAAGCCTGGCGCAATTTTGT
429	GATAAGACACATACATGTCTCCCTGTCCCGCTCCGGAGGCAGCCGGTG GGCCTTCAGTTTTCTTGTTCCTCCCGCAAGCCTAAGGACACGTTGATGATA TCCCGAACACCAGAGGTCACATGCGTCGTCGTGGACGTCTCACACGAGG ACCCTGAAGTGAAATTCAACTGGTATGTAGACGGGGTCGAAGTTCACAA TGCGAAAACCTAAACCTCGCGAGGAGCAATATAACTCAACATACCGCGTA GTGTCCGTCTTGACTGTCTTCATCAGGATTGGCTGAATGGTAAAGAATA TAAATGTAAAGTTTCTAATAAAGCGCTTGCGGCACCCATTGAGAAGACA ATTTCCAAAGCCAAAGGCCAACCCCGAGAGCCTCAGGTATATACGCTGC CTCCGTCTCGAGATGAGTTGACAAAAAATCAAGTCAGCTTGACTTGTCTT GTAAAGGGGTCTATCCGTGACACATAGCAGTGGAGTGGGAATCCAACG GGCAACCAGAAAATAATTACAAACCACTCCGCCCCGTGCTTGACTCAGA TGGGAGCTTCTTCCTTTATAGCAAACTTACGGTAGATAAATCCAGATGGC AGCAAGGCAACGTATTCAGCTGTAGTGTGCTGCATGAAGCGCTTCACTC CCATTATACTCAAAAATCTCTTTCTGTGTCACCGGGCGAGGGCGGAAGTG ATAGTTGGCAGGAAGAGGTCATCAAGCTCTGTGGGAGAGAGCTTGTACG CGCTCAGATTGCTATATGCGGCCAGTCAACTGCAAGCGATGCAGCGGGT GCCGATGCCCCAAGCGGGGGCACGGCAACTCTACTCAGCCCTCGCGAATA AATGTTGTCATGTAGGGTGTACTAAGAGAAGCCTCGCGCAATTTTGT
430	GATAAAACGCATACTTGCCCCCGCTGCCAGCACCTGAGGCAGCCGGCG GCCCTAGTGTCTTCTTGTTCCTCCCGCCCAAGCCCAAGGATACACTCATGATC TCCCGAACGCCAGAGGTCACATGCGTAGTTGTTGACGTTTCCCATGAGG ACCCTGAAGTGAAATTTAACTGGTACGTCGACGGCGTTGAGGTTCAAA CGCTAAGACTAAGCCAAGAGAGGAACAGTACAATTCAACTTATAGAGTG GTGTCTGTATTGACAGTTCTCCATCAGGATTGGCTGAACGGAAAAAGAA ATAAGTGCAAGGTCTCAAAATAAGGCGCTCGCTGCACCCATAGAAAAAAC CATATCAAAAGCGAAGGGGCAACCAAGAGAACCCAGGTGTACACGCT

SEQ ID NO:	Sequence
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431	GACAAGACTCATACTTGTCCGCCCTGCCCCGCTCCTGAGGCTGCCGGAG GCCCTTCAGTATTCTTGTTTCCGCCGAAACCGAAGGATACCTTGATGATT AGTAGGACACCGGAAGTCACCTGCGTAGTGGTGGACGTAAGCCACGAA GATCCCGAAGTAAAGTTTAATTGGTATGTTGATGGCGTAGAGGTGCATA ATGCGAAAACCAACCTAGGGAGGAACAGTACAATAGTACTTACCGCGT AGTGTCAAGTGCTTACCGTGCTGCATCAGGACTGGCTTAATGGGAAGGAA TACAAATGTAAAGTATCCAATAAAGCGCTGGCGGCTCCCATCGAGAAAA CGATCTCAAAAGCCAAAGGACAACACGGAACCGCAGGTCTATACTCT GCCACCTTCAAGAGACGAACTTACCAAGAACCAAGTCTCATTGACGTGC TTGGTAAAAGGTTTTATCCGTCTGACATCGCTGTTGAATGGGAGTCTAA CGGCCAGCCGGAGAACAATTACAAAACAACCTCCACCAGTCTTGGATTCA GATGGGTCTTTTTTTTTGTATTCAAAGCTTACCGTTGACAAAAGCCGCTG GCAACAAGGAAACGTTTTACGCTGCAGTGTGCTGCACGAAGCGCTCCAC AGTCATTATACCCAGAAATCTTTGAGCCTGTCTCCAGGGGAAGGTGGGA GTGACTCTTGGCAAGAAGAGGTTATCAAACCTTGCAGGGCGGGAGCTGGT AAGGGCCCCAAATTGCAATATGCGGCAAAAGTACTGCATCTGATGCCGCT GGGGCCGATGCTAACGCGGGCGCAAGACAACCTTTATAGCGCGTTGGCGA ACAAATGCTGTCATGTGGGATGCACCAAAACAAAGTTTGGCGCAATTTTG T
432	GATAAACTCACACGTGTCCGCCATGCCCCGCACCTGAAGCGGCGGGTG GTCCGAGCGTGTTTTTGTTCGCCCTAAGCCCAAGGATACCCTGATGATT AGTCGGACACCCGAAGTAACATGTGTCTCGTGGATGTAAGTCACGAGG ATCCCGAAGTGAAATTCAACTGGTATGTGGATGGAGTTGAAGTCCATAA TGCGAAAACAAAACCGAGAGAGGAACAGTACAACCTCAACATACCGGGT GGTAAGTGTACTGACGGTACTCCACCAGGACTGGCTGAATGGTAAGGAG TACAAATGCAAAGTTTCAAATAAGGCGCTCGCTGCCCCCATCGAGAAAA CCATTAGTAAGGCTAAAGGTCAACCTAGGGAGCCACAAGTATATACATT GCCGCCTTCTAGAGATGAGCTGACCAAAAACAGGTCAGCCTGACCTGT TTGGTGAAAGGCTTCTATCCAAGCGACATTGCTGTGAGTGGGAGTCAA ATGGGCAGCCGGAAAATAACTATAAAACGACTCCTCCTGTTCTCGACTC CGATGGTTCATTCTTCTCTACTCAAAGCTTACCGTGGATAAATCCAGGT GGCAACAAGGTAACGTGTTCTCATGTTCCGTTCTGCACGAAGCACTGCAT TCCATTATACAAAAAATCCCTGAGCCTCTACCTGGGGAGGGCGGAA GCGATAGTTGGCAAGAGGAAGTAATAAAGCTGTGTGGCAGGGAACCTCGT AAGGGCTCAGATTGCGATATGTGGAAAAAGCACTGCTTCTGACGCCGCA

SEQ ID NO:	Sequence
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433	GACAAAACCCACACTTGTCCGCCCTGTCCCGCTCCGGAGGCTGCAGGCG GCCCAAGTGTGTTTCTTTTCCCCCAAAGCCGAAAGACACCTTGATGATA TCCCGCACACCCGAAGTGACTTGCCTTGTCTGACGTGTCTCATGAGGA CCCAGAAGTCAAGTTTAATTGGTACGTTGATGGCGTGGAAGTTCACAAT GCGAAAACCTAAGCCCAGAGAGGAGCAATATAACTCAACCTACCGGGTG GTAAGTGTTCTGACAGTTCTCCACCAGGACTGGTTGAACGGAAAAGAAT ACAAATGCAAAGTGAGTAACAAAGCCCTGGCTGCCCTATCGAAAAGAC CATATCCAAAGCGAAGGGCCAGCCACGGGAACCGCAAGTATATACACTT CCACCATCTAGAGATGAGCTTACAAAGAACCAGGTGTCCCTTACCTGCC TTGTCAAAGGCTTCTATCCCTCTGACATCGCAGTGGAGTGGGAGTCCAAC GGACAACCAGAGAACAACCTATAAGACAACGCCGCCAGTACTGGATTCA GATGGTTCAATTCTTCTTGTATTCTAAACTGACTGTTGATAAATCCCGATG GCAGCAGGGCAACGTTTTTAGTTGTAGTGTCTGCACGAAGCCCTTCATT CCCATTATACACAAAATCTCTTTCCCTCAGCCCAGGCGAGGGAGGAAG TGACAGTTGGCAAGAGGAGGTGATAAAGCTCTGTGGGAGGGAGCTGGT ACGCGCACAGATTGCAATCTGCGGAAAGAGCACAGCAAGCGATGCTGCT GGGGCCGATGCCGATGCTGGCGCTCGACAATTGTATTACGCTCTTGCTAA CAAATGCTGTACGTAGGATGCACTAAACAGAGCCTTGCTCAATTTTGT
434	GATAAGACCCACACATGTCCACCATGCCAGCCCCAGAAGCGGCAGGTG GTCTTCTGTGTTTCTCTTTCTCCCAAACCGAAAGATACTCTGATGATA AGCCGGACCCAGAAAGTTACGTGCGTTGTAGTAGACGTGTCTCACGAGG ACCCAGAAGTGAAGTTTAACTGGTATGTGACGGTGTAGAAGTTCATAA TGCGAAAACAAAGCCCAGGGAAGAACAATATAATTCAACGTACCGGGT CGTTTCCGTGCTGACAGTTCTGCACCAAGATTGGCTCAACGGGAAAGAG TACAAATGCAAAGTATCAAATAAGGCCTTGGCTGCGCCGATTGAAAAGA CGATTTCCAAAGCAAAGGGCCAGCCAAGGGAACCCAGGTCTATACCTT CCCTCCTAGCAGAGATGAACTTACAAAAACCAAGTCTCCCTCACCTGC CTGGTCAAAGGATTCTATCCCTCAGATATAGCAGTAGAATGGGAAAGTA ACGGGCAGCCCGAAAACAATTATAAGACCACTCCTCCAGTACTCGATT AGACGGTAGCTTCTTTCTGTATTCCAAGCTGACCGTAGATAAAAGTAGGT GGCAGCAAGGTAATGTCTTCTCATGTAGTGTACTTCATGAGGCGTTGCAT TCCATTACACGCAAAAGTCTTTGAGTCTCAGTCCGGGTGAAGGAGGTA GCGATTCTTGGCAGGAAGAAGTAATTAAGCTGTGCGGCCGGGAGCTCGT CAGGGCTCAGATAGCTATATGCGGCAAGAGCACGGCCAGTGATGCTGCT GGTGCAGAGGCTGAAGCAGGTGCCAGGCAGTTGTACAGCGCACTCGCTA ATAAGTGTTGCCACGTGGGGTGTACAAAGCAATCTTTGGCACAAATTCTGT
435	GATAAGACCCATACTTGTCTCCTCGCCGACCAAGAGGCTGCGGGTG GCCCATCCGTTTTCTGTTTCCGCCAAAGCCTAAGGATACTCTGATGATT TCACGCACACCCGAAGTGACCTGCGTGGTGGTCGACGTATCTCACGAAG ACCCAGAGGTAAAATTCAATTGGTACGTGGACGGCGTCGAGGTTCAATA CGCGAAAACCTAAGCCGAGAGAAGAGCAGTACAACCTCTACGTATCGCGTG GTGTCCGTACTGACAGTATTGCATCAGGACTGGTTGAATGGCAAGGAGT ATAAGTGCAAGGTATCTAATAAGGCATTGGCTGCCCCAATAGAGAAAAC GATCAGCAAAGCAAAGGGGCAGCCGCGCGAGCCGCAGGTATATACACT

SEQ ID NO:	Sequence
	TCCACCATCACGGGATGAGTTGACGAAAAATCAAGTCTCTCTCACATGT CTGGTAAAAGGTTTCTATCCTTCTGATATCGCCGTGGAATGGGAAAGCA ACGGCCAACCCGAAAACAACATAAAGACGACGCCGCCGGTACTCGACA GCGACGGAAGCTTTTTCTTGTATTCCAAGTTGACAGTGGACAAGTCTCGA TGGCAGCAAGGAAACGTGTTCTCATGTTCTGTTCTTCACGAAGCCCTTCA TAGCCATTATACTCAGAAATCTCTCTCACTCTCCCCAGGTGAAGGGGGA AGTGACTCTTGGCAAGAAGAAGTCATTAAGCTTTGCGGTCGAGAATTGG TTCGGGCTCAAATAGCTATTTGTGGCAAGTCCACGGCAAGTGATGCAGC GGGGGCTCAGGCAGACGCGGGCGCAAGGCAGCTTTATTCCGCACTTGCA AATAAGTGCTGTCACGTCGGATGTACTAAACAATCACTTGCACAATTCTG C
436	GACAAGACACATACATGTCCCCATGCCCTGCACCCGAAGCTGCTGGGG GGCCCAGCGTGTTCCTGTTTCCGCCGAAGCCCAAGGACACATTGATGATT AGTAGAACCCAGAGGTAACCTTGTGTTGTGGTCGATGTGTCACATGAAG ACCCCGAGGTAAAGTTTAACTGGTATGTGGATGGGGTAGAGGTACATAA TGCAAAAACCAAGCCGCGGGAGGAGCAGTATAATTCAACCTATCGAGTC GTGTCAGTCTTGACCGTGCTCCACCAGGACTGGCTTAACGGTAAGGAGT ATAAATGCAAAGTCAGTAATAAGGCATTGGCCGCCCCCATTGAGAAGAC CATCAGTAAAGCTAAGGGGCAACCTAGAGAGCCACAGGTTTACACCCTC CCTCCCTCCCGGGATGAACCTACCAAAAACCAGGTGTCCCTTACTTGT GGTAAAGGGCTTTTATCCTTCTGATATTGCTGTTGAATGGGAGTCTAACG GGCAACCTGAAAATAACTACAAAACAACCCCCCGTTCTGGACTCTGA TGGGTCATTCTTCCTTTATTCAAAATTGACAGTTGATAAGAGTAGATGGC AACAAAGGCAACGTATTTTCATGTTCTGTGCTCCACGAGGCTCTCCATTCC CACTACACACAGAAAAGTCTCTCACTGTCCCCAGGAGAGGGCGGGAGCG ACTCTTGGCAGGAAGAAGTAATCAAGTTGTGTGGCAGGGAACCTCGTACG CGCTCAGATTGCAATATGCGGGAAATCCACGGCAAGTGACGCTGCCGGG GCCGACGCGCAAGCAGGGGACGCGCAGCTTTACTCCGCCCTCGCAAATA AATGTTGTCATGTGGGATGCACTAAACAGTCCCTTGCCCAGTTTTGC
437	GATAAAACCCATACCTGTCCACCATGCCCCGCGCCAGAGGCAGCGGGTG GTCCAAGCGTTTTCTTTTCCACCAGAAACCAAAAGATACACTTATGATA TCAAGGACCCCCGAGGTAACGTGCGTCGTAGTTGACGTTTCTCACGAAG ATCCCGAGGTGAAATTCAATTGGTACGTAGATGGTGTAGAGGTACACAA TGCGAAGACAAAACCGCGGGAAGAGCAGTATAATAGCACATACAGAGT CGTGAGCGTCTCACCCTACTTCACCAAGATTGGCTGAATGGAAAGGAG TACAAATGTAAGGTAAGTAATAAAGCACTTGCGGCCCCCATCGAGAAAA CTATCAGTAAAGCAAAAGGGCAACCACGAGAACCCAGGTCTACACTTT GCCACCATCACGGGATGAACTGACAAAAAATCAGGTGTCACTCACTTGC CTTGTTAAAGGGTTCTATCCTAGTGACATAGCGGTAGAATGGGAGTCTA ACGGGCAGCCTGAGAACAAATTATAAACTACGCCCCCTGTTCTTGATTCC GATGGATCATTTTTTCTCTACTCCAACTCACCGTAGACAAATCCCGCTG GCAGCAGGGCAACGTGTTTAGTTGCAGCGTTCTTCACGAAGCACTTCACT CACATTACACACAAAAGTCCCTGAGCTTGAGTCCTGGGGAGGGTGGATC TGATTCTTGGCAGGAAGAAGTTATAAACTTTGTGGCAGAGAGTTGGTC CGCGCACAAATCGCCATATGTGGTAAAAGCACAGCGTCTGACGCGGCGG

SEQ ID NO:	Sequence
	GAGCGCAAGCCCAGGCGGGGGCTCGGCAACTCTACTCAGCCCTGGCTAA CAAGTGCTGTACGTGGGATGCACTAAACAAAGTCTGGCGCAGTTCTGC
438	GACAAAACCCATACGTGTCCCCCGTGTCCGGCTCCAGAGGCTGCGGGAG GACCGTCTGTGTTCTTGTTCGCCGGAAGCCTAAAGATACGCTGATGATT AGTCGGACCCCCGAGGTGACCTGCGTGGTAGTAGACGTATCTCATGAAG ATCCGGAAGTAAAGTTTAACTGGTACGTAGACGGCGTCGAGGTACATAA TGCCAAGACGAAACCCAGAGAAGAGCAATATAATAGCACTTATCGAGTT GTAAGCGTATTGACGGTCCTTCACCAGGACTGGTTGAACGGCAAAGAGT ACAAATGTAAGGTATCCAATAAAGCATTGGCTGCGCCAATTGAAAAGAC AATTTCCAAAGCGAAGGGGCAACCTCGAGAGCCGCAAGTCTACACGCTG CCACCGAGTAGGGATGAATTGACTAAGAATCAGGTGAGTCTCACGTGTC TCGTGAAGGGGTTTTACCCAGTGATATTGCGGTAGAATGGGAGTCCAA CGGTCAGCCAGAAAATAATTATAAAACAACGCCCCCTGTATTGGATTCT GACGGGAGCTTTTTCTGTACTCAAACTCACCGTAGATAAGAGTCGCT GGCAACAGGGCAACGTATTCTCATGTAGCGTTCTGCACGAGGCGCTGCA CTCTCACTACACACAGAAGAGTTTGAGTTTGTCCCTGGCGAAGGAGGT TCTGATTCTTGGCAGGAGGAGGTGATTAAGCTGTGTGGCCGCGAATTGG TGAGGGCTCAAATTGCTATTTGCGGACAGAGCACAGCGTCCGATGCCGC CGGCGCAGATGCTAATGCCGTGCAAGGCAACTGTACTCCGCTCTCGCC AATAAGTGTTGTCATGTCGGCTGCACCAAGCAATCCCTGGCCCAGTTTTG C
439	GACAAGACTCACACTTGTCCCCCATGTCCAGCACCGGAAGCTGCCGGCG GTCCCTCAGTTTTCTTTTCCCCCCAAACCCAAGGACACCTTATGATTT CAAGGACACCAGAGGTAAAGTTTAACTGGTACGTGGATGGGGTAGAGGTTCA TGCTAAAACAAAACACGCGAGGAACAGTACAATAGTACGTATAGAGT GGTCTCCGTTCTTACGGTGCTGCATCAGGACTGGCTGAACGGAAAAGAG TACAAGTGTAAGGTTAGCAATAAGGCGCTGGCGGCCCCAATCGAAAAGA CGATTTCTAAGGCCAAAGGCCAGCCAAGGGAGCCACAAGTATATACCCT TCCCCCTTCCCGAGATGAGCTGACTAAGAATCAAGTCAGTCTCACCTGCC TTGTCAAAGGGTTCTACCCATCCGATATTGCTGTTGAATGGGAGTCTAAT GGCCAGCCGGAGAACAATTACAAGACAACCTCCGCCTGTATTGGATTCCG ACGGGTCTTTTTTCTCTATTCAAACTCACAGTAGACAAAAGTCGATGG CAGCAAGGTAACGTGTTTTCTTGCTCTGTGTTGCATGAAGCACTTCATTC TCATTATACTCAAAAATCATTGAGCCTCAGTCCAGGCGAAGGGGGTAGT GACTCATGGCAGGAGGAGGTAATCAAGCTTTGCGGACGAGAGTTGGTCA GGGCCCAGATAGCTATTTGTGGTCAGTCCACGGCGAGTGACGCAGCAGG GGCGAATGCCGATGCAGGAGCAAGACAACGTATTCTGCTCTGGCCAAC AAGTGTTGTCATGTAGGGTGTACTAAACAAAGTCTCGCCCAGTTCTGC
440	GATAAAACCCACACCTGTCCCCCATGTCCGGCTCCCGAAGCAGCGGGGG GCCCTTCAGTTTTTCTTTTCCCCCCAAACCGAAAGACACGCTGATGATT AGCAGAACTCCAGAGGTTACCTGTGTAGTTGTGGACGTTTCACACGAGG ATCCCGAGGTTAAATTCAACTGGTATGTGGACGGCGTCGAAGTGCATAA TGCAAAAACAAAGCCCCGGAAGAACAATATAATAGTACCTATAGGGTC GTTTCCGTACTGACCGTACTTCATCAAGATTGGCTCAATGGGAAGGAAT ACAAATGTAAGGTGAGTAATAAAGCCCTGGCGGCACCGATCGAAAAA

SEQ ID NO:	Sequence
	CCATTTCAAAGGCTAAGGGACAACCGCGCGAACCTCAGGTCTATACCTT GCCCCCTTCACGCGACGAGCTTACGAAGAATCAGGTAAGCCTTACTTGT CTTGTCAAGGGTTTTTACCCCAGCGACATAGCTGTGCGAGTGGAATCCA ATGGCCAACCGGAGAATAATTACAAAACCTACCCCTCCTGTTCTTGATAG CGACGGAAGCTTCTTCTTGTATTCCAACTCACAGTAGATAAAAAGTAGG TGGCAGCAGGGCAATGTATTTTCTTGCAGCGTCCTGCATGAAGCACTGC ATAGCCATTATACTCAAAAGTCCCTGTCTTTGTCTCCTGGAGAGGGCGGA AGCGATTCTTGGCAAGAGGAAGTTATTAAGCTGTGCGGGCGCGAACTTG TGAGGGCTCAAATAGCGATATGTGGTCAGAGCACCGCTAGCGATGCGGC TGGTGCAGACGCCGATGCCGGTGCTAGGCAACTTTACAGTGCACCTTGCG AATAAGTGCTGTCACGTCGGATGTACTAAACAAAGCCTCGCCCAGTTCT GC
441	GATAAAACACATACTTGCCCTCCTTGTCCGGCTCCCGAAGCCGCAGGTG GACCTTCCGTCTTTCTTTTCCCACCCAAACCTAAAGACACTTTGATGATT AGCCGGACCCCGAGGTAACCTGTGTCGTAGTTGACGTTTCCCATGAAG ACCCCGAAGTTAAGTTCAACTGGTATGTCGACGGCGTCGAGGTGCACAA CGCGAAGACTAAGCCAAGAGAGGAGCAATACAATTCAACTTACAGGGT CGTGTCCTGCTTGACAGTGCTTCATCAAGACTGGCTTAATGGAAAGGAA TACAAATGTAAAGTCTCCAACAAGGCTCTCGCAGCGCCATTGAGAAAA CGATATCCAAAGCGAAGGGTCAACCAAGAGAACCCAGGTTTACACCCT CCCCCCTAGTCGGGACGAGCTTACGAAGAACCAGGTCAGTTTGACATGC CTGGTGAAAGGCTTCTATCCGTCAGACATCGCCGTAGAGTGGGAAAGCA ACGGGCAACCCGAGAACAATAAGACGACTCCCCCGGTGTTGGATAG CGATGGCTCTTTCTTCTGTACTCTAAGCTGACCGTAGATAAATCCAGGT GGCAACAGGGGAACGTGTTTTATGCTCAGTGCTCCATGAAGCCCTCCA TTCACACTATACACAAAAGTCTTTGTCACTGTCCCCCGGTGAAGGCGGCA GTGATAGCTGGCAAGAAGAAGTCATAAAGCTCTGTGGTCGCGAGCTTGT TAGGGCCCAAATTGCGATCTGTGGTCAGTCAACGGCTTCTGACGCCGCC GGAGCGGAAGCCGAGGCGGGTGCTCGGCAATTGTATTACGACTGGCGA ACAATGTTGCCATGTTGGTTGTACTAAACAAAGCCTGGCCCAGTTTGC
442	GACAAGACTCACACTTGTCCACCCTGTCCAGCACCTGAAGCCGCTGGTG GACCATCTGTCTTTCTGTTCCCCCTAAACCAAAGGATACACTTATGATC AGCAGAACACCTGAAGTCAATGCGTTGTGGTAGACGTTTCCCACGAGG ATCCTGAAGTGAAGTTTAACTGGTACGTGGATGGCGTTGAGGTTCTATA TGCCAAGACGAAACCTCGGGAGGAGCAGTATAATTCTACTTATAGGGTG GTAAGCGTACTGACAGTCTCCATCAAGACTGGTTGAACGGGAAGGAAT ACAAGTGTAAGTTTCCAACAAAGCTCTGGCGGCGCCTATAGAAAAGAC AATATCAAAAGCGAAAGGGCAACCCAGAGAGCCTCAAGTATATACATTG CCCCCTAGCAGAGACGAATTGACGAAAAATCAGGTCTCTCTCACGTGCC TCGTGAAGGGCTTCTATCCTAGTGATATAGCTGTGGAATGGGAATCCAA TGGACAGCCAGAAAACAATAAGACCACGCCCCCGTCTTGGATTCC GACGGGTCAATTCTTCTGTACAGCAAGCTGACTGTCGACAAGAGTCGAT GGCAACAGGGCAACGTCTTTAGCTGCAGCGTCCTGCACGAAGCTCTGCA TAGTCATTACACCCAAAAGTCCCTTCTCTCTCCCCTGGTGAAGGCGGTT CCGATTTCATGGCAAGAAGAAGTAATTAAGCTCTGTGGACGAGAGCTTGT CCGAGCACAAATTGCGATCTGCGGGCAGAGTACCGCATCTGACGCTGCT

SEQ ID NO:	Sequence
	GGCGCGCAGGCAGATGCGGGTGCACGGCAGCTTTATTCAGCTCTCGCCA ACAAGTGTTGTCATGTGGGGTGTACAAAGCAGAGCCTTGCCCAGTTTTGT
443	GATAAGACCCATACGTGTCCCCCTTGCCCTGCACCCGAGGCGGCTGGGG GCCCTTCCGTATTCTTGTTTCCTCCTAAGCCCAAAGATACCTTGATGATA AGTCGAACGCCAGAAGTGACTTGCGTTGTTGTGGATGTCTCCACGAGG ATCCAGAAGTCAAATTTAACTGGTATGTCGATGGGGTCGAAGTGCATAA TGCTAAAACGAAACCCAGAGAGGAACAATAACAATTCAACATACCGCGTA GTCAGTGTTCTTACTGTGCTCCATCAGGATTGGCTCAATGGGAAAGAATA CAAGTGTAAGTCTCAAATAAAGCATTGGCGGCCCTATAGAGAAGACC ATAAGCAAGGCTAAAGGTCAGCCTAGGGAGCCTCAAGTATATACCTTGC CTCCTAGCAGAGATGAGTTGACCAAGAACCAGGTCAGCCTCACATGCCT GGTGAAAGGGTTTTACCCATCTGATATTGCCGTCGAGTGGGAAAGTAAT GGGCAGCCAGAGAACAACCTACAAGACGACACCACCGGTACTGGATAGT GACGGAAGTTTTTTCTTTACAGTAAGCTCACAGTCGACAAAAGCCGGT GGCAACAAGGAAATGTATTTTCATGTAGCGTACTTCATGAAGCCCTCCA CTCTCATTACACGCAGAAGTCACTTTCACTTAGTCCGGGTGAGGGTGA AGCGATAGCTGGCAAGAGGAGGTTATCAAGCTCTGTGGACGAGAACTCG TGAGAGCGCAAATTGCAATCTGCGGGCAGAGCACGCGCAGTGATGCGG CCGGGGCGGACGCGCAAGCAGGAGCACGACAACTTTATAGTGCTTTGGC TAATAAATGTTGCCACGTTGGATGTACTAAACAGAGCTTGGCACAGTTTT GC
444	GATAAAACGCACACTTGTCCGCCATGTCCGGCACCTGAGGCAGCGGGAG GACCGTCCGTGTTTCTGTTTCCCCCTAAACCAAAGGACACGCTGATGATC AGCCGAACACCTGAAGTAACATGCGTGGTCGTTGACGTGTCTCACGAGG ATCCAGAAGTAAAGTTCAATTGGTATGTTGACGGAGTTGAAGTACATAA TGCTAAGACTAAACCCCGCGAAGAACAATAAATTCTACGTACAGAGTT GTATCCGTGCTCACGGTACTTCACCAAGATTGGCTTAACGGGAAAGAAT ATAAGTGTAAGGTCTCAAATAAGGCCCTGGCTGCTCCGATCGAAAAAC GATATCAAAGGCAAAGGGTCAACCTCGGGAGCCTCAAGTATATACCTC CCCCATCTAGGGATGAGCTGACAAAGAACCAAGTTTCACTGACCTGTC TCGTAAAGGGTTTCTATCCTTCTGACATCGCAGTTGAATGGGAGTCCAAC GGCCAAACCAGAGAACAACATAAGACGACACCCCCCGTGTTGGACAGTG ACGGAAGTTTTTTCTGTACTCCAAGCTGACGGTTGATAAAAGTAGATG GCAACAAGGAAATGTTTTCAAGTTGTTCTGTGTTGCACGAGGCCCTCCACT CACACTATACCCAAAAAAGTTTGTCTCTGAGTCCCGGTGAAGGCGGGAG CGATTCATGGCAGGAGGAAGTAATCAAACCTTTGTGGGCGAGAACTGGTC AGGGCGCAAATAGCGATATGTGGGCAAAGCACAGCTTCAGATGCAGCC GGTGCTCAAGCTCAGGCTGGAGCTCGACAGCTTTATAGCGCCTTGGCTA ATAAATGTTGTACGTTGGCTGTACGAAGCAGAGCCTGGCACAGTTCTG C
445	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAACCTGTGTCGTTGTGGATGTGTCACATGAGG ATCCCAGGTTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA

SEQ ID NO:	Sequence
	CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTCTTTATTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCTTTTCTTGCAGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCAATTGTCCCCAGGTAAGGGCGGAAGCG ACTCATACCAAGAAGAAGTCATTAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTGTGCACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
446	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAACCTTGTGTCGTTGTGGATGTGTACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTCTTTATTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCTTTTCTTGCAGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCAATTGTCCCCAGGTAAGGGCGGAAGCG ACTCATTCAAGAAGAAGTCATTAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTGTGCACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
447	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAACCTTGTGTCGTTGTGGATGTGTACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTCTTTATTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCTTTTCTTGCAGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCAATTGTCCCCAGGTAAGGGCGGAAGCG ACTCACTTCAAGAAGAAGTCATTAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC

SEQ ID NO:	Sequence
	GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTGTGCACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
448	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTCCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAAGTTGTGTCGTTGTGGATGTGTACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTTCTTTATTTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCCTTTCTTGACGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCATTGTCCCCAGGTAAGGGCGGAAGCG ACTCAATTCAAGAAGAAGTCATTAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTGTGCACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
449	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTCCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAAGTTGTGTCGTTGTGGATGTGTACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTTCTTTATTTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCCTTTCTTGACGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCATTGTCCCCAGGTAAGGGCGGAAGCG ACTCATGGCAAGAAGAAGTCATTAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTGTGTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
450	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTCCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAAGTTGTGTCGTTGTGGATGTGTACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC

SEQ ID NO:	Sequence
	CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTTCTTTATTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCTTTTCTTGACGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCAATTGTCCCCAGGTAAGGGCGGAAGCG ACTCATGGCAAGAAGAAGTCATTAAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTTGTCTTGTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
451	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAACCTTGTGTCGTTGTGGATGTGTACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTTCTTTATTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCTTTTCTTGACGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCAATTGTCCCCAGGTAAGGGCGGAAGCG ACTCATGGCAAGAAGAAGTCATTAAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTTGTCAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
452	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAACCTTGTGTCGTTGTGGATGTGTACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTTCTTTATTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCTTTTCTTGACGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCAATTGTCCCCAGGTAAGGGCGGAAGCG ACTCATGGCAAGAAGAAGTCATTAAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTTGTAAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC

SEQ ID NO:	Sequence
453	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAG GACCTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATC TCTCGGACACCGGAAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGG ATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAA CGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGGTT GTCTCAGTTCTCACAGTTCTTCATCAGGATTGGTTGAATGGAAAGGAGTA CAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACG ATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTTGC CTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTT GGTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATG GCCAGCCTGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGA CGGCTCCTTTTTCTTTATTCAAACTCACAGTGGACAAATCCAGGTGGC AGCAGGGTAACGTCTTTCTTGACGCGTGCTCCACGAAGCTTTGCATTCA CATTATACGCAAAAATCCTTGTCATTGTCCCCAGGTGAAGGCGGAAGCG ACTCATACCAAGAAGAAGTCATTAACTTTGTGGACGGGAGCTGGTTAG GGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAGCGGGC GCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACA AGTGTGTTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
454	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAG CGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTAAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
455	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG

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456	GATAAAACCCACACTTGCCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGAGAAGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTAAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
457	GATAAAACCCACACTTGCCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGATCTGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
458	GATAAAACCCACACTTGCCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC

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459	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAG CGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACAAAG TGTTGTTACGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
460	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGACGCAG CGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAACAAAG TGTTGTAAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
461	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA

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462	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGAGAAGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTAAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
463	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGATCTGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTTACGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
464	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA

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465	GATAAAACACACACGTGTCCCCCTGCCCGCTCCAGAGGCGGCTGGTGGTCCCAG CGTATTCTTGTTCCTCCCAAACCTAAGGATACGCTCATGATATCCCGCACCCCAG AAGTTACGTGTGTAGTCGTCGACGTCAGTCACGAAGATCCAGAGGTCAAATTTAAC TGGTATGTGACGGAGTAGAGGTCCACAATGCGAAAACCAAGCCCAGAGAAGAGCA GTACAACTCCACGTATCGCGTCGTCTCCGTCTCACCCTACTCCATCAAGATTGGC TGAATGGGAAAGAGTATAAATGCAAAGTATCTAACAAGGCTCTGCCAGCTCCGATA GAAAAGACTATATCAAAGGCCAAGGGGCAGCCAAGGGAGCCTCAAGTCTATACTTT GCCCCATCTCGGGATGAGCTTACGAAAAACCAGGTCAGCCTTACCTGTCTTGTAA AAGGTTTTTTATCCGAGTGACATCGCAGTGGAATGGGAATCTAATGGTCAACCTGAA AACAATTACAAAACACACCGCCAGTATTGGACAGCGATGGTAGTTTTTTTCTTTA CTCAAACTGACTGTAGATAAAAAGCAGATGGCAGCAGGGCAATGTCTTTTCATGTA GCGTTATGCATGAGGCTCTTCACAACCACTATAACCAAAAGTCATTGTCTCTTAGT CCCGGAAAGGGCGGAAGTGATTCTTGAAGGAGGAGGTAATCAAGTTGTGCGGGCG AGAGTTGGTACGGGCACAGATCGCGATATGCGGAAAATCCACAGGTGGGGGCGAAG GAGGAGGTGAGGGTGGAGGTGAAGGACGACAGTTGTATTCCGCCTTGGCAAACAAG TGTTGCCATGTGGGTTGCACAAAACGCAGTCTTGCCCGCTTCTGT
466	GATAAGACACATACATGCCCTCCCTGTCCGGCTCCAGAGGCAGCCGGGGGTCCATC AGTCTTCTTTTTCCGCCTAAACCTAAGGATACACTGATGATCTCTCGAACACCGG AGGTCACCTTGTGTGTGTCGTTGACGTATCACATGAGGATCCCGAAGTAAAGTTCAAC TGGTATGTGATGGTGTGGAGGTTCAATGCTAAAACTAAACCACGGGAGGAGCA ATATAATTCCACATATAGGGTCGTGAGCGTGTTGACGGTGCTTCATCAAGACTGGC TTAATGGGAAGGAATATAAATGCAAAGTGTCAAATAAAGCACTTCCCTGCGCCAATC GAGAAAACAATTAGTAAGGCAAAGGGGCAGCCGCGAGAACCTCAGGTGTACACCTT GCCGCCTTCTAGAGACGAGCTCACAAAGAACCAAGTTTCCCTGACTTGCCCTCGTTA AGGGGTTTTATCCGTCCGATATAGCCGTGGAGTGGGAGTCAAACGGCCAACCGGAA AATAATTACAAAACGACACCCCAAGTATTGGATAGTGACGGCTCTTTTTTCTTTTA TTCTAAGCTGACTGTGGACAAAAGCCGCTGGCAGCAGGGCAATGTCTTTTCATGCA GCGTAATGCATGAAGCCCTGCACAACCACTACACGCAAAAATCCCTTTCCTTGTCA CCCGGCAAGGGCGGCTCTGACTCCTGGAAAGAGGAAGTTATAAACTCTGTGGCCG AGAAGTTGTTGAGCTCAAATCGCGATTGTGGTAAGTCAACGGGTGGGGGCGAAG GTGGAGGCGAGGGTGGGGGAGAAGGAGGAGGCCAGTTGTACTCAGCTCTTGCAAAAT AAGTGTTGCCACGTTGGTTGTACGAAGCGGAGCCTTGCTCGCTTCTGC
467	GACAAAACACATACCTTGTCCGCCTTGCCCGGCACCCGAAGCGGCCGGCGGACCCAG TGTCTTTCTCTTCCCACCAAAACCGAAAGACACTCTGATGATTTCCAGGACGCCTG AAGTGACCTGCGTTGTAGTTGATGTATCACACGAGGATCCCGAGGTCAAGTTCAAT TGGTATGTAGATGGGGTGGAGGTCCATAATGCAAAGACGAAGCCACGGGAGGAACA GTACAACTCTACGTACAGAGTTGTCAGTGTTTTGACCGTCCTTCATCAGGATTGGC TGAACGGTAAAGAATATAAATGCAAGGTAGCAATAAAGCTTTGCCCGCCCTATA GAGAAAACGATCAGTAAGGCGAAGGGGCAGCCTAGGGAACCCAGGTATATACCTT GCCGCCAAGTCGAGATGAGCTGACGAAGAACCAAGTGAGTCTGACATGCCTCGTGA AGGGCTTCTATCCGAGCGATATCGCTGTGCAATGGGAGAGCAATGGGCAGCCTGAG

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468	GACAAGACGCACACTTGTCCACCTTGCCCTGCGCCGGAAGCTGCTGGAGGCCCCAG TGTCTTTTTTGTTCGCCCCAAACCGAAGGACACTTTGATGATAAGTCGCACGCCCG AGGTTACCTGTGTGGTTGTTCGATGTCTCACACGAAGATCCGGAGGTGAAGTTTAAAT TGGTATGTAGATGGCGTGGAGGTTTCATAACGCCAAAACGAAACCCAGAGAAGAACA ATATAACAGTACATATCGAGTAGTATCCGTTCTCACTGTCTGCATCAAGACTGGT TGAACGGGAAGGAATATAAGTGCAAGGTGAGCAATAAAGCACTCCCGGCCCAATC GAAAAGACCATCAGCAAAGCGAAGGGGCAACCTCGAGAACCCAGGTATATACGCT CCCCCTAGTCGGGATGAACCTACTAAAAATCAGGTTAGCCTCACTGCCTTGTTA AAGGGTTCTATCCAGTGATATTGCCGTGCAATGGGAATCAAACGGGCGAGCCGGA AATAACTACAAGACAACCCCTCCTGTGCTCGATAGCGATGGCTCTTTTTTCCTCTA CAGCAAACCTTACCGTTGATAAGAGCCGGTGGCAACAAGGTAATGTTTTCTCTGCT CCGTTATGCATGAAGCACTCCATAACCATTAACCAAAAAAGCCTGTCACTTAGT CCGGGTAAAGGAGGTAGTGATTCTTGGCAGGAGGAGGTAATCAAACCTTTGTGGGAG GGAGCTGGTACGAGCTCAGATTGCTATATGTGGAAAAAGCACGGGCGGAGGAGAAG GAGGTGGCGAAGGCGGGGTGAAGGTGCGCAACTCTACTCCGCTCTCGCTAATAAG TGCTGCCACGTTCGGGTGTACGAAGCGCTCCCTGGCGCGATTCTGC
469	GATAAAACGCACACGTGTCCGCCCTGCCAGCGCCTGAAGCCGCAGGCGGGCCGTC CGTCTTCTCTTTCTCCAAAACCCAAAGACACACTTATGATCAGTAGGACCCAG AGGTAACTGCGTTCGTGGTCGACGTTTCCCATGAAGACCCAGAGGTCAAGTTCAAC TGGTACGTTCGACGGTGTGAAAGTACATAATGCTAAAACGAAGCCTCGGGAAGAGCA GTACAACCTCTACCTACCGCGTCGTTTCCGTAACCTCACCCTACTTACCAGGACTGGC TTAACGGTAAAGAGTATAAATGCAAAGTATCTAATAAGGCTCTCGCCGCGCCGATT GAGAAGACAATTTCAAAGGCCAAGGGGCAGCCGCGGGAGCCCCAAGTGATACCTT GCCCCGTCCCGAGATGAGCTGACTAAAAACCAAGTAAGCTTGACTTGCTTGGTCA AAGGCTTCTACCTTCCGATATAGCTGTGCAATGGGAGTCAAATGGCCAACCAGAG ACAATTATAAACTACACCCCGGTCTTGGATTCTGATGGCTCATTTTTTCTCTA TTCTAAACTGACCGTGGATAAGTCTCGCTGGCAGCAAGGTAACGTGTTCAAGTTGCT CTGTTCTTACGAAGCACTGCACAGTCATTACACTCAGAAGAGTCTTAGCCTGAGC CCTGGTAAAGGGGGTTCTGATTCTTGGCAGGAGGAAGTAATAAACTCTGTGGCCG GGAGTTGGTACGGGCGCAGATTGCGATATGCGGTAAGAGCACCGGCGGAGGCGAAG GCGGTGGGGAAGGAGGAGGAGAAGGGAGACAACCTCTATTCCGCATTGGCAAATAAG TGCTGCCACGTTCGGGTGTACCAAACGATCCCTTGACGCGTTCTGT
470	GATAAGACCCATACGTGCCCCCTTGCCCTGCGCCTGAGGCAGCGGGTGGCCCATC AGTCTTTTTTGTTCGCCCAAGCCAAAGGACACCCTCATGATTAGTAGAACACCGG AGGTTACGTGCGTCGTAGTGGATGTCAGCCACGAGGATCCCGAGGTTAAGTTTAAAC TGGTACGTTGATGGGGTTGAGGTCCATAATGCGAAGACTAAGCCGAGAGAGGAACA GTACAATTCCACGTATAGAGTTGTCTCTGTACTGACTGTGCTGCATCAAGATTGGC TTAACGGTAAGGAGTACAAGTGCAAAGTCTCTAATAAGGCTCTTCTGCACCCATT GAGAAACTATAAGCAAAGCAAAAGGTCAACCTCGCGAACCTCAGGTGTACACACT GCCACCCTCTAGGGACGAGCTTACCAAAAATCAAGTATCTCTTACCTGCCTTGTGA

SEQ ID NO:	Sequence
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471	GACAAGACGCATACATGCCCGCCATGCCCGCCCCCGAAGCTGCTGGGGGACCATC CGTATTCCCTCTTCCCTCCCAAACCAAAAGACACGTTGATGATAAGTAGAACACCAG AGGTAACGTGCGTGGTTGTCTGATGTTTCCACGAAGATCCGGAGGTAAAATTCAAT TGGTATGTAGATGGGGTGGAAAGTGACAATGCCAAAACAAAGCCGCGAGAAGAACA ATACAATAGTACTTACCGGGTTGTGAGCGTGCTCACGGTGTGTCACCAAGACTGGC TCAACGGCAAGGAATACAAGTGCAAAGTATCTAATAAAGCTCTGCCTGCGCCGATA GAGAAGACCATCAGTAAGGCCAAAGGGCAGCCCCGAGAGCCGCAAGTTTACACTCT TCCTCCGAGCAGAGATGAATTGACCAAGAACCAAGTAAGTTTGACGTGCCTGGTGA AGGGCTTCTACCCCTCAGACATTGCGGTGGAGTGGGAAAGTAATGGTCAACCGGAA AACAACTACAAGACCACGCCCGCCGTCTCTGACTCCGATGGGTCTTTCTTTCTTTA TTCAAAGTTGACAGTAGATAAGTCAAGGTGGCAGCAAGGTAACGTGTTTAGTTGTA GTGTAATGCACGAGGCCCTGCATAATCATTATACCCAAAAGAGTTTGAGCCTCTCA CCAGGAAAAGGCGGATCAGACAGCTGGCAGGAGGAGGTAATTAAATTGTGTGGACG GGAGTTGGTCAGGGCGCAAATAGCCATCTGCGGTAAGAGCACGGGTGGAGGAGAGG GTGGAGGGGAAGGTGGGGGAGAAGGCGGCGGGCAGCTCTATTCTGCACTCGCCAAC AAGTGTGTCTACGTCCGATGCACAAAGAGATCTCTTGCTCGATTCTGC
472	GACAAAACACACACCTGTCCGCCTTGCCCGGCTCCTGAAGCCGCGGGTGGCCCTAG TGTGTTTTTTGTTTTCCGCCGAAACCTAAGGATACCTCATGATAAGCCGACGCCCG AGGTTACCTGTGTCTGTTGGTTCGATGTTAGTCATGAGGATCCAGAAGTCAAGTTTAAT TGGTACGTGACGGCGTTGAAAGTCCACAATGCAAAAACCTAAACCGCGAGAAGAACA GTACAACCTCCACCTACAGAGTTGTCTCAGTTTTGACAGTTCTCCATCAGGATTGGC TCAATGGAAAGGAATATAAGTGCAAGGTGAGCAATAAAGCGCTTGCCGCCCTATA GAGAAGACCATTAGCAAGGCGAAAGGACAGCCCCGCGAGCCCCAGGTCTATACGCT GCCTCCTAGCAGAGATGAGCTCACGAAAAATCAGGTGAGCTTGACATGCTTGGTGA AGGGCTTCTACCCAGTGACATCGCAGTTGAATGGGAGAGCAACGGCCAACCTGAG AACAACTACAAAACAACGCCCGGGTTCTTGACAGCGATGGGTCTTCTTTCTTTA CTCTAAGCTTACAGTTGATAAAAGCAGGTGGCAGCAGGGGAATGTGTTCTCATGTT CCGTACTGCATGAGGCTCTGCATTCTCACTACACCAAAAAAGCCTTAGCCTGAGC CCCGGTAAGGGAGGTAGTGACTCATGGCAAGAGGAAGTGATTAAGCTCTGCGGCCG GGAGTTGGTGAGAGCCCAAATCGCCATTTGCGGTAAAAGTACCGGAGGGGGCGAGG GAGGAGGCGAAGGTGGAGGTGAAGGAGGTGGACAGTTGTACTCAGCTCTTGCAAAT AAATGTTGTCTATGTTGGTTGCACGAAAAGATCTCTTGCGAGGTTCTGT
473	GATAAGACGCATACCTTGTCCACCGTGCCCCGCACCGGAAGCGGCTGGTGGTCCATC AGTTTTTCTGTTCACCGAAACCTAAGGACACGTTGATGATATCACGGACACCAG AGGTTACGTGCGTAGTGGTGGATGTGAGCCACGAGGATCCAGAAGTTAAATTTAAT TGGTACGTAGATGGAGTGGAGGTTGATAATGCGAAGACAAAGCCTCGCGAGGAACA GTATAATTCCACCTATCGCGTCGTATCTGTGCTTACGGTACTTCACCAAGACTGGT TGAACGGTAAGGAATATAAATGCAAGGTTTCCAATAAAGCACTTCCTGCGCCAATT GAGAAGACAATATCCAAAGCTAAAGGTCAACCCAGGGAACCGCAAGTCTACACTCT

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	CCCCCGTCTCGCGATGAATTGACGAAGAACCAGGTTAGTCTCACCTGCCTGGTCA AGGGGTTTTACCCCTCTGACATAGCTGTAGAATGGGAGTCTAATGGACAGCCAGAG AACAAATTACAAAACGACCCCCCGGTCCCTCGATTCTGATGGGAGTTTTTTCTTTA TTCAAAATTGACTGTCGATAAGTCAAGATGGCAACAGGGTAACGTATTTTTCTTGCA GTGTTATGCATGAAGCATTGCACAACCACTATACACAAAATCATTGAGTTTGAGT CCCGGTAAAGGGGGAAGCGACTCATGGATGGAAGAAGTAATCAAGCTGTGCGGGCG AGAGCTTGTGCGAGCTCAGATAGCAATCTGTGGTAAGTCTACAGGTGGAGAGGGTG GCGGTGAAGAAGGCGGGGAGAGGGAGGCCAGCTTTATTCTGCCCTGGCTAACAAAG TGCTGTCACGTTGGATGCACGAAGCGCTCCCTGGCCCGATTCTGC
474	GATAAGACGCATAC'TTGTCCCCATGTCCCCTCCGGAAGCCGCTGGCGGCCCTC CGTTTTTCTGTTCCCGCCGAAACCGAAAAGACACCCTGATGATATCACGCACTCCCG AGGTCACTTGCCTGGTAGTCGATGTTAGTCATGAAGATCCTGAGGTCAAATTCAT TGGTATGTAGATGGCGTTGAGGTACACAACGCGAAGACAAAACCCCGAGAAGAACA GTATAACTCAACCTACCGCGTAGTTTCAGTTCCTACCCTACTGCACCAAGACTGGT TGAACGGTAAAGAGTACAAATGTAAAGTCAGCAATAAAGCTTTGCCAGCACCTATC GAAAAAACCATCAGTAAGGCCAAGGGTCAACCCAGGGAGCCGCAAGTGACACTCT TCCCCCTAGCAGGGATGAATTGACCAAGAATCAGGTCTCTTTGACGTGCCTCGTTA AGGGTTTCTATCCAGCGATATAGCCGTAGAATGGGAGTCTAACGGTCAGCCAGAA AATAACTATAAGACAACCCCGCTGTTTTGGATTCCGACGGCTCTTTTTTCTCTA CTCTAAGTTGACCGTTGATAAGAGCAGATGGCAGCAGGGAAACGTATTTTCTTGT CCGTGATGCACGAAGCCCTGCACAATCACTATACGCAAAAGTCTCTGAGCTTGAGT CCGGGTAAAGGCGGTTCTGACTCCTGGCAGGAGGAAGTCATAAACTCTGCGGAAG AGAGCTCGTAAGGGCGCAATCGCTATTTGTGGTAAGAGCACCGGTGGGAAGGAG GCGGTGAAGAGGGTGGCGGCGAGGGTGGGCAATTGTATTCCGCGCTTGCCAATAAA TGTTGTCACGTAGGCTGCACAAAGCGAAGTCTCGCTAGGTTCTGC
475	GACAAGACCCACACATGTCCCCGTGTCCGGCACCAAGCAGCGGGGGACCGTC AGTATTCTTGTTCACCGAAGCCAAAAGACACATTGATGATTTACGAACCTCTG AAGTTACCTGTGTGGTTGTAGATGTATCACACGAAGACCCAGAAGTCAAATTCAT TGGTATGTGACGGGGTTGAAGTTCACAATGCGAAGACGAAGCCCCGGGAGGAACA GTACAACAGCACGTACAGGGTTGTGAGCGTTCTTACTGTATTGCACCAGGATTGGC TCAACGGCAAGGAGTATAAATGTAAAGTTTCTAATAAGGCTCTTCCTGCCCCAATT GAAAAGACGATATCTAAAGCGAAGGGCCAACCACGGGAACCTCAGGTGTACACACT TCCGCCTAGCAGGGATGAGTTGACCAAGAATCAAGTCTCTTTGACGTGCCTGGTCA AGGGGTTTTACCCATCAGATATCGCCGTGCAATGGGAGTCAAACGGACAACCCGAA AATAACTATAAACTACTCCACCAGTTCTGGATAGCGACGGCTCATTTTTTCTGTA TTCAAAGCTCACTGTAGACAAGTCTAGGTGGCAGCAGGGTAATGTCTTCTCCTGCT CAGTAATGCATGAGGCTCTTACAACCACTATACTCAAAAGAGCCTTTCCCTGTCA CCTGGCGGTGGAAGCGACTCATGGATGGAGGAGGTAATAAAGCTCTGCGGAAGAGA ACTGGTACGCGCACAAATCGCAATTTGTGGTAAGAGTACTGGCGGGGAAGGAGGTG GGGAAGAAGGGGCGGTGAGGGCGGACAGCTCTATTCTGCACTTGCAAACAAATGT TGCCACGTGGGATGTACTAAGCGAAGCCTTGCAAGATTCTGC
476	GATAAAACCCACACATGCCCTCCATGCCCTGCTCCAGAGGCCGCCGGTGGGCCATC AGTTTTCTTGTTCGCCCTAAACCAAAGGACACGCTTATGATCTCCAGGACCCCCG AAGTTACGTGTGTGGTGGTTGATGTTAGTCACGAGGACCCGGAAGTCAAGTTCAAC TGGTACGTTGATGGTGTAGAGGTGCACAATGCAAAGACGAAGCCACGCGAAGAACA ATACAACAGCACATATCGAGTTGTGAGCGTACTCACGGTACTGCATCAGGACTGGC TGAACGGTAAAGAATACAAATGTAAAGTCTCCAATAAGGCACTTCTGCGCCGATA

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	GAAAAACGATCAGTAAGGCCAAGGGCCAACCCCGAGAACCACAGGTATATACGCT CCCACCGTCACGAGACGAGTTGACAAAAAATCAGGTCTCCCTGACTGCGCTCGTGA AAGGTTTTTATCCCTCAGATATTGCTGTTGAGTGGGAAAGCAATGGGCAGCCAGAG AATAATTATAAGACGACTCCTCCGGTTTTGGATTCCGACGGTAGTTTTTCTTGTA TAGTAAGCTTACTGTAGACAAGTCAAGATGGCAACAAGGTAATGTGTTCTCTTGCT CAGTTATGCATGAAGCTCTTCATAACCATTACACGCAAAAGAGTCTCAGTCTGAGC CCCGGTGGCGGTAGCGACAGTTGGCAGGAAGAGGTGATTAAGTTGTGCGGTGCGGA GCTCGTTCGGGCCCCAAATTGCAATCTGCGGAAAATCTACGGGCGGAGAGGGCGGGG GTGAGGAGGGTGGGGGTGAAGGTGGGCAGCTCTATAGCGCCCTTGCGAATAAATGT TGTCACGTCCGATGCACAAAGAGGTCCCTCGCCAGGTTCTGC
477	GATAAGACCCACACTTGCCCCCTTGCCCTGCCCCGAAGCGGCCGAGGTCCTTC AGTATTTTTGTTTTCCACCGAAACCCAAAGATACTTTGATGATATCAAGAACTCCTG AAGTCACCTGCGTGGTAGTTGACGTATCTCATGAGGATCCCGAGGTGAAGTTCAAT TGGTACGTCGATGGCGTCGAGGTTCAACGCTAAGACTAAGCCGAGGGAAGAGCA ATATAATTCACCTTATAGGGTGGTGTCCGTCTTGACTGTTTTGCACAGGATTGGT TGAACGGGAAAGAGTACAAATGTAAGGTGAGTAATAAAGCTTTGGCTGCTCCCATC GAAAAGACAATAAGCAAGGCCAAGGGGCAACCTCGGGAGCCGCAGGTGTACACCCT TCCTCCCAGTAGAGACGAACTGACAAAAAACAGGTGTCCCTGACCTGCCTTGTGA AGGGGTTTTACCCGAGCGACATAGCGGTTGAATGGGAGAGCAACGGGCAACCCGAG AACAACCTACAAACTACACCGCTGTCTGGACTCCGATGGAAGCTTCTTCCTCTA CTCCAAACTGACCGTGGACAAAAGCAGATGGCAACAAGGAAACGTATTCTCATGCT CAGTAATGCACGAAGCATTGCACAATCACTACACCCAAAAGTCCCTCTCACTCTCC CCTGGTAAGGGCGGATCAGACTCATGGCAAGAGGAGGTAATTAAGTTGTGCGGGAG GGAGCTCGTCCGCGCGCAATAGCCATTTGTGGCAAGTCCACTGGAGGAGGCGAGG GTGGAGGAGAGGGTGGTGGGGAGGGCAGGCAACTCTACAGTGCCTCGCCAATAAA TGCTGCCATGTTGGGTGCACGAAGCGCAGTCTCGCACAAATTCTGC
478	GATAAGACCCACACGTGTCTCCATGTCCGGCACCGGAGGCTGCTGGCGGGCCTTC TGTATTCCTCTTCCCACCCAAAGCCAAAAGACACATTGATGATATCAAGGACGCCGG AAGTCACCTGTGTTGTTGTGGACGTTTCCCATGAAGACCCAGAGGTAATAATTCAT TGGTATGTGGACGGCGTAGAGGTTCAACACGCCAAAACCAAACCCGAGAGGAACA GTATAATAGCACATATCGAGTAGTATCTGTTCTCACAGTGCTCCATCAAGACTGGC TTAATGGTAAAGAGTATAAATGCAAAGTTTCCAATAAAGCCCTCGCTGCACCGATC GAGAAGACAATCAGTAAAGCGAAGGGCCAGCCTCGGGAACCGCAGGTGTATACTCT TCCACCCTCAAGAGACGAGCTCACTAAAAACCAAGTTTCATTGACATGCCTCGTCA AAGGTTTCTACCCATCAGACATCGCGGTGCAATGGGAAAGTAATGGGCAGCCGGAA AACAACCTATAAAACGACGCCGCCCGTCTTGGATTCTGATGGTTCATTTTTCTTTA CTCTAAATTGACCGTCGATAAAAGTAGGTGGCAACAAGGAAATGTTTTTCTGCT CCGTCTGCATGAAGCGTTGCACAGTCACTATAACCCAGAAGAGTCTTTCTTTGTCA CCCGGAAAAGGCGGTTTCAGATTCATGGCAGGAAGAAGTAATTAACCTCTGTGGCCG CGAGCTTGTTAGGGCGCAGATAGCCATATGTGGTAAAAGCACCGGAGGAGGTGAAG GCGGAGGCGAAGGAGGTGGGGAAGGAAGACAATTGTATTCTGCACTTGCAATAAAA TGCTGTCATGTGGGTGCACGAAACGCAGTCTTGACAATTTTGT
479	GACAAAACCCATACCTGCCCCCTTGCCCTGCACCAGAAGCGGCGGGAGGACCTAG CGTTTTTCTTTTTCTCCGAAACCGAAAAGATACCCTCATGATATCAAGAACACCTG AGGTTACTTGCGTTGTCTGGACGTGAGTCACGAAGACCCGAGGTGAAGTTCAAC TGGTATGTAGATGGAGTGGAGGTCCATAATGCAAAAACGAAACCGAGAGAAGAACA ATACAACCTACATATCGAGTCGTGTGAGTACTCACGGTTTTGCATCAAGATTGGC

SEQ ID NO:	Sequence
	TGAACGGTAAGGAGTACAAGTGTAAAGTTAGCAACAAGGCTCTCGCGGCGCCGATA GAAAAGACTATAAGTAAAGCAAAAGGCCAGCCAGAGAACCTCAAGTTTACACTCT GCCTCCCAGCAGAGATGAACTGACTAAAAATCAGGTTTCATTGACCTGTCTCGTCA AGGGTTTTTATCCAAGCGACATAGCAGTTGAATGGGAAAGCAACGGTCAACCAGAA AATAATTACAAAACCACTCCACCAGTCTTGGACTCTGACGGATCCTTCTTTCTCTA TTCAAAATTGACGGTGGATAAACTAGGTGGCAGCAAGGCAACGTCTTCTCTTGTA GCGTTATGCATGAGGCGCTGCACAACCACTACACACAAAAGTCTCTTAGTTTGAGC CCGGGCGGCGGAAGCGACTCTTGGCAAGAGGAAGTGATAAAACTCTGTGGTCGAGA ATTGGTACGCGCGCAGATCGCTATCTGCGGCAAGTCCACAGGGGGAGGGGAAGGTG GCGGGGAAGGTGGTGGCGAGGGCAGGCAGTTGTATAGTGAAGTCCCAACAAGTGC TGCCATGTGGGGTGCACCAAGCGCAGTTTGGCACGGTCTGC
480	GATAAACTCACACTTGTCCCCGTGTCCGGCACCAGAAGCCGCAGGAGGGCCATC TGTCTTTCTTTTTCCCCCAAAACCAAGGATACACTGATGATCTCCCGCACTCCCG AAGTTACTTGTGTCTAGTAGACGTTTCTCACGAGGACCCAGAGGTGAAATTCAAT TGGTATGTTGACGGAGTAGAGGTGCATAATGCCAAGACAAAGCCCCGAGAGGAACA ATACAATTCAACCTACAGAGTAGTGTCCGTTCTTACGGTTCTCCATCAGGATTGGC TCAACGGTAAGGAATATAAGTGCAAGGTAAGCAACAAAGCGCTGGCCGCACCCATT GAGAAAACCATTTCAAAGCTAAAGGCCAACCCCGCAACCACAAGTTTATACTCT CCCCCAAGTCGCGATGAACCTACAAAAAATCAAGTCTCATTGACGTGCTTGGTCA AAGGCTTCTACCCGAGCGATATCGCTGTTGAATGGGAGTCTAATGGACAACCGGAA AATAACTATAAACTACACCCCAAGTCTCGATTGAGACGGCAGCTTCTTCTCTGTA TTCAAACTGACGGTTGACAAATCACGCTGGCAACAGGGTAACGTTTTTCTCTGTA GCGTTCTTTCATGAAGCCTTGACAGTCACTACACCCAGAAGTCCCTTAGCTTGTCA CCTGGCGGGGGTTCAGACTCTTGGCAGGAGGAGGTAAATCAAATGTGCGGAAGAGA ACTGGTGAGGGCTCAGATTGCAATTTGTGGGAAGAGCACGGGTGGCGGTGAAGGAG GTGGCGAGGGCGGAGGAGAGGGGAGGCAACTCTACAGTGCCTTGGCTAATAAATGC TGTCACGTGCGCTGTACTAAGAGAAGCCTCGCCAGATTTTGC
481	GACAAGACGCATACCTGCCCTCCGTGCCCTGCACCAGAAGCCGCTGGTGGCCCATC TGTGTTTTTGTTCCCCCCTAAGCCAAAAGACACATTGATGATTTACGAACTCCAG AAGTGACTTGCGTAGTTGTTGACGTATCACACGAAGACCCCGAGGTTAAATTTAAT TGGTATGTGGACGGGGTCGAGGTGCATAACGCCAAAACCAACCCCGGGAGGAACA ATATAACTCTACGTATCGGGTCGTATCTGTGTTGACCGTCCTTACCAAGATTGGT TGAACGGCAAGGAATATAAGTGTAAAGTGTCTAATAAAGCATTGGCTGCCCGATA GAAAAGACGATCTCTAAAGCCAAGGGCCAACCCAGAGAGCCTCAAGTATATACTCT CCCACCGAGTCGAGATGAGCTCACTAAGAACCAGGTGTCACTCACGTGTCTGGTTA AAGGATTTTACCCTAGTGATATAGCCGTGAGTGGAATCAAATGGGCAGCCGGAG AATAACTATAAGACCACGCCTCCAGTTCTCGATTCCGATGGTAGCTTTTTCTTTTA CTCTAAACTTACGGTCGACAAGTCCAGGTGGCAACAGGGCAATGTATTTTCTTGCT CCGTGATGCACGAGGCTTTGCACAACCATTACACGCAAAAGTCACTGTCCCTGTCT CCTGGAGGCGGTTCTGACAGTTGGCAGGAGGAGGTAAATCAAATTGTGTGGCGGGA GTTGGTTAGGGCGCAAATTGCTATTTGCGGCAAAAGTACTGGGGGCGGTGAAGGCG GAGGCGAGGGAGGAGGAGAAGGTGCACAAGTGTATTCTGCCTTGGCGAACAAATGC TGTCACGTGCGCTGTACGAAACGGTCTTTGGCCAGTTTTGT
482	GATAAGACACACACTTGTCCGCCATGCCCTGCGCCGGAAGCGGCGGGAGGACCGTC CGTTTTTCTGTTCCTCCCAAAACCCAAAAGACACGTTGATGATTAGTCGCACGCCAG AAGTTACGTGCGTTGTCGTAGATGTATCCACGAAGACCCCGAGGTGAAGTTCAAT TGGTATGTAGATGGGGTGGAGGTCCATAACGCTAAGACCAAACACGCGAGGAACA

SEQ ID NO:	Sequence
	ATATAATTCTACGTACCGCGTAGTGAGCGTTCTCACAGTTCTTCACCAGGATTGGC TTAACGGCAAGGAGTATAAGTGTAAAGGTGTCTAATAAGGCCTTGGCTGCCCCGATC GAAAAACGATAAGTAAAGCAAAGGGTCAACCTAGAGAAACCCCAAGTGTACACTCT CCCGCCATCACGGGATGAATTGACTAAGAACCAAGTGTCACCTCACGTGTCTTGTAA AGGGCTTCTACCCATCCGATATAGCCGTTGAGTGGGAATCCAATGGTCAGCCAGAG AACAACATAAGACAACCTCCGCCCGTACTTGATAGTGACGGTTCCTTTTCCCTTTA CAGTAAATTGACGGTAGATAAGTCTCGCTGGCAGCAAGGAAACGTCTTTTCTTGT CAGTGCTTCATGAGGCGTTCACCTCACACTATACTCAGAAGAGTTTGTAGTTTGTCT CCAGGTGGAGGCAGCGACTCATGGCAAGAGGAAGTAATCAAACGTGTGTGGTCGCGA ATTGGTACGAGCACAGATCGCGATCTGCGGGAAATCAACAGGTGGCGGCGAAGGCG GCGGGGAAGGCGGCGGCGAAGGTAGGCAACTTTACTCAGCCCTTGCGAACAAATGT TGCCACGTAGGCTGTACTAAGAGAAGTCTCGCCAGTTTGC
483	GACAAGACTCATACCTGCCCCCTTGTCCAGCACCAGAAGCAGCTGGCGGGCCAAG CGTGTTCCCTGTTTTCCACCTAAGCCCAAAGATACGTTGATGATCAGCCGCACCCCG AAGTAACCTGTGTAGTAGTAGTGTGTCCCACGAAGACCCGAAGTAAAGTTAAT TGGTACGTGATGGTGTGCGAAGTACATAACGCTAAAACGAAGCCCCGAGAAGAGCA GTACAACAGTACTTACAGAGTAGTTTCTGTTCTTACAGTGCTGCATCAGGATTGGC TGAACGGGAAGGAGTATAAATGTAAAGTCTCAAACAAGGCACTTGCGGCACCAATA GAGAAGACAATATCTAAGGCCAAAGGGCAGCCTAGAGAGCCACAAGTATATACGCT GCCCCCAGCAGGGACGAGCTGACAAAGAACCAAGTGTCACTGACCTGCCTTGTTA AGGGCTTCTATCCGAGTGATATTGCTGTTGAATGGGAAAGTAACGGACAGCCGGAG AACAACATAAACTACTCCACCCGTGTTGGATAGTGACGGTAGCTTTTTTCTGTA CTCCAAGTTGACGGTAGACAAAAGTCCGGTGGCAGCAGGGGAACGTATTTTCTTGT CTGTATGCACGAAGCTCTTCACAATCACTATACGCAGAAGTCCCTCTCTCTCTCT CCTGGGAAGGGTGGTTCCGACAGCTGGCAGGAGGAGGTCAATAACTGTGTGGTAG AGAGTGGTACGGGCTCAAATTGCAATTTGTGGTAAGAGTACTGGCGGTGGCGAGG AAGGGGGTGGGAGGAGGGCGGAGGTAGGCAGCTCTACTCTGCTCTCGCCAACAAG TGTTGTACAGTCGGGTGTACTAAAAGATCACTTGCCCGCTTTTGT
484	GACAAAACACATACATGCCCCCGGTGTCCGGCGCCTGAAGCAGCAGGAGGCCCCAG TGTATTCCCTTTTCCCTCCAAAGCCAAAAGATACGTTGATGATATCTAGGACACCTG AGGTTACCTGCGTCGTAGTGGACGTATCCCACGAAGACCCAGAAGTCAAGTTTAAAC TGGTATGTGGACGGAGTGGAGGTACACAATGCAAAGACAAAGCCGCGAGAGGAACA ATATAATTCCACCTATAGAGTCGTGTCACTCCTTACGGTCTTGACACAGGACTGGC TCAATGGTAAGGAGTATAAGTGCAAAGTATCAAACAAAGCTCTCGCAGCGCCCATC GAAAAGACCATCAGCAAAGCTAAGGGCCAGCCAAGAGAGCCTCAAGTGTACACGTT GCCGCCTTCAAGGGACGAGCTCACTAAAAATCAGGTATCACTTACGTGTCTTGTCA AAGGGTTTTATCCTTCCGACATCGCGGTTGAATGGGAGAGCAATGGACAGCCGGAG AATAATTATAAAAACGACGCCGCCGGTCCCTTGACAGCGATGGTTCATTTTTCCCTTTA CTCAAAGCTGACGGTTGATAAGTCTAGGTGGCAGCAGGGGAACGTCTTTTCCCTGTA GTGTACTTCATGAGGCGCTCCATTCTCATTACACTCAGAAGTCACTGAGCCTTTCA CCCGGCAAAGGTGGATCAGACTCCTGGCAAGAAGAGGTAATCAAACCTCTGTGGGAG GGAACCTCGTTCGAGCCCAGATTGCAATCTGTGGGAAAAGCACAGGCGGAGGGGAAG AAGGGGGTGGCGAAGAAGGTGGGGGCAGGCAGCTCTATTAGCTCTTGCCAACAAA TGCTGTATGTAGGCTGCACAAAGCGATCACTGGCGAGATTCTGT
485	GATAAACTCATACTTGCCACCTGCCCCGGCTCCCGAGGCAGCAGGTGGACCCTC AGTATTTTTGTTCCCTCCGAAACCTAAAGATACACTTATGATTAGCCGGACCCCTG AGGTAACGTGTGTGGTGGTTGACGTAAAGTCATGAAGATCCAGAAGTAAAGTTTAAAC

SEQ ID NO:	Sequence
	TGGTACGTAGACGGTGTGGAGGTACATAATGCGAAGACAAAACCACGAGAGGAACA GTATAACTCTACCTACCGCGTAGTAAGCGTACTTACTGTGCTCCACCAAGACTGGC TTAACGGGAAAAGAGTATAAGTGTAAAGTCAGTAATAAAGCACTGGCCGCCCGATC GAAAAACAATCAGCAAGGCCAAAGGACAACCAAGGGAGCCTCAGGTCTATACTCT TCCCCGAGTAGGGATGAGCTTACCAAGAACCAGGTGTCTCTGACATGCCTTGTCA AGGGATTTTACCCGAGTGACATAGCCGTAGAATGGGAGTCAAACGGCCAACCTGAA AACAACTATAAGACCACGCCTCCCGTACTCGACTCAGATGGAAGCTTTTTCTCTA TAGCAAGCTGACCGTCGACAAAAGTAGGTGGCAACAGGGAAACGTCTTTAGTTGT CCGTTCATGCACGAAGCTTTCATATAACCATACACCCAGAAGAGTCTTCCCTTCC CCTGGCAAGGGGGCTCCGACTCCTGGCAAGAGGAAGTAATCAAACGTGTGTGGGCG CGAGCTTGTCCGCGCGCAAATAGCCATTTGCGGAAAAAGTACTGGAGGAGGAGAGG AAGGCGGCGGCGAGGAAGGTGGGGGCAGGCAGCTGTACAGTGCCTTGGCTAACAA TGCTGCCATGTTCGGCTGTACGAAAAGGTCTCTTGCTCAATTCTGT
486	GATAAGACACATACCTGTCCACCCTGCCAGCACCTGAAGCTGCAGGCGGCCCCAG CGTATTCCTGTTTTCTCCGAAGCCGAAAGACACACTTATGATTTCCCGACGCCTG AGGTAACCTTGCCTCGTAGTAGATGTGTCTCACGAAGACCCGAGGTGAAATTC AAC TGGTACGTTGATGGTGTGGAAGTTCATAATGCGAAAACTAAACCACGAGAGGAGCA ATATAACTCAACTTATAGAGTTGTGAGCGTCTTGACGGTACTGCACCAGGACTGGC TGAATGGCAAAGAGTACAAATGCAAAGTCTCAAATAAGGCGTTGGCGGCTCCCAT GAGAAAATATCAGCAAAGCCAAGGGTCAACCTCGGGAGCCACAAGTGTATACTCT TCCGCCTAGTCGCGACGAGCTCACAAAGAATCAGGTGAGTCTTACTTGTGTGTTA AGGGTTTTCTACCCAGTGACATTGCGGTTCGAGTGGGAAAGTAACGGACAGCCTGAA AACAACTATAAAACAACGCCTCCAGTACTCGATTGAGATGGTTTCTTTCTTTA TTCCAAACTCACAGTCGACAAGAGTAGATGGCAACAAGGGAACGTGTTTAGCTGTA GCGTACTCCATGAGGCACTCCACTCTCACTATAACCCAAAAGTCTCTCAGCTTGTCA CCCGGAAAAGGCGTTCTGACAGTTGGCAAGAGGAAGTGATTAATTTGTGTGGGCG GGAACCTTGTGAGGGCTCAAATCGCGATTTGCGGCAAGTCCACTGGTGGCGGCGAGG AAGGAGGAGGTGAAGAAGGAGGAGGTAGGCAACTGTATTGAGCGTTGGCGAATAAA TGCTGCCATGTTGGATGTACTAAACGGAGCCTTGCTCAGTTCTGC
487	GATAAAACGCATACCTTGCCCTCCTTGCCCGGCACCTGAAGCTGCCGGAGGTCTTTC CGTGTTCCTGTTCCACCTAAGCCAAAAGACACACTTATGATTTCTCGCACACCAG AAGTAACGTGCGTCGTAGTTGACGTCTCCCATGAAGACCCGGAGGTAAAATTTAAT TGGTACGTCGACGGGGTAGAAGTTCATAACGCAAAGACTAAACCACGAGAAGAGCA ATACAACCTCTACATACAGAGTAGTAAGCGTTCTCACCGTTCTTCATCAAGATTGGC TCAACGGAAAGGAGTATAAGTGTAAAGGTGTCCAATAAAGCGTTGGCCGCACCAATC GAAAAGACCATAAGCAAAGCCAAAGGCCAACCCCGCAACCGCAGGTGTACACACT TCCCCCGTCCAGGGATGAATTGACAAAAAACCAAGTTTCCCTCACGTGTCTCGTCA AGGGATTCTACCCGAGTGATATCGCAGTTGAATGGGAAAGCAATGGTCAGCCCGAG AATAACTACAAGACTACTCCCCCTGTGTTGGACTCAGACGGCTCATTTCTTCTCTA CAGTAAGTTGACTGTGGACAAAAGTCGGTGGCAGCAAGGCAATGTCTTCAGTTGTA GTGTAATGCATGAAGCACTCCACAATCATTACACCCAAAAATCCCTGAGCCTGTCC CCGGGCGGAGGTTGAGATTCATGGCAGGAGGAAGTTATAAACTGTGCGGGCGCGA GTTGGTGAGGGCGCAGATCGCAATCTGTGGAAAGAGTACGGGAGGTGGCGAAGAGG GTGGTGGAGAAGAGGGAGGAGGTGCAAACTGTATTCCGCGCTCGCGAACAAGTGT TGCCACGTTGGCTGCACCAACGAAGCCTGGCTCGATTTTGC
488	GACAAGACACACACTTGTCCACCTTGCCCGGCTCCCGAGGCGGCAGGAGGACCAAG CGTTTTTCTGTTCCCTCCCAAACCAAAGGATACGCTTATGATCTCTCGAACGCCGG

SEQ ID NO:	Sequence
	AAGTTACTTGCGTAGTAGTTGATGTCTCCCATGAAGATCCCGAAGTGAAGTTC AAC TGGTATGTAGATGGTGTGGAAGTTCATAACGCGAAAAACCAAACACGCGAAGAACA GTATAACAGTACTTATCGGGTTGTTTCAGTACTCACGGTGCTCCATCAAGACTGGC TTAATGGAAAGGAGTATAAATGTAAGGTAAGTAACAAGGCATTGGCGGCTCCCATC GAGAAGACAATCTCCAAAGCAAAAGGGCAACCACGGGAGCCTCAGGTGTATACGTT GCCGCCAGCAGAGATGAACTACTAAGAATCAGGTGAGTCTCACTTGTCTCGTCA AGGGCTTCTATCCAGCGATATAGCCGTAGAATGGGAGAGTAACGGTCAGCCGGAG AACAACTACAAAACAACCCCGCTGTTTTGGACTCCGATGGGAGTTTTTTTCTCTA CAGCAAACCTCACGGTAGACAAAAGCAGGTGGCAGCAGGGCAATGTTTTCAGTTGCT CTGTTCTCCACGAAGCCCTCCACTCCCACTATACTCAGAAGTCTCTGAGTCTCTCA CCAGGGGGAGGTAGCGATAGCTGGCAGGAGGAAGTGATCAAGTTGTGCGGGGCGCA ACTCGTGCGGGCACAAATTGCTATATGCGGTAAAAGTACGGGAGGTGGAGAGGAGG GTGGAGGTGAAGAAGGCGGTGGTAGACAATTGTATAGTGCGCTCGCCAACAAGTGT TGTCATGTGCGGTGTACGAAACGGTCCTTGCGCGGTTTTGC
489	GACAAGACACATACTTGTCCACCATGTCCCGCCCCAGAAGCTGCGGGAGGACCATC AGTTTTTTTTGTTCCCCCGAAACCGAAGGATACCCTCATGATAAGTCGAACGCCCG AAGTCACTTGCGTGGTGGTTGATGTTAGCCACGAGGACCCAGAAGTGAAGTTC AAC TGGTACGTGGACGGGGTCGAAGTTCATAATGCGAAAACAAAGCCTCGCGAGGAACA GTACAACCTCTACATACAGGGTTGTGTCTGTTTTGACAGTCTTGACCAAGATTGGC TCAACGGGAAGGAATATAAGTGTAAGGTAAGCAATAAAGCACTGGCGGCCCGCATC GAAAAAACGATATCCAAGGCCAAGGGCCAGCCCCGAGAGCCTCAGGTATATACTCT GCCGCCAAGCCGGGATGAACTGACTAAAAAACAGGTCTCTTTGACTTGTCTTGTCA AGGGATTTTACCCAAGTGACATTGCGGTAGAGTGGGAAAGCAACGGTCAACCAGAA AACAAATTACAAGACGACACCGCCGGTACTCGACTCAGATGGATCCTTTTTCTGTGA TAGCAAGCTGACAGTGGACAAGTCCCGGTGGCAGCAAGGGAACGTATTTTCATGCA CGGTGATGCATGAGGCTCTTACAACCATTAACACACAGAAAAGTCTGTCAATTGAGC CCTGGCGGGCGGAGCGATTCTTGCGCAAGAAGAAGTTATAAAACTTTGCGGTCGAGA GCTGGTTGCGGCACAAATTGCTATCTGCGGAAAATCTACAGGAGGAGGCGAGGAGG GAGGGGGCGAAGAAGGCGGGGGGAGACAGTTGTACAGTGCGCTCGCTAACAAGTGT TGCCACGTGCGTTGCACAAAGAGATCCCTGGCTCAATTCTGT
490	GATAAAACTCACACCTGTCCCCGTGTCCCGCACCAGAAGCGGCCGGTGGTCCCTC CGTTTTTCTCTTCCCTCCTAAACCTAAGGACACACTTATGATTAGCAGAACTCCAG AAGTTACGTGCGTAGTCGTTGACGTTAGTCATGAAGATCCTGAGGTTAAGTTC AAC TGGTACGTAGACGGAGTAGAGGTCCACAACGCCAAGACGAAACCCCGAGAAGAGCA GTATAATTCTACCTATCGAGTTGTTTCAGTATTGACGGTGCTTCACCAAGATTGGC TGAATGGCAAAGAGTATAAGTGCAAGGTAAGCAACAAAGCACTCGCGGCTCCTATC GAGAAAACCTATTTCCAAAGCTAAGGGCCAGCCTCGCGAACCACAAGTCTATACCT GCCACCGAGTCGGGACGAACTCACCAAGAACCAAGTGTCTCTTACTTGCCCTCGTTA AAGGTTTTTATCCAGCGACATAGCCGTGGAATGGGAGTCCAATGGCCAACCTGAG AACAACTATAAACTACCCCTCCTGTACTTGATAGCGACGGAAGTTTTTCTCTCTA TTCAAACTCACAGTTGATAAGTCTCGATGGCAACAGGGCAACGTCTTCTCTTGCA GTGTGTTGCATGAAGCTCTGCACTCTCATTACACACAGAAGAGTTTGTCTCTCAGT CCAGGTGGCGGCTCAGATAGCTGGCAGGAAGAAGTAATCAAGTTGTGCGGCAGGGA ACTGGTAAGGGCACAGATAGCCATTTGTGGAAAATCTACGGGTGGCGGTGAGGAAG GCGGCGGAGAAGAAGGGGGAGGTGCGGAGCTGTATAGTGCACTCGCAAACAAGTGC TGCCATGTGCGGTGCACCAAGCGATCCCTTGCCAGTTTTGC

SEQ ID NO:	Sequence
491	GATAAGACGCACACATGCCCCACCCTGTCCTGCGCCTGAAGCCGCGGGGGGACCCAG CGTTTTTCTCTTCCCGCCGAAACCGAAAGACACACTTATGATCAGCCGGACTCCCG AGGTTACCTGCGTGGTGGTAGATGTATCTCACGAGGATCCCGAGGTCAAATTCAAC TGGTACGTTGATGGGGTTGAAGTTCATAATGCCAAAACGAAGCCAAGAGAAGAGCA GTATAACTCCACATATAGAGTTGTTTTCCGTCTTGACTGTTCTTCACCAAGATTGGC TGAATGGGAAGGAGTACAAATGTAAAGTTAGCAACAAGGCACTCGCCGCTCCCATTT GAAAAAACTATAAGCAAAGCTAAGGGCCAACCGCGCGAACCACAGGTCTACACGTT GCCGCCCTCTAGGGACGAACTCACGAAGAATCAGGTTTTCCCTTACCTGCCTCGTTA AAGGATTCTACCCCTCTGACATAGCGGTTGAATGGGAGAGCAACGGTCAGCCTGAG AACAACTACAAAACGACGCCTCCGGTGTGGATTCCGACGGTAGTTTTTCTCTCTA TAGTAAGCTGACAGTGGATAAACTCTCGGTGGCAGCAAGGGAATGTATTCTCCTGTT CAGTCCTGCATGAAGCCCTCCACTCCCATATACACAGAAATCTCTTCTCTGAGT CCCGGTAAAGGTGGGAGTGACTCTTGGCAGGAAGAGGTAATTAAGTTGTGTGGAAG GGAGCTGGTAAGAGCACAGATTGCCATCTGTGGCAAATCCACGGCGGCGAAGGTG AGGGGGGTGAGGGGGAAGGGGGTCCAGACAACGTATTCTGCTCTGGCGAATAAG TGTTGCCATGTAGGGTGCCTAAACGGTCTTGGCGCAGTTCTGT
492	GATAAACTCATACGTGCCCCACCTTGCCCCGCACCGGAGGCTGCTGGAGGACCCCTC TGTCTTCTGTTCCCGCCGAAGCCTAAAGACACATTGATGATCAGTCGAACACCGG AAGTCACCTGTGTAGTGGTTGATGTGAGCCATGAGGACCCTGAAGTAAATTTAAC TGGTATGTTGATGGCGTAGAAGTACACAACGCGAAGACTAAACCAAGGGAAGAGCA ATACAACTCTACCTATAGGGTCGTTAGCGTACTGACTGTGCTTCACCAAGACTGGC TTAACGGGAAGGAGTACAAGTGCAAAAGTGAAGCAATAAGGCCCTCGCCGCGCCTATC GAGAAAACCATTTCCAAAGCCAAGGGTCAACCAAGGGAGCCTCAGGTTTACACCCCT GCCCCCTTCAAGGGATGAGTTGACAAAAAACAGGTAAGTCTGACGTGTCTCGTTA AGGGATTCTACCCGTCAGATATCGCGGTAGAGTGGGAGAGCAACGGTCAGCCAGAA AATAATTACAAAACAACACCTCCAGTTTTTGGACTCTGATGGGAGTTTTTTTTCTTTA TTCTAAGTTGACAGTGGATAAGTCACGCTGGCAACAGGGGAACGTATTTAGCTGCT CAGTACTTCATGAAGCGTTGCATTCTCACTACACACAGAAGAGCCTCTCCTTGAGT CCCGGAGGTGGCTCTGATTCTTGGCAGGAGGAGGTAATAAACTTTGTGGTAGAGA ACTGGTTCGCGCTCAGATAGCTATTTGTGGAAAATCCACTGGCGGTGAAGGTGAAG GTGGAGAAGGAGAGGGCGGAAGCCGCGCAGTTGTACTCTGCCCTGGCTAATAAGTGC TGTCACGTGGGCTGCACTAAGCGGAGCTTGGCAAGATTTTGC
493	GATAAACTCATACCTGTCCACCTTGTCCTGCGCCTGAGGCAGCTGGAGGGCCTAG CGTGTTTCTGTTCCCCCCCCAAACCCAAAGACACGCTCATGATTAGCCGAACCCCTG AAGTGACCTGCGTTGTTGTGGACGTAAGCCACGAAGACCCCGAAGTTAAGTTTAAAT TGGTACGTCGACGGTGTGAGGTTCAACGCGAAGACTAAGCCGAGAGAGGAGCA ATATAACAGCACCTACCGCGTAGTCTCAGTTCTTACCGTGCTCCACCAGGACTGGC TTAACGGGAAGGAATACAAATGCAAAGTTTCCAACAAAGCCTTGGCAGCCCCAATA GAGAAGACAATATCTAAGGCGAAAGGCCAACCGCGGGAACCGCAAGTTTATACCCT CCCACCGAGCAGGGATGAGCTGACAAAAAATCAGGTTTCCCTCACTTGTCTGGTCA AGGGATTTTATCCTTCAGACATAGCCGTTGAATGGGAGAGTAATGGGCAGCCGGAG AATAATTACAAGACCACCCCCCGGTGTTGGACAGCGACGGTTCCTTCTTTCTCTA TTCTAAACTTACCGTCGACAAATCACGGTGGCAACAAGGAAATGTATTCTCATGCA GTGTATTGCACGAAGCTCTGCACTCTCATTACACCCAAAAATCCCTCTCTCTCAGC CCTGGCGGTGGATCTGATTCTTGGCAGGAAGAGGTGATTAACTGTGTGGCGGAGA GCTTGTCCGAGCTCAGATCGCTATTTGTGGCAAGAGTACCGGAGGCGAGGGTGAGG

SEQ ID NO:	Sequence
	GAGGCGAAGGCGAGGGCGGAAGCCGGCAACTCTATAGCGCACTCGCTAATAAATGT TGTCATGTGGCTGCACGAAGCGCTCACTGGCGCAGTTCTGC
499	GATAAAACCCATACGTGTCTCCATGCCAGCTCCCGAGCTGCTCGGTGGTCCTTC AGTGTTTCTCTTTCCCCCAAAGCCGAAGGACACGCTCATGATTAGTCGAACGCCAG AGGTGACATGTGTGGTCGTTGATGTTTCCCATGAGGATCCGGAAGTTAAGTTCAAC TGGTACGTAGATGGCGTGGAGGTTACAATGCAAAAACCAAGCCCCGCGAGGAGCA GTATAACTCAACCTACAGAGTAGTATCTGTGCTCACGGTCTTGTCATCAGGATTGGT TGAACGGGAAGGAATACAAGTGTAAAGTAAGTAATAAGGCACTGCCGGCCCCATA GAAAAAACTATCAGCAAAGCTAAAGGTGAGCCGCGGGAGCCACAAGTTTACACTCT TCCTCCTAGTAGAGACGAGCTGACGAAGAATCAAGTTTCTTTGACTTGCTCTCGTGA AGGGATTCTACCCAAGCGATATAGCTGTAGAGTGGGAAAGCAACGGACAACCAGAA AATAACTACAAGACTACACCCCCGTCTCGATTCTGATGGCTCATTCTTCTTGTA CTCAAAATTGACAGTTGACAAATCTCGATGGCAGCAGGGTAACGTATTTAGTTGCT CTGTTATGCACGAAGCGTTGCATAACCACTACACACAGAAGTCATTGTCACTGAGC CCAGGAAAAGGTGGTGGCGGGTCCGCGGGTGGAGGTAGCGGTGGCGGGGGCTCCCA GCTTTATAGTGCCCTTGCAACAAATGTTGCCACGTGCGATGTACGAAGCGCAGTT TGGCGAGATTCTGTGGAGGGGGCGGATCCGGAGGCGGGGGGTCCGGAGGAGGAGGT AGCTCATGGATGGAAGAGGTAATAAACTGTGCGGACGCGAGCTTGTGAGGGCCCA AATCGCAATTTGTGGCATGAGCACATGGAGT
532	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTGCTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAAGTACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCTATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAAG TGTTGTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
533	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTGCTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAAGTACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCTATTGTCC

SEQ ID NO:	Sequence
	CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAAG TGTTGTCAAGTTGGGTGTACCAAGCGGTCCCTTGC GCAATTCTGC
534	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAAG TGTTGTCAAGTTGGGTGTACCAAGCAATCCCTTGC GCAATTCTGC
535	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAAG TGTTGTCAAGTTGGGTGTACCAAGCAATCCCTTGC GCAATTCTGC
536	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATACCTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAAG TGTTGTCAAGTTGGGTGTACCAAGCAATCCCTTGC GCAATTCTGC

SEQ ID NO:	Sequence
	GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGATCTGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
537	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGATCTGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTCAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
538	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGATCTGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTACGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
539	GATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAG TGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGG AAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAAT TGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCA GTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGATTGGT TGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATT GAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATACTTT GCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTGGTTA AGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCCTGAG AATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTCTTTA TTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGATCTGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTACGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC

SEQ ID NO:	Sequence
	TTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCTTGCA GCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCTATTGTCC CCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAAACTTTGTGGACG GGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAAGGCT CTGGAGGCGAAGGATCTGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAACAAG TGTTGTCAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC

[0191] In some embodiments, the vector comprises a polynucleotide sequence that is at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or 99% identical to a sequence recited in Table 10, below. In some embodiments, the vector comprises a polynucleotide sequence that comprises or consists of a sequence recited in Table 10, below.

Table 10. Nucleotide Sequences Encoding Fusion Proteins and Peptide Components

SEQ ID NO:	Sequence
194	ATGGAGACTGACACACTCCTCCTTTGGGTTTTGCTGTTGTGGGTGCCTGGATCTAC TGGCGACAAGACCCATACATGTCCGCCTTGTCTGCGCCTGAGGCAGCAGGGCGGAC CATCAGTCTTCTTGTTCCTCCCAAGCCGAAGGACACCCTTATGATCTCACGCACC CCCGAAGTAACTTGTGTAGTCGTTGATGTCTCACACGAAGACCCGGAAGTAAAGTT TAATTGGTATGTCGATGGTGTGAGGTCCACAACGCTAAAACGAAACCGCGGGAAG AACAATACAACCTCCACATATCGAGTAGTCTCCGTCCTGACTGTTCTTCACAGGAC TGGCTGAATGGTAAAGAATACAAATGTAAAGTGAGTAACAAGGCCCTTGCAGCACC CATCGAGAAGACGATATCCAAAGCCAAGGGGCAACCGCGGAGCCACAAGTTTACA CGCTCCCACCCTCAAGAGACGAACTACCAAAAATCAAGTGTCCCTGACATGTCTG GTGAAAGGATTCTATCCAGCGACATAGCTGTAGAATGGGAGAGTAATGGCCAACC CGAAAACAATTACAAAACCTACCCCCCGTTTTGGATAGTGATGGTTCATTCTTCC TCTATAGTAACTTACCGTGGATAAGTCTCGGTGGCAGCAGGGGAACGTGTTTAGC TGTTTCAGTCCCTCCATGAGGCACTCCATAGTCACTATACGCAAAAGTCATTGTCCCT TTCTCCGGGCAAGGGCGGGTCAGACTCCTGGCAGGAAGAGGTAATTAAGCTTTGTG GGCGAGAACTCGTTAGGGCACAGATAGCAATCTGCGGGAAAAGTACAGCTTCCGAT GCTGCCGGGGCTGACGCCAATGCGGGAGCACGCCAGCTCTACTCAGCCCTCGCCAA CAAGTGTTGTGTCATGTAGGTTGCACCAAAAAGAAGTCTGGCACAGTTTTGC
195	ATGGAAACAGACACTCTTCTTTTGTGGGTCTTGTTGCTCTGGGTCCCTGGCTCAAC AGGCGACAAGACGCATACTTGTCTCCCTGCCCAGCTCCCGAAGCGGCTGGGGGGC CCTCTGTCTTTCTGTTTCCGCCTAAGCCCAAGGACACGCTCATGATAAGTCGCACT CCGGAAGTCACCTGTGTTGTCGTCGATGTTAGCCATGAAGATCCAGAGGTGAAATT TAACTGGTACGTCGACGGAGTGGAGGTTACAATGCTAAAACCAACCGCGAGAAG AGCAATACAATTCCACGTATAGGGTCGTCTCCGTCCTGACAGTACTCCATCAGGAT TGGCTGAATGGAAGAATACAAAGTGCAAGGTTTCCAATAAAGCCTTGCCCGCAC

SEQ ID NO:	Sequence
	TATTGAGAAAACGATATCAAAAGCTAAGGGACAACCTCGGGAGCCGCAAGTATATACACTCCCCCTTCTAGGGACGAACTGACAAAAAACCAAGTTAGTCTGACTTGTCTTGTGAAAGGTTTTTACCCGAGTGATATAGCCGTAGAATGGGAGAGCAATGGCCAGCCGAAAAACAATTACAAAACAACCTCCCCCAGTATTGGACAGTGACGGGTCATTTTTTTTGTATTCTAAATTGACCGTAGACAAGTCACGCTGGCAACAAGGGAATGTATTTAGCTGTTCCGTCCTTCATGAGGCGCTCCATAGCCATTACACTCAGAAGTCTTTGTCACGTGTCACCGGGCAAGGGTGGTTCTGATTCATGGCAAGAGGAAGTGATTAAGCTGTGCGTCCGGAGTTGGTAAGAGCTCAAATTGCGATTTGTGGCAAGAGCACTGCGTCCGATGCCGCAGGTGCTAATGCCGACGCCGGTGCGAGACAGCTTTATTCTGCGCTGGCCAACAAGTGCTGCCACGTCGGATGCACCAAACGGAGCCTTGCTCAGTTTTGC
196	ATGGAAACCGACACCCTGCTTCTCTGGGTGCTGCTGCTCTGGGTACCAGGGTCTACAGGTGACAAAACCTCATACTTGTCACCATTGCCCAGCCCCGAGGCGGCTGGCGGCCCCAGCGTATTCTTTTTCCCCCAAAACCTAAGGACACGCTTATGATATCTAGAACCCTGGAGGTCACATGTGTCGTCGTAGACGTAAGTCACGAAGATCCTGAAGTCAAGTTAACAGTATAATTCTACCTATCGCGTAGTCTCTGTCCTCACCGTCTTGTCATCAAGACTGGTTGAACGGCAAGGAGTACAAGTGTAAGGTTTTCAAACAAAGCCCTTGCCGCGCCGATAGAGAAAACAATTAGCAAAGCGAAGGGGCAGCCGAGAGAGCCGCAAGTGATATACCTTCTCTAGTAGAGACGAGTTGACCAAAAACAGGTGTCACTTACATGCCTC GTGAAAGGCTTCTACCCGAGTGATATTGCAGTCGAGTGGGAATCCAACGGCCAGCCCGAGAATAACTACAAAACGACGCCGCCCGTACTGGACAGTGATGGAAGTTTTTTTTTGTACTCAAAACTCACGGTTGACAAAAGTCGGTGGCAGCAAGGGAACGTTTTTTAGCTGCTCTGTCTCCATGAAGCACTCCATTCTCATTATACCCAGAAGTCTCTGTCTCTCTCCCCCTGGTAAGGGAGGTTCTGACAGTTGGCAGGAAGAGGTAATAAAACTCTGCGTCCGAGAGCTTGTTCGAGCACAAATTGCTATATGTGGAAAATCTACCGCTTCAGAGCCGCGGAGCTGATGCGGATGCCGGGCTCGCCAGCTCTATAGCGCCTTGCCCAA CAATGTTGTCACGTTGGCTGCACGAAGCGCTCCCTGGCTCAGTTTTGC
197	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCACAGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGACCTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACACCGGAAGTAACCTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATTTAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGGAGCAGTATAATTCTACATACCGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCCGATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCAACCCCAAGTATATACCTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATGGCAAGAAGAAGTCATTAACCTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTCACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
198	ATGGGAGACTGATACACTTCTTCTCTGGGTCTCTCTCTGGGTCCAGGCTCAACAGGTGATAAAACCTCATACTTGCCCCCTGCCCCGCGCCTGAAGCTGCAGGGGGGC CATCAGTCTTCTTGTTCACCAAAAACCTAAGGATACTCTCATGATTAGCCGGACC

SEQ ID NO:	Sequence
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199	ATGGAAACCGATACCTTGCTCCTTTGGGTTCTGCTCCTTTGGGTCCCTGGAAGTAC AGGGGATAAGACACACACGTGCCACCCTGCCCTGCCCGAGAGGCAGCCGGAGGTCT CTAGTGTGTTTCTGTTCCCCCAAAGCCCAAGGACACCCTTATGATATCTAGGACA CCAGAAGTTACGTGCGTCGTTGTGGACGTTAGCCACGAAGACCCAGAAGTGAAGTT TAATTGGTACGTTGATGGAGTCGAAGTGCACAATGCAAAAACAAAACACGAGAAG AGCAGTATAACAGTACTTATAGAGTAGTCAGCGTCCTTACTGTATTGCATCAGGAT TGGCTGAATGGGAAGGAATATAAATGTAAGGTTAGCAATAAAGCCCTTGCGGCTCC TATCGAGAAAACCTATTAGCAAAGCAAAGGGCCAACCCCGAGAGCCCCAAGTTTATA CACTGCCACCCAGTCGAGATGAGCTGACTAAAAATCAAGTATCCCTGACCTGCTTG GTTAAGGGGTTTTATCCTAGTGACATCGCGGTTGAGTGGGAATCCAACGGCCAACC GGAGAATAATTACAAAACACGCCACCTGTATTGGATTCCGATGGTAGCTTCTTTCA TCTATAAGTAACTTACAGTCGATAAGTCAAGATGGCAGCAGGGAAACGTATTTTCA TGCTCAGTTCTGCATGAGGCCTTGCACTCCCATTAACACTCAAAAATCACTGAGCCT CAGTCCTGGTAAGGGTGGCTCTGACTCATGGCAGGAGGAAGTAATCAAGCTGTGTG GGAGGGAATTGGTAAGGGCTCAGATTGCAATTTGTGGAAAGAGCACAGCGTCTGAC GCTGCAGGTGCCGACGCACAGGCGGGCGGAGGCAGCTCTACAGTGCTCTTGCGAA CAAGTGTTGTGATGTAGGTTGCACGAAACGAAGTTTGGCGCAATTCTGT
200	ATGGGAGACTGACACTCTCCTTCTTTGGGTGCTGTTGCTCTGGGTTCCCGGAAGCAC GGGGGATAAAACACACACCTGCCCCCTTGCCAGCACCTGAAGCAGCGGGTGGTC CCAGCGTTTTTCTTTTCCCCCTAAGCCAAAGGACACGCTCATGATAAGTCGCACC CCGGAGGTCACCTGCGTCGTTGTTGACGTATCACATGAAGATCCTGAGGTGAAGTT TAATTGGTACGTAGATGGTGTGAGGTCCACAACGCAAAGACGAAACCGAGGGAAG AACAGTACAACAGTACTTATCGCGTAGTCTCCGTTCTGACTGTCCTGCATCAAGAT TGGTTGAACGGGAAGGAGTACAAGTGCAAAGTTAGTAACAAGGCTCTCGCGGCCCC AATTGAGAAGACGATATCCAAAGCGAAAAGGACAGCCGAGAGAGCCCCAAGTCTACA CTCTGCCCCCTTCCAGGGATGAGCTCACCAAAAATCAGGTCAGTCTCACGTGCCTG GTTAAGGGATTCTACCCAAGTGATATAGCAGTTGAATGGGAGAGTAACGGCCAGCC CGAGAACAACATAAACTACACCGCCCGTTCTTGATTCCGATGGGTCTTTCTTCC TTTATAGTAAGCTCACCGTTGATAAGTCCCGATGGCAGCAAGGTAATGTCTTCTCA TGTTTCAGTTCTTCATGAAGCCCTGCATTCCCATTAACACAAAAGAGCTTGTCTCT GTCACCGGGCAAAGGCGGTAGCGATTCTTGGCAAGAAGAAGTTATAAAGTTGTGCG GTAGGGAACGGTACGCGCTCAATAGCTATATGCGGTAAGTCTACTGCTTCAGAT

SEQ ID NO:	Sequence
	GCGGCTGGCGCACAGGCACAGGCCGGTGCTAGACAACTCTATAGTGCCTGGCCAA CAAGTGCTGCCATGTGGGGTGTACAAAACGGAGTCTTGCCAGTTTTGT
201	ATGGAAACTGACACGCTTTTGCTTTGGGTCCTCCTTCTTTGGGTTCCCGGCTCTAC TGGAGACAAAACCTATACATGCCCCCATGCCCAGCACCCGAAGCGGCCGGAGGTC CGTCTGTCTTTCTGTTTCCGCCGAAACCTAAAGATACGTTGATGATTAGCAGAACC CCTGAGGTAACATGTGTGGTAGTCGATGTCTCCCATGAGGACCCCGAGGTAAAGTT CAATTGGTATGTTGACGGCGTCGAAGTCCATAACGCAAAAACGAAGCCCCGAGAGG AGCAATATAACTCTACCTATCGCGTTGTTTCTGTTTTGACTGTGTTGCACCAGGAT TGGCTCAACGGCAAGGAATACAAATGTAAAGTGTCCAACAAGGCCCTTGCTGCACC TATCGAAAAAACGATTAGTAAGGCAAAGGGACAACCGCGCGAACCACAGGTATATA CTTTGCCGCCTAGCAGAGATGAACTCACCAAGAATCAAGTTTCCCTTACCTGTTTG GTTAAAGGATTTTACCCGTCGTGACATAGCTGTTGAATGGGAGAGCAATGGTCAGCC GGAAAATAATTATAAAACCACCCCGCCAGTATTGGATTGAGATGGGTCCTTTTTCT TGTATTCTAACTTACCGTGGATAAGTCTAGGTGGCAACAGGGAAACGTCTTTTCA TGTAAGTGTACTTCATGAAGCCCTCCATAGTCACTACACGCAGAAATCCTTGTCTCT TAGTCCGGGTGAAGGTGGGTCTGATTCTGTCAGGAAGAGGTGATAAAGCTCTGTG GTCGGGAACTTGTTAGGGCGCAGATCGCTATTTGCGGCAAATCTACAGCATCAGAT GCCGCCGGAGCTGATGCGAACGCAGGAGCGAGGCAGCTGTACTCCGCACTTGCTAA CAAGTGTTGCCATGTCGGCTGCACCAAGAGGAGTCTTGCTCAATTCTGC
202	ATGGAAACCGACACCCTCCTTCTTTGGGTCCTGCTGCTTTGGGTTCTGCTTCTAC TGGAGATAAGACCCATACATGCCCAGCATGTCCCGCACCCGAGGCAGCGGGTGGAC CCTCTGTCTTTCTGTTCCCTCCAAAGCCAAAAGATACCCTGATGATTAGCCGAACC CCGGAGGTGACTTGTGTCGTAGTAGATGTCAGTCACGAGGATCCCGAAGTAAAGTT TAATTGGTATGTGGACGGTGTGGAGGTACATAACGCTAAGACGAAACCCCGAGAGG AACAATACAACCTCTACGTACAGGGTCGTCTCAGTGCTCACGGTCTGCACCAGGAC TGGCTTAATGGGAAGGAATATAAATGCAAAGTCTCTAATAAGGCGCTTGCTGCACC TATTGAAAAAACGATTTCTAAGGCGAAGGGACAACCCCGGAGCCACAAGTCTACA CCCTTCTCCAAGCAGAGATGAGCTTACGAAAAATCAAGTGTCTCTTACGTGCCTC GTAAAGGGCTTTTACCCATCCGACATTGCGGTGGAGTGGGAATCAAACGGGCAGCC GGAAAATAACTACAAAACAACGCCGCTGTATTGGATTCCGACGGCTCTTTCTTCC TTTACAGCAAACCTGACAGTCGATAAATCCAGATGGCAACAAGGGAACGTTTTTTCA TGTTCCGTTCTGCATGAAGCCCTTCACAGTCATTACACCCAAAAGTCACTTTCACT TTCACCGGGCGAGGGGGGTGAGACTCCTGGCAAGAGGAAGTTATAAAGTTGTGCG GCAGGGAACCTGGTTAGAGCGCAGATAGCGATTTGCGGAAAAATCTACTGCGAGTGAT GCTGCGGGAGCGAATGCGGACGCCGGGGCCCGACAGCTCTATTCCGCACTCGCCAA TAAGTGCTGCCATGTTGGTTGTACGAAGAGAAGTCTTGACACAATTTTGC
203	ATGGAAACAGACACGCTGCTTTTGTGGGTACTGTTGCTTTGGGTCCCAGGATCCAC AGGTGATAAGACACATACATGCCCCCCTGCCCAGCTCCCGAAGCTGCCGGGGGAC CGTCAGTGTTTTTGTTCGCCCAAGCCGAAGGATACTTTGATGATTAGTCGGACA CCAGAAGTGACATGTGTTGTCGTTGACGTGAGTCACGAGGATCCCGAGGTCAAGTT CAACTGGTACGTTGATGGGGTTGAAGTTCACAACGCTAAAACGAAACCCCGCAAG AGCAGTATAACTCCACTTACCGGGTCGTGAGTGTCTGACGGTCTTGACCAGGAC TGGCTGAATGGAAAGGAATACAAGTGTAAAGTTTCCAATAAAGCACTGGCCGCCCC GATCGAAAAACAATTTCCAAAGCTAAGGGACAGCCAGGGAACCGCAAGTTTATA CTCTTCCACCCTCCCGGGATGAACTGACCAAAAACCAAGTGTCTTTGACGTGCCTC GTAAAGGGCTTCTACCCGTCAGACATAGCTGTGCAATGGGAGTCTAATGGACAGCC GGAAAACAATTATAAGACTACACCGCCGGTGCTTGATAGTGATGGAAGTTTCTTTT

SEQ ID NO:	Sequence
	TGTA CTCCAACTTACGGTCGATAAAAGCCGGTGGCAGCAGGGAAACGTATTCAGT TGTA GCGTTCTGCATGAAGCTCTTCATTCTCACTACACCCAGAAGTCTCTGTCTCT GAGCCCCGGAGAGGGTGGATCTGATTCTTGGCAGGAAGAAGTGATAAAGTTGTGCG GCCGGGAATTGGTACGCGCCAGATAGCCATTTGCGGGAAGTCTACGGCGAGTGAC GCAGCAGGTGCTGACGCGGACGCTGGTGCTAGACAGCTGTATTCTGCCCTGGCTAA TAAGTGTTGCCACGTTGGCTGCACCAAGAGATCCCTGGCCCAATTCTGT
204	ATGGAACTGACACTTTGCTGTTGTGGGTCTCTGTTGTGGGTCCCCGGAAGTAC AGGAGACAAGACACATACTTGTCCCCCTGCCAGCTCCAGAAGCTGCCGGAGGGC CGTCAGTCTTCCTTTTCCCTCCAAACCTAAGGATACGCTTATGATTTCTCGAACG CCAGAGGTTACGTGTGTAGTCGTGGACGTTTCCACAGAGGATCCTGAGGTCAAGTT TAACTGGTATGTAGACGGGGTTGAGGTCCATAATGCCAAGACAAAGCCGCGGAGG ACAATACAACAGTACATATAGGGTGGTGAGCGTCTCACAGTCTTGCATCAAGAT TGGCTCAACGGCAAAGAGTACAAATGTAAGGTTAGCAACAAAGCCCTCGCTGCTCC CATCGAAAAGACGATTTCTAAGGCGAAGGGCCAACCACGAGAACCGCAAGTATATA CTCTTCCCCCTTACGGGACGAGCTGACCAAAAACAGGTATCCTTGACTTGCCTG GTCAAAGGATTTTACCCCTCTGATATTGCGGTGAGTGGGAGAGTAATGGGCAACC AGAAAATAATTATAAAACGACCCCCCGGTACTCGACAGTGATGGGTCTTTTTTCC TGTA TTCTAAGCTTACGGTTGATAAGTCTAGATGGCAGCAAGGGAATGTCTTCTCA TGTA GTGTTCTGCATGAAGCACTTCATTCTCACTATACTCAGAAATCTCTTTCCCT TAGTCCGGGAGAAGGTGGGAGCGATAGTTGGCAAGAGGAGGTGATAAACTGTGTG GTCCGGGAGCTGGTGAGAGCCCAATAGCTATCTGCGGCAAATCAACAGCAAGTGAT GCGGCAGGAGCGGAAGCGGAGCGGGAGCGCGGCAATTGTATAGTGCCCTTGCTAA TAAATGCTGTACGTTGGGTGTACTAAACGATCTCTTGCTCAATTCTGC
205	ATGGAGACGGATACGTTGTTGCTTTGGGTCTCTGTTGTGGGTGCCCGGCTCTAC CGGTGATAAAACCCATACATGTCCTCCGTGTCCCGCTCCAGAAGCCGCTGGCGGGC CATCTGTGTTTTTGTTCCTCCCAAGCCTAAGGATACGTTGATGATCAGCAGGACC CCGGAGGTTACATGCGTAGTAGTTGACGTTTCTCATGAAGACCCAGAAGTAAATTT TAACTGGTATGTCGATGGCGTCGAAGTACATAATGCTAAAACTAAGCCCAGGGAAG AGCAATACAATTCAACGTACCGAGTTGTGAGTGTCTTACGGTCTTGCACCAAGAC TGGTTGAACGGCAAAGAGTACAAATGCAAAGTGTCTAACAAGGCATTGGCCGCGCC TATAGAAAAGACCATTAGCAAAGCAAAAGGGCAGCCTCGGGAACCCAGGTCTACA CGCTGCCACCTTCCCGAGATGAATTGACGAAAAACAGGTCTCTTTGACCTGCTTG GTTAAAGGCTTCTACCCAAGCGACATTGCAGTGGAGTGGGAGTCTAACGGGCAACC CGAAAACA ACTATAAGACGACTCCCCCTGTTCTTGATTCTGATGGGAGTTTTTTTC TGTA CAGTAAGTTGACAGTGGATAAATCAAGATGGCAGCAAGGTAATGTCTTCTCT TGTT CAGTGCTTACGAAGCATTGCATTCTCACTACACACAAAAGTCTTTGTCCTT GTCTCCAGGTGAAGGCGGTAGCGATTGATGGCAAGAAGAAGTCATTAAGCTGTGTG GAAGGGAAC TGGTTAGGGCCCAAATTGCGATATGTGGAAAGTCTACGGCGAGTGAT GCGGCCGGTGCTCAAGCGGATGCGGGTGCTAGACAGTTGTA CTAGCCCTTGCGAA CAAATGTTGTACGTTGGCTGTACGAAACGAGCCTTGCTCAATTCTGC
206	ATGGAACTGACACCCTTCTGCTCTGGGTACTCTTGTTGTGGGTCCCCGGCAGTAC AGGCGATAAAACTCACACATGCCCCCATGCCCAGCACCGGAAGCTGCCGGAGGAC CGTCTGTATTCTCTTTCCGCCCAAACCGAAAGACACGTTGATGATTTCTCGGACT CCCGAGGTAAC TTGTGTCGTGGTGCAGCTCTCACACAGGACCCGGAGGTCAAAT TAACTGGTATGTCGATGGGGTGGAGGTCCATAATGCTAAGACGAAGCCAGAGAAG AACAGTATAACTCTACTTATAGAGTTGTAAGCGTGCTCACTGTATTGCACCAGGAC TGGCTCAACGGGAAAGAATATAAGTGTAAGGTCTCAAACAAAGCTCTCGCAGCCCC

SEQ ID NO:	Sequence
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207	ATGGAAACGGACACACTTCTCTTGTGGGTCTTCTGCTCTGGGTTCCCGGCAGTAC AGGCGACAAAACACATACATGCCCCCTTGCCCGGTCCCGAGGCCGCCGGTGGTC CTAGCGTCTTTCTTTTCCCTCCCAAACCCAAAGACACACTTATGATTAGCAGAACT CCCGAGGTAACATGTGTGGTCTGTAGACGTAAGTACGAAGATCCCGAAGTTAAATT CAACTGGTACGTTGATGGTGTGGAAGTTTATAATGCAAAAACCAACCCGCGAGAGG AACAGTATAACTCTACCTACCGCGTGGTCTCAGTGCTGACTGTCTGTCATCAGGAC TGGCTCAACGGGAAGGAATATAAGTGCAAAGTGAGTAATAAGGCCCTTGCAGCTCC CATAGAAAAGACGATATCAAAGGCTAAAGGACAGCCGAGGGAGCCACAGGTGTACA CTTTGCCCTCCGAGTAGAGATGAACTCACTAAAAACCAAGTAAGTTTGACATGCCTG GTCAAAGGTTTTTACCCAGTGATATAGCGGTTGAGTGGGAGTCCAATGGGCAACC GGAGAACAACATATAAGACTACTCCACCTGTCTGGATAGCGATGGAAGTTTTTTTC TTTACTCAAAGCTGACGGTGGATAAGAGTCGATGGCAGCAGGGCAATGTGTTTAGC TGTTCTGTGCTTCACGAAGCACTTCACTCTCATTATACCCAGAAGTCATTGAGCCT TTCCCCCTGGTGAAGGAGGGTCAGATTCTTGGCAGGAGGAGGTTATAAAGCTGTGTG GCCGGGAACTCGTGCGAGCTCAAATTGCGATCTGTGGAAAATCCACCGCTAGTGAT GCGGCGGGAGCACAAGCTCAAGCGGGCGCTCGACAACCTTTATAGCGCTTTGGCTAA TAAGTGCTGCCATGTGGGTTGTACAAAAGCGCAGCCTCGCTCAATTTTGC
208	ATGGAAACAGACACTCTCCTCCTGTGGGTACTTCTCTTGTGGGTACCAGGATCCAC CGGGGATAAGACGCACACTTGCCCTCCTTGCCCGGCACCCGAAGCCGCTGGTGGGC CTAGTGTATTCTGTTCCTTCCCGGGAAGCCGAAGGATACTCTTATGATTTACGCACG CCCGAGGTTACATGCGTAGTAGTGGACGTATCTCACGAAGATCCCGAAGTCAAGTT CAATTGGTATGTGACGGAGTAGAAGTTTACAACGCAAAGACAAAACCGCGGGAAG AGCAATACAACCTCCACGTACCGCGTCGTTTCTGTTCTTACGGTCTTGCACCAGGAC TGGCTCAATGGCAAGGAGTATAAGTGCAAGGTATCCAACAAGGCCCTTGCCGCACC TATTGAAAAGACTATCAGCAAGGCCAAGGGACAGCCAAGGGAGCCTCAAGTCTACA CGCTCCCGCCTAGTAGAGACGAGTTGACAAAGAATCAAGTGAGTTTGACTTGTCTG GTTAAAGGTTTTTACCCGTCAGATATTGCAGTAGAATGGGAATCTAACGGACAACC CGAAAACAACATATAAAAACGACGCTCCTGTGTTGGATTGAGATGGGTCAATTTTTTC TCTACTCAAAGCTCACGGTAGATAAATCAAGATGGCAACAAGGCAATGTATTTTCC TGCTCCGTGCTCCACGAGGCTCTGCACAGCCATTATACGCAAAAGAGTCTGTCTTT GAGCCCAGGTGAGGGTGGCTCCGATTCTTGGCAGGAGGAAGTAATTAAGTTGTGCG GCAGGGAACTTGTTCGCGCACAAATAGCCATTTGTGGTCAGAGCACAGCATCAGAT GCCGCCGAGCCGACGCCAACGCAGGTGCCCCGCCAACTTTATTCTGCCCTCGCAAA CAAATGCTGCCACGTGCGGTGCACGAAGAGGAGCCTCGCCCAATTTTGC
209	ATGGAAACAGACACGCTGCTCCTCTGGGTGTTGCTTCTCTGGGTGCCTGGCAGTAC AGGTGATAAGACCCATACGTGCCCGCATGTCCAGCCCCCGAGGCAGCCGGAGGTC CTTCCGTTTTCTTTTCCCCCTAAGCCCAAGGACACTCTGATGATCTCCCGGACG

SEQ ID NO:	Sequence
	CCTGAAGTCACTTGCGTAGTCGTAGACGTTTCACATGAGGATCCAGAAGTTAAATT TAACTGGTACGTCGATGGCGTCGAGGTCCATAACGCGAAAACCAAGCCCAGGGAGG AACAATATAACTCCACCTATAGGGTCGTGAGTGTGCTCACCCTTTTGCACCAAGAC TGGCTCAACGGGAAAAGGTACAAATGTAAAGTTTCAAATAAGGCTTTGGCCGCCCC AATAGAGAAGACTATATCCAAGGCTAAGGGACAGCCTCGAGAACCGCAGGTATATA CGCTTCCTCCGTCTAGGGATGAACTCACAAAAAACAGGTTTCTTTGACCTGCTTG GTAAAGGGATTTTATCCCTCCGACATTGCGGTGCAATGGGAGAGCAACGGACAGCC GGAAAACAATTACAAAACGACACCCCGGTTTGGACTCTGATGGAAGCTTCTTCC TCTATAGTAAGTTGACCGTAGACAAGTCTCGCTGGCAGCAGGGAAACGTCTTCAGT TGCTCAGTTCTCCATGAGGCGTTGCATAGTCACTATACACAGAAGAGTCTTAGTTT GTCTCCAGGAGAAGGAGGTTCTGATTCTTGGCAAGAGGAGGTAATCAAATTGTGTG GCCGAGAACTTGTTAGAGCTCAGATAGCCATCTGCGGACAGTCTACGGCGTCCGAT CCGGCCGGAGCTAATGCTGACGCAGGTGCGCGACAGCTGTACTCCGCACGTGGCGAA TAAAGTGCTGCCACGTGGGATGCACTAAGCGGTCTCTCGCGCAATTCTGT
210	ATGGAGACCGACACTCTTTTGCTCTGGGTGCTGTTGCTGTGGGTTCCAGGTTCAAC GGGAGATAAAACCCACACCTGTCCACCATGCCC GGCGCCGGAAGCCGCCGGGGGAC CCAGCGTATTTCTTTTCCCCC CAAGCCAAAGACACGCTGATGATTTACGAACG CCGGAGGTGACTTGCGTGGTAGTGACGCTCTCCATGAGGATCCCGAAGTTAAATT TAATTGGTATGTAGATGGTGTGAGGTCCATAATGCTAAAACAAAGCCGCGGGAAG AGCAATATAACTCCACCTATAGAGTGGTCTCTGTACTCACTGTCCTGCACCAGGAT TGGCTGAATGGGAAAGAGTACAAGTGTAAGTTAGCAACAAAGCGCTCGCCGCGCC TATCGAAAAACGATTTCCAAAGCAAAGGGCCAACCACGAGAACCCAGGTTTACA CCCTGCCACCCAGTCGAGATGAACTCACTAAGAATCAGGTGTCCCTTACATGCCCTC GTCAAGGGATTCTATCCGAGCGATATAGCGGTGGAATGGGAGAGTAACGGTCAACC CGAAAATAACTATAAAACCACTCCGCCGGTACTCGATTCTGACGGTTCTTCTTTTC TTTATTCCAAACTGACTGTAGACAAATCACGGTGGCAGCAGGGCAACGTGTTTAGC TGCTCTGTACTCCATGAGGCTTGCATTCTCATTATACTCAAAGAGTCTGAGTCT GAGTCCAGGTGAAGGGGGTTCCGATTCTATGGCAAGAGGAAGTCATTAAACTCTGCG GAAGGGAACTTGTAAGAGCACAAATCGCGATTTGTGGGCAATCTACCGCATCCGAC GCGGCTGGAGCAGATGCAGATGCCGAGCGAGGCAGCTGTATTGAGCATTGGCTAA CAAATGTTGCCATGTTGGATGTACGAAGAGATCACTTGACAGTTCTGT
211	ATGGAAACTGACACCCTCCTTCTCTGGGTACTGCTCTTGTGGGTTCCAGGCTCTAC TGGCGATAAGACTCATACCTGCCCGCCCTGTCCCGCACCCGAGGCTGCCGGAGGGC CATCAGTGTTCTTTTCCCACCAAAGCCGAAGGATACACTTATGATCAGCAGGACA CCCGAAGTGACCTGTGTAGTCGTAGACGTGTCCACGAAGACCCGAAGTAAATTT TAATTGGTATGTCGATGGCGTAGAGGTCCACAACGCGAAAACGAAACCCCGCGAAG AACAATATAATTCCACATACCGAGTTGTGAGCGTCCTCACTGTTCTCCATCAGGAC TGGCTGAATGGGAAGGAATATAAGTGCAAGGTCTCAAACAAGGCGCTGGCGGCCCC CATAGAGAAAACGATTTCTAAGGCCAAAAGGACAGCCACGGGAACCGCAGGTCTATA CGCTCCCACCTAGTAGGGATGAGTTGACCAAGAATCAGGTATCCCTCACATGTCTC GTCAAGGGATTCTATCCCAGCGACATAGCCGTGGAGTGGGAATCTAACGGTCAACC TGAGAATAACTATAAAACAACCCCGGTCCTCGACTCCGATGGTAGCTTCTTTTC TGTATTCCAACTGACGGTAGATAAAAGCCGATGGCAACAGGGTAACGTCTTTAGT TGTTCTGTATTGCACGAGGCGCTCCATAGTCACTACACACAGAAGTCTTTGAGCCT CTCACCTGGGGAGGGGGTAGCGATTCTTGGCAGGAGGAAGTGATCAAACGTGTGCG GCAGGGAACTGGTCAGAGCACAGATAGCAATATGCGGTGAGGTACGGCCTCTGAC

SEQ ID NO:	Sequence
	GCCGCCGGTGCGGAGGCTGAGGCAGGGGCGAGACAGCTCTACAGCGCTCTTGCAAA TAAGTGTTGTACGTGGGGTGACAAAGAGATCCTTGGCGCAATTTGT
212	ATGGAAACCGATACATTGCTTTGTGGGTCTTGTGCTGTGGGTGCCCGGTTCTAC TGGTGATAAGACCCACACATGTCCGCCATGTCCAGCCCCAGAGGCAGCAGGGGGCC CGTCCGTATTCTTGTTCCTCCCGAAACCCAAAGATACCCTTATGATTAGTCGAACT CCAGAAGTCACGTGTGTGGTGGTGGACGTATCCCACGAGGACCCCGAAGTGAAATT CAATTGGTATGTGGACGGGGTGGAAGTCCATAACGCTAAGACGAAGCCAGAGAGG AGCAGTACAATTCTACCTATCGGGTGTATCTGTGCTTACTGTTCTCCATCAAGAT TGGCTGAACGGGAAGGAATACAAATGTAAAGTTAGTAACAAAGCATTGGCAGCTCC TATCGAAAAGACGATAAGCAAGGCTAAAGGTCAACCCCGAGAGCCTCAGGTCTACA CTTTGCCGCCCTCCAGGGATGAGCTTACCAAGAACCAAGTGAGCTTGACGTGTCTC GTGAAGGGATTCTACCCATCAGATATAGCGGTAGAATGGGAGTCTAATGGGCAGCC CGAGAACAATAAGACCACCCCTCCCGTTCTTGACTCCGACGGTTCCTTTTTCT TGTACTCCAACTCACGGTCGACAAGTCTAGGTGGCAGCAAGGCAATGTTTTAGT TGTTCCGTGCTGCACGAAGCTCTTCACTTCTACATACGCAAAAAGCCTGAGTCT TTCACCTGGAGAGGGGGGTTCGATTCTTGGCAGGAAGAAGTCATTAAGCTGTGCG GCAGAGAACTTGTGCGCGCACAAATTGCTATTTGTGGACAGTCAACTGCATCTGAC GCCGCTGGAGCCCAAGCGGACGCAGGGGCAAGGCAGCTTTATTAGCGCTTGCAGAA TAAGTGTTGCCATGTGGGTGCACGAAACGAAGCCTGGCGCAATTTGT
213	ATGGAGACTGATACATTGTTGCTTTGGGTACTCTTGCTTTGGGTGCCCGGAAGTAC AGGGGATAAGACACATACATGTCTCCCTGTCCCGCTCCGGAGGCAGCCGGTGGGC CTTCAGTTTTCTTGTTCCTCCCGCAAGCCTAAGGACACGTTGATGATATCCCGAACA CCAGAGGTCACATGCGTCGTCGTGGACGTCTCACACGAGGACCCTGAAGTGAAATT CAACTGGTATGTAGACGGGGTCGAAGTTCACAATGCGAAAATAAACCTCGCGAGG AGCAATATAACTCAACATACCGCGTAGTGTCCGTCTTGACTGTCTTCATCAGGAT TGGCTGAATGGTAAAGAATATAAATGTAAAGTTCTAATAAAGCGCTTGGCGCACC CATTGAGAAGACAATTTCCAAAGCCAAAGGCCAACCCGAGAGCCTCAGGTATATA CGCTGCCTCCGTCTCGAGATGAGTTGACAAAAAATCAAGTCAGCTTGACTTGTCTT GTAAAGGGGTCTATCCGTGACACATAGCAGTGGAGTGGGAATCCAACGGGCAACC AGAAAATAATTACAAAACCACTCCGCCCCTGCTTGACTCAGATGGGAGCTTCTTCC TTTATAGCAAATACGGTAGATAAATCCAGATGGCAGCAAGGCAACGTATTAGC TGTAAGTGTGCTGCATGAAGCGCTTCACTCCCATTAATACTCAAAAATCTCTTCTCT GTCACCGGGCGAGGGCGGAAGTGATAGTTGGCAGGAAGAGGTCATCAAGCTCTGTG GGAGAGAGCTTGTACGCGCTCAGATTGCTATATGCGGCCAGTCAACTGCAAGCGAT GCAGCGGGTGCCGATGCCAAGCGGGGGCACGGCAACTCTACTCAGCCCTCGCGAA TAAATGTTGTATGTAGGGTGTACTAAGAGAAGCCTCGCGCAATTTGT
214	ATGGAAACTGATACTCTTCTTTGTGGGTACTGTTGTTGTGGGTCCCAGGAAGTAC CGGCGATAAAACGCATACCTTGCCCGCCGTGCCAGCACCTGAGGCAGCCGGCGGCC CTAGTGTCTTCTTGTTCCTCCCGCCCAAGCCCAAGGATACACTCATGATCTCCCGAACG CCAGAGGTCACATGCGTAGTTGTTGACGTTTCCCATGAGGACCCTGAAGTGAAATT TAAGTGGTACGTCGACGGCGTTGAGGTTCAACACGCTAAGACTAAGCCAAGAGAGG AACAGTACAATTCAACTTATAGAGTGGTGTCTGTATTGACAGTTCTCCATCAGGAT TGGCTGAACGGAAAAGAATATAAGTGCAAGGTCTCAAATAAGGCGCTCGCTGCACC CATAGAAAAAACCATATCAAAGCGAAGGGGCAACCAAGAGAACCCAGGTGTACA CGCTCCCCCGTCCAGAGATGAACTCACGAAGAATCAAGTGTCACTCACATGTCTT GTAAAGGGGTCTACCCCTCTGATATTGCCGTAGAATGGGAAAGCAACGGACAGCC CGAGAATAACTACAAGACGACACCGCCAGTTCTTGATTCTGACGGAAGCTTTTTCC

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215	ATGGAAACAGATACGCTCCTTTTGTGGGTACTGTTGTTGTGGGTGCCCCGGCTCTACGGGCGACAAGACTCATACTTGTCCGCCCTGCCCCGCTCCTGAGGCTGCCGGAGGCCCTTCAGTATTCTTGTTCGCGCGAAACCGAAGGATACCTTGATGATTAGTAGGACACCGGAAGTCACCTGCGTAGTGGTGGACGTAAGCCACGAAGATCCCGAAGTAAAGTTTAATTGGTATGTTGATGGCGTAGAGGTGCATAATGCGAAAACCAAACCTAGGGAGGAACAGTACAATAGTACTTACCGCGTAGTGTGAGTGCTTACCGTGCTGCATCAGGACTGGCTTAATGGGAAGGAATACAAATGTAAAGTATCCAATAAAGCGCTGGCGGCTCCATCTGAGAAAAACGATCTCAAAAGCCAAAGGACAACCACGGGAACCGCAGGTCTATCTCTGCCACCTTCAAGAGACGAACTTACCAAGAACCAAGTCTCATTGACGCTTGTAATAAGGTTTTATCCGCTGACATCGCTGTTGAATGGGAGTCTAACGGCCAGCCGGAGAACAATTACAAAACAACTCCACCAGTCTTGGATTGAGATGGGTCTTTTTTTTTTGTATTCAAAGCTTACCGTTGACAAAAGCCGCTGGCAACAAGGAAACGTTTTTCAGCTGCAGTGTGCTGCACGAAGCGCTCCACAGTCATTATACCCAGAAATCTTTGAGCCTGTCTCCAGGGGAAGGTGGGAGTGACTCTTGGCAAGAAGAGGTTATCAAACCTTTGCGGGCGGGAGCTGGTAAGGGCCCAAATTGCAATATGCGGCAAAAGTACTGCATCTGATGCCGCTGGGGCCGATGCTAACGCGGGCGCAAGACAACCTTTATAGCGCGTTGGCGAACAAATGCTGTATGTGGGATGCACCAACAAAGTTTGGCGCAATTTTGT
216	ATGGAAACCGATACCTTGCTGCTTTGGGTGCTCTTGCTGTGGGTGCCGGTTCCACGGGTGATAAACTCACACGTGTCCGCCATGCCCCGCACCTGAAGCGGCGGGTGGTCCGAGCGTGTTTTTGTTCGCGCTAAGCCCCAAGGATACCTTGATGATTAGTCGGACACCCGAAGTAACATGTGTCTGCTGGATGTAAGTACAGAGGATCCCGAAGTGAATTCAACTGGTATGTGGATGGAGTTGAAGTCCATAATGCGAAAACAAAACCGAGAGAGGAACAGTACAACATAACCGGGTGGTAAGTGTACTGACGGTACTCCACCAGGACTGGCTGAATGGTAAGGAGTACAAATGCAAAGTTTCAAATAAGGCGCTCGCTGCCCCATCGAGAAAACCATTAGTAAGGCTAAAGGTCAACCTAGGGAGCCACAAGTATATACATTGCCGCTTCTAGAGATGAGCTGACCAAAAACAGGTGAGCCTGACCTGTTTGTGAAAGGCTTCTATCCAAGCGACATTGCTGTGAGTGGGAGTCAAATGGGCAGCCGGAAAATAACTATAAAACGACTCCTCCTGTTCTCGACTCCGATGGTTTATTCTTCTCTACTCAAAGCTTACCGTGGATAAATCCAGGTGGCAACAAGGTAACGTGTTCTCATGTTCCGTTCTGCACGAAGCACTGCATTCCCATTATACACAAAAATCCCTGAGCCTCTCACCTGGGGAGGGCGGAAGCGATAGTTGGCAAGAGGAAGTAATAAAGCTGTGTGACAGGAACTCGTAAGGGCTCAGATTGCGATATGTGGAAAAAGCACTGCTTCTGACGCCGAGGGGCCAACGCAGATGCTGGCGCCCGACAACCTCTATTCTGCGCTTGCGAACAAAGTGTTGTATGTAGGATGTACCAAGCAAAGCCTTGCTCAGTTCTGT
217	ATGGAGACCGATACACTCTTGCTCTGGGTCTCTTCTTTGGGTTCAGGCTCCACAGGAGACAAAACCCACACTTGTCCGCCCTGTCCGCTCCGGAGGCTGCAGGCGGCCCAAGTGTGTTTCTTTTCCCCCAAAGCCGAAAGACACCTTGATGATATCCCGCACACCCGAAGTGACTTGCGTTGTCGTGACGTGTCTCATGAGGACCCAGAAGTCAAGTTTAATTGGTACGTTGATGGCGTGGAAGTTCACAATGCGAAAACAAAGCCAGAGAGGAGCAATATAACTCAACCTACCGGGTGGTAAGTGTTCTGACAGTTCTCCACCAGGACTGGTTGAACGGAAGAATACAAATGCAAAGTGAGTAACAAAGCCCTGGCTGCCCC

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218	ATGGAAACCGACACTCTTCTGCTGTGGGTCTTCTCCTGTGGGTGCCTGGATCAACCGGAGATAAGACCCACACATGTCCACCATGCCCAGCCCCAGAAGCGGCAGGTGGTCTTCTGTGTTTCTCTTTCCCTCCCAAACCGAAAGATACTCTGATGATAAGCCGGACC CAGAAGTTACGTGCGTTGTAGTAGACGTGTCTCACGAGGACCCAGAAGTGAAGTTTAACTGGTATGTCGACGGTGTAGAAGTTTATAATGCGAAAAACAAAGCCAGGGAAGAACAATATAATTCAACGTACCGGGTCGTTTCCGTGCTGACAGTTCTGCACCAAGATTGGCTCAACGGGAAAGAGTACAAATGCAAAGTATCAAATAAGGCCTTGGCTGCGCCGATTGAAAAGACGATTTCCAAAGCAAAGGGCCAGCCAAGGGAACCCAGGTCTATACCTCCCTCCTAGCAGAGATGAACTTACAAAAACCAAGTCTCCCTCACCTGCCTGTCAAAGGATTCTATCCCTCAGATATAGCAGTAGAATGGGAAAGTAACGGGCAGCCCGAAAAACAATTATAAGACCACTCCTCCAGTACTCGATTGACAGCGGTAGCTTCTTCTGTATTCCAAGCTGACCGTAGATAAAAAGTAGGTGGCAGCAAGGTAATGTCTTCTCATGTAGTGTACTTCATGAGGCGTTGCATTCCCATTACACGCAAAAGTCTTTGAGTCTCAGTCCGGGTGAAGGAGGTAGCGATTCTTGGCAGGAAGAAGTAATTAAGCTGTGCGGCCGGGAGCTCGTCAGGGCTCAGATAGCTATATGCGGCAAGAGCACGGCCAGTGATGCTGCTGGTGCAGAGGCTGAAGCAGGTGCCAGGCAGTTGTACAGCGCACTCGCTAAATAAGTGTGCCACGTGGGGTGTACAAAGCAATCTTTGGCACAATTCTGT
219	ATGGAGACTGATACTTTGCTGCTGTGGGTCTCCTTCTTTGGGTCCCAGGTTCCACAGGAGATAAGACCCATACTTGTCTCCGTGCCCCGGCACCAGAGGCTGCGGGTGGCCCATCCGTTTTTCTGTTTTCCGCCAAAGCCTAAGGATACTCTGATGATTTACGCACACCCGAAGTGACCTGCGTGGTGGTGCAGCTATCTCACGAAGACCCAGAGGTAAATTCAATTGGTACGTGGACGGCGTCGAGGTTTATAACGCGAAAACTAAGCCGAGAGAAGAGCAGTACAACCTACGTATCGCGTGGTGTCCGTACTGACAGTATTGCATCAGGACTGGTTGAATGGCAAGGAGTATAAGTGCAAGGTATCTAATAAGGCATTGGCTGCCCCAATAGAGAAAACGATCAGCAAAGCAAAGGGGCAGCCGCGCGAGCCGAGGTATATACACTTCCACCATCACGGGATGAGTTGACGAAAAATCAAGTCTCTCTCACATGTCTGTAAAAGGTTTTCTATCCTTCTGATATCGCCGTGGAATGGGAAAGCAACGGCCAACC CGAAAAACAACATAAGACGACGCCGCCGCTACTCGACAGCGACGGAAGCTTTTTCTTGATTCCAAGTTGACAGTGGACAAGTCTCGATGGCAGCAAGGAAACGTGTTCTCATGTTCTGTTCTTCACGAAGCCCTTCATAGCCATTATACTCAGAAATCTCTCTCACTCTCCCCAGGTGAAGGGGGAAGTGACTCTTGGCAAGAAGAAGTCATTAAGCTTTGCGGTGCGAGAATTGGTTCGGGCTCAAATAGCTATTTGTGGCAAGTCCACGGCAAGTGATGCAGCGGGGGCTCAGGCAGACGCGGGCGCAAGGCAGCTTTATTCCGCACCTTGCAAAATAAGTGTGTCACGTGCGATGTACTAAACAATCACTTGACACAATTCTGC
220	ATGGAGACCGACACACTTCTCCTCTGGGTCTGCTCCTTTGGGTGCCAGGCAGTACAGGTGACAAGACACATACATGTCCCCCATGCCCTGCACCCGAAGCTGCTGGGGGGCCAGCGTGTTCTGTTTTCCGCCGAAGCCCAAGGACACATTGATGATTAGTAGAACC

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221	ATGGAGACAGATACACTGCTTCTGTGGGTGCTCTTGCTTTGGGTCCCGGTTCCAC AGGCGATAAAACCCATACCTGTCCACCATGCCCCGCGCCAGAGGCAGCGGGTGGTC CAAGCGTTTTCTTTTTCCACCGAAAACCAAAAGATACACTTATGATATCAAGGACC CCCGAGGTAACGTGCGTCGTAGTTGACGTTTCTCACGAAGATCCCGAGGTGAAATT CAATTGGTACGTAGATGGTGTAGAGGTACACAATGCGAAGACAAAACCGCGGGAAG AGCAGTATAATAGCACATACAGAGTCGTGAGCGTCCTCACCCTACTTCACCAAGAT TGGCTGAATGGAAGGAGTACAAATGTAAGGTAAGTAATAAAGCACTTGCGGCCCC CATCGAGAAAACATCAGTAAAGCAAAAAGGGCAACCACGAGAACCCAGGTCTACA CTTTGCCACCATCACGGGATGAACTGACAAAAAATCAGGTGTCACTCACTTGCCCTT GTTAAAGGGTCTATCCTAGTGACATAGCGGTAGAATGGGAGTCTAACGGGCAGCC TGAGAACAAATTATAAACTACGCCCCCTGTTCTTGATTCCGATGGATCATTTTTTC TCTACTCCAAACTCACCCTAGACAAATCCCGCTGGCAGCAGGGCAACGTGTTTAGT TGACAGCGTTCTTCACGAAGCACTTCACTCACATTACACACAAAAGTCCCTGAGCTT GAGTCCTGGGGAGGGTGGATCTGATTCTTGGCAGGAAGAAGTTATAAACTTTGTG GCAGAGAGTTGGTCCGCGCACAAATCGCCATATGTGGTAAAAGCACAGCGTCTGAC GCGGCGGGAGCGCAAGCCCAGGCGGGGGCTCGGCAACTCTACTCAGCCCTGGCTAA CAAGTGCTGTGTCAGTGGGATGCACTAAACAAAGTCTGGCGCAGTTCTGC
222	ATGGAGACCGATACGTTGCTGTTGTGGGTTTTGTTGCTGTGGGTACCTGGATCTAC AGGTGACAAAACCCATACGTGTCCCCCGTGTCCGGCTCCAGAGGCTGCGGGAGGAC CGTCTGTGTTCTTGTTCGCCCGAAGCCTAAAGATACGCTGATGATTAGTCGGACC CCCGAGGTGACCTGCGTGGTAGTAGACGTATCTCATGAAGATCCGGAAGTAAAGTT TAACTGGTACGTAGACGGCGTCGAGGTACATAATGCCAAGACGAAACCCAGAGAAG AGCAATATAATAGCACTTATCGAGTTGTAAGCGTATTGACGGTCCTTCACCAGGAC TGGTTGAACGGCAAAGAGTACAAATGTAAGGTATCCAATAAAGCATTGGCTGCGCC AATTGAAAAGACAATTTCCAAAGCGAAGGGGCAACCTCGAGAGCCGCAAGTCTACA CGCTGCCACCGAGTAGGGATGAATTGACTAAGAATCAGGTGAGTCTCACGTGTCTC GTGAAGGGGTTTTACCCAGTGATATTGCGGTAGAATGGGAGTCCAACGGTCAGCC AGAAAATAATTATAAAACAACGCCCCCTGTATTGGATTCTGACGGGAGCTTTTTTC TGTAATCAAACTCACCCTAGATAAGAGTCGCTGGCAACAGGGCAACGTATTTCTCA TGTAAGCGTTCTGCACGAGGCGCTGCACTCTCACTACACACAGAAGAGTTTGAGTTT GTCCCCTGGCGAAGGAGGTTCTGATTCTTGGCAGGAGGAGGTGATTAAGCTGTGTG GCCGCGAATTGGTGAGGGCTCAAATTGCTATTTGCGGACAGAGCACAGCGTCCGAT

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223	ATGGAGACAGATACGCTCTTGCTGTGGGTACTCCTCCTCTGGGTCCCAGGCTCAAC GGGCGACAAGACTCACACTTGTCCTCCCATGTCCAGCACCGGAAGTGCCGGCGGTC CCTCAGTTTTCTTTTCCCCCACAAGGACACCCTTATGATTTCAAGGACA CCAGAGGTAACGTGCGTAGTGGTGGACGTCAGTCATGAAGACCCAGAGGTAAGTT TAACTGGTACGTGGATGGGGTAGAGGTTTATAATGCTAAAACAAAACACGCGAGG AACAGTACAATAGTACGTATAGAGTGGTCTCCGTTCTTACGGTGTGTCATCAGGAC TGGCTGAACGGAAAAGAGTACAAGTGAAGGTTAGCAATAAGGCGCTGGCGGCCCC AATCGAAAAGACGATTTCTAAGGCCAAAGGCCAGCCAAGGGAGCCACAAGTATATA CCCTTCCCCCTTCCCAGATGAGCTGACTAAGAATCAAGTCAGTCTCACCTGCCTT GTCAAAGGTTCTACCCATCCGATATTGCTGTTGAATGGGAGTCTAATGGCCAGCC GGAGAACAATTACAAGACAACTCCGCCTGTATTGGATTCCGACGGGTCTTTTTTCC TCTATTCAAACTCACAGTAGACAAAAGTCGATGGCAGCAAGGTAACGTGTTTTCT TGCTCTGTGTTGCATGAAGCACTTCATTCTCATTATACTCAAAAATCATTGAGCCT CAGTCCAGGCGAAGGGGGTAGTGACTCATGGCAGGAGGAGGTAATCAAGCTTTGCG GACGAGAGTTGGTCAGGGCCCAGATAGCTATTTGTGGTCAGTCCACGGCGAGTGAC GCAGCAGGGGCGAATGCCGATGCAGGAGCAAGACAACTGTATTCTGCTCTGGCCAA CAAGTGTTGTCATGTAGGGTGTACTAAACAAAGTCTCGCCCAGTTCTGC
224	ATGGAAACGGATACGCTGTTGTTGTGGGTCTTGCTCCTGTGGGTCCCCGGATCCAC AGGTGATAAAACCCACACCTGTCCCCATGTCCGGCTCCCGAAGCAGCGGGGGGCC CTTCAGTTTTTCTCTTTCCCCCACAAGGACACGCTGATGATTAGCAGAACT CCAGAGGTTACCTGTGTAGTTGTGGACGTTTACACGAGGATCCCGAGGTTAAATT CAACTGGTATGTGGACGGCGTCGAAGTGCATAATGCAAAAACAAAGCCCCGGGAAG AACAATATAATAGTACCTATAGGGTCGTTTCCGTACTGACCGTACTTCATCAAGAT TGGCTCAATGGGAAGGAATACAAATGTAAAGTGAGTAATAAAGCCCTGGCGGCACC GATCGAAAAAACCATTTCAAAGGCTAAGGGACAACCGCGCAACCTCAGGTTCTATA CCTTGCCCCCTTACGCGACGAGCTTACGAAGAATCAGGTAAGCCTTACTTGTCTT GTCAAGGGTTTTTACCCAGCGACATAGCTGTGAGTGGAATCCAATGGCCAACC GGAGAATAATTACAACTACCCCTCCTGTTCTTGATAGCGACGGAAGCTTCTTCT TGTATTCCAACTCACAGTAGATAAAAGTAGGTGGCAGCAGGGCAATGTATTTTCT TGCAGCGTCCTGCATGAAGCACTGCATAGCCATTATACTCAAAAGTCCCTGTCTTT GTCTCCTGGAGAGGGCGGAAGCGATTCTTGGCAAGAGGAAGTTATTAAGCTGTGCG GGCGGCAACTTGTGAGGGCTCAAAATAGCGATATGTGGTCAGAGCACCGCTAGCGAT GCGGCTGGTGCAGACGCCGATGCCGGTGCTAGGCAACTTTACAGTGCATTGCCGAA TAAGTGCTGTCACGTCGGATGTACTAAACAAAGCCTCGCCCAGTTCTGC
225	ATGGAAACGGATACTCTTCTTTGTGGGTCTTCTTCTGTGGGTACCAGGAAGTAC TGGTGATAAAACACATACTTGCCCTCCTTGTCGGCTCCCGAAGCCGAGGTGGAC CTTCCGTCTTTCTTTTCCACCCAAACCTAAAGACACTTTGATGATTAGCCGGACC CCCAGGTAACCTGTGTCGTAGTTGACGTTTCCCATGAAGACCCCGAAGTTAAGTT CAACTGGTATGTGACGGCGTCGAGGTGCACAACGCGAAGACTAAGCCAAGAGAGG AGCAATACAATTCAACTTACAGGGTCGTGTCCGTCTTGACAGTGCTTCATCAAGAC TGGCTTAATGGAAAGGAATACAAATGTAAAGTCTCCAACAAGGCTCTCGCAGCGCC CATTGAGAAAACGATATCCAAGCGAAGGGTCAACCAAGAGAACCCAGGTTTACA CCCTCCCCCTAGTCGGGACGAGCTTACGAAGAACCAGGTCAGTTTGACATGCCTG GTGAAAGGCTTCTATCCGTGACACATCGCCGTAGAGTGGGAAAGCAACGGGCAACC CGAGAACAATAAGACGACTCCCCGGTGTTGGATAGCGATGGCTCTTTCTTCC

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226	ATGGAGACCGATACCTTGTTGCTGTGGGTGCTTCTTCTCTGGGTCCGGGATCTAC AGGAGACAAGACTCACACTTGTCACCCCTGTCCAGCACCTGAAGCCGCTGGTGGAC CATCTGTCTTTCTGTTCCCCCTAAACCAAAGGATACACTTATGATCAGCAGAACA CCTGAAGTCACATGCGTTGTGGTAGACGTTTCCACGAGGATCCTGAAGTGAAGTT TAACTGGTACGTGGATGGCGTTGAGGTTTATAATGCCAAGACGAAACCTCGGGAGG AGCAGTATAATTCTACTTATAGGGTGGTAAGCGTACTGACAGTCTCCATCAAGAC TGGTTGAACGGGAAGGAATACAAGTGTAAGTTTCCAACAAAGCTCTGGCGGCGCC TATAGAAAAGACAATATCAAAAGCGAAAGGGCAACCCAGAGAGCCTCAAGTATATA CATTGCCCCCTAGCAGAGACGAATTGACGAAAAATCAGGTCTCTCTCACGTGCCTC GTGAAGGGCTTCTATCCTAGTGATATAGCTGTGGAATGGGAATCCAATGGACAGCC AGAAAACAACACTACAAGACCACGCCCCCGTCTTGGATTCCGACGGGTCACTCTTCC TGTACAGCAAGCTGACTGTCGACAAGAGTCGATGGCAACAGGGCAACGTCTTTAGC TGCAGCGTCTGTCACGAAGCTCTGCATAGTCATTACACCCAAAAGTCCCTTTCTCT CTCCCCTGGTGAAGGCGGTTCCGATTATGCGCAAGAAGAAGTAATTAAGCTCTGTG GACGAGAGCTTGTCCGAGCACAAATTGCGATCTGCGGGCAGAGTACCGCATCTGAC GCTGCTGGCGCGCAGGCAGATGCGGGTGACGGCAGCTTTATTACGCTCTCGCCAA CAAGTGTTGTATGTGGGGTGTAACAAAGCAGAGCCTTGCCAGTTTTGT
227	ATGGAAACGGACACACTGCTGCTTTGGGTCTCTTGCTGTGGGTCCCAGGCTCTAC AGGGGATAAGACCCATACGTGTCCCCCTTGCCCTGCACCCGAGGCGGCTGGGGGCC CTTCCGTATTCTTGTTTCCCTAAGCCCAAAGATACCTTGATGATAAGTCGAACG CCAGAAGTGACTTGCGTTGTTGTGGATGTCTCCACGAGGATCCAGAAGTCAAATT TAACTGGTATGTCGATGGGGTCGAAGTGATAATGCTAAAACGAAACCCAGAGAGG AACAATACAATTCAACATACCGCGTAGTCAGTGTTCTTACTGTGCTCCATCAGGAT TGGCTCAATGGGAAAGAATACAAGTGTAAGTCTCAAATAAAGCATTGGCGGCCCC TATAGAGAAGACCATAAGCAAGGCTAAAGGTGAGCCTAGGGAGCCTCAAGTATATA CCTTGCCCTCCTAGCAGAGATGAGTTGACCAAGAACCAGGTGAGCCTCACATGCCTG GTGAAAGGGTTTTACCCATCTGATATTGCCGTGAGTGGGAAAGTAATGGGCAGCC AGAGAACAACACTACAAGACGACACCACCGGTACTGGATAGTGACGGAAGTTTTTTTC TTTACAGTAAGCTCACAGTCGACAAAAGCCGGTGGCAACAAGGAAATGTATTTTCA TGTAGCGTACTTCATGAAGCCCTCCACTCTCATTACACGCAGAAGTCACTTTCCT TAGTCCGGGTGAGGGTGGAAAGCGATAGCTGGCAAGAGGAGGTTATCAAGCTCTGTG GACGAGAACTCGTGAGAGCGCAAATTGCAATCTGCGGGCAGAGCACGGCGAGTGAT GCGGCCGGGGCGGACGCGCAAGCAGGAGCACGACAACCTTTATAGTGCTTTGGCTAA TAAATGTTGCCACGTTGGATGTACTAAACAGAGCTTGGCACAGTTTTGC
228	ATGGAGACTGATACACTGCTTCTGTGGGTATTGTTGTTGTGGGTCCCCGGTTCAC AGGTGATAAAACGCACACTTGTCGCCATGTCCGGCACCTGAGGCAGCGGGAGGAC CGTCCGTGTTTCTGTTTCCCCCTAAACCAAAGGACACGCTGATGATCAGCCGAACA CCTGAAGTAACATGCGTGGTCGTTGACGTGTCTCACGAGGATCCAGAAGTAAAGTT CAATTGGTATGTTGACGGAGTTGAAGTACATAATGCTAAGACTAAACCCCGCGAAG AACAATATAATTCTACGTACAGAGTTGTATCCGTGCTCACGGTACTTCACCAAGAT TGGCTTAACGGGAAAGAATATAAGTGTAAGGTCTCAAATAAGGCCCTGGCTGCTCC

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229	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTTC TTTATTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
230	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTTC TTTATTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATTTCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
231	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA

SEQ ID NO:	Sequence
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232	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCTATT GTCCCCAGGTAAGGGCGGAAGCGACTCAATTCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
233	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCTATT GTCCCCAGGTAAGGGCGGAAGCGACTCATGGCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC

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235	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACCTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATGGCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTCAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
236	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACCTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC

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237	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAAC TTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAAT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC TTTATTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
238	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAAC TTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAAT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC TTTATTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTAAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
239	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAAC TTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAAT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTTAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC TTTATTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTAAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC

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240	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTAAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAAATAACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTTC TTTATTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGAGAAGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTTAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
241	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTAAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAAATAACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTTC TTTATTCAAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGATCTGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
242	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA

SEQ ID NO:	Sequence
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243	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTTACGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
244	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTGAAGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGCTAGTGAC

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	GCAGCGGGCGCCGAAGCGGAAGCTGGTGCAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTAAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
245	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAAGTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTAAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGAGAAGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTTACGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
246	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAAGTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTAAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGAGAAGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTAAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
247	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAAGTTGTGTCGTTGTGGATGTGTACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTAAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC

SEQ ID NO:	Sequence
	TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGATCTGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTACGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
248	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAAC'TTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAAT'T TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTGTTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTC TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGATCTGGGGGCGGAAGACAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTAAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
381	ATGGAGACGGACACTTTGCTGCTTTGGGTACTGCTGCTTTGGGTTCCTGGATCTAC TGGCGATAAAACACACACGTGTCCCCCTGCCCCGCTCCAGAGGCGGCTGGTGGTC CCAGCGTATTCTTGTTCCTCCCAAACCTAAGGATACGCTCATGATATCCCGCACC CCAGAAGTTACGTGTGTAGTCTGACGTCAGTCACGAAGATCCAGAGGTCAAAT'T TAAGTGGTATGTCGACGGAGTAGAGGTCCACAATGCGAAAACCAAGCCAGAGAAG AGCAGTACAACCTCCACGTATCGCGTCGTCTCCGTCCTCACCCTACTCCATCAAGAT TGGCTGAATGGGAAAGAGTATAAATGCAAAGTATCTAACAAGGCTCTGCCAGCTCC GATAGAAAAGACTATATCAAAGGCCAAGGGGCGCAAGGGAGCCTCAAGTCTATA CTTTGCCCCCATCTCGGGATGAGCTTACGAAAAACAGGTGAGCCTTACCTGTCTT GTTAAAGGTTTTTATCCGAGTGACATCGCAGTGGAATGGGAATCTAATGGTCAACC TGAAAACAATTACAAAACCAACCGCCAGTATTGGACAGCGATGGTAGTTTTTTTC TTTACTCAAACTGACTGTAGATAAAAGCAGATGGCAGCAGGGCAATGTCTTTTCA TGTAGCGTTATGCATGAGGCTCTTCAACCACTATACCCAAAAGTCATTGTCTCT TAGTCCCGGAAAGGGCGGAAGTGATTCTTGGAAGGAGGAGGTAATCAAGTTGTGCG GGCGAGAGTTGGTACGGGCACAGATCGCGATATGCGGAAAATCCACAGGTGGGGGC GAAGGAGGAGGTGAGGGTGGAGGTGAAGGACGACAGTTGTATTCCGCCTTGGCAAA CAAGTGTTGCCATGTGGGTGTCACAAAACGAGTCTTGCCCGCTTCTGT
382	ATGGAGACCGATACGCTGTTGCTGTGGGTATTGCTTCTCTGGGTGCCCGGCTCAAC TGGGGATAAGACACATACATGCCCTCCCTGTCCGGCTCCAGAGGCAGCCGGGGGTC CATCAGTCTTCTTTTTCCGCTAAACCTAAGGATACACTGATGATCTCTCGAACA CCGGAGGTCACTTGTGTTGTCGTTGACGTATCACATGAGGATCCCGAAGTAAAGTT CAACTGGTATGTCGATGGTGTGGAGGTTATAATGCTAAAATAAACCACGGGAGG AGCAATATAATTCCACATATAGGGTCGTGAGCGTGTTGACGGTGCTTCATCAAGAC TGGCTTAATGGGAAGGAATATAAATGCAAAGTGTCAAATAAAGCACTTCTGCGCC

SEQ ID NO:	Sequence
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383	ATGGAAACTGATACTCTTCTGCTGTGGGTCTGCTGCTGTGGGTCCAGGATCTAC TGGAGACAAAACACATACTTGTCCGCTTGCCCGGCACCCGAAGCGCCGGCGGAC CCAGTGTCTTTCTCTTCCACCCAAACCGAAAGACACTCTGATGATTTCCAGGACG CCTGAAGTGACCTGCGTTGTAGTTGATGTATCACACGAGGATCCCGAGGTCAAGTT CAATTGGTATGTAGATGGGGTGGAGGTCCATAATGCAAAGACGAAGCCACGGGAGG AACAGTACAACCTCTACGTACAGAGTTGTGAGTGTGTTTTGACCGTCCTTCATCAGGAT TGGCTGAACGGTAAAGAATATAAATGCAAGGTAGCAATAAAGCTTTGCCCGCCCC TATAGAGAAAACGATCAGTAAGGCGAAGGGGCAGCCTAGGGAACCCAGGTATATA CCTTGCCGCCAAGTCGAGATGAGCTGACGAAGAACCAAGTGAGTCTGACATGCCTC GTGAAGGGCTTCTATCCGAGCGATATCGCTGTGCAATGGGAGAGCAATGGGCAGCC TGAGAATAACTATAAAACAACGCCACCCGTCTCGACTCCGATGGCTCATTCTTCC TGTACAGTAACTTACAGTAGATAAGAGTAGATGGCAGCAGGGTAACGTCTTTAGT TGCTCCGTGATGCACGAGGCATTGCACAATCATTAACCTCAAAAATCTCTGTCCCT GAGTCCGGGCAAAGGCGGTTTCAATAGCTGGATGGAGGAGGTATAAAGCTTTGTG GACGAGAACTCGTTTCGCGCCAGATAGCTATTTGTGGGAAATCAACCGGGGGTGA GAAGGTGGCGGAGAAGGGGGAGGCGAAGGGCGCCAAGTGTATTCTGCTAGGCTAA TAAGTGCTGTCACGTAGGATGTACAAAAAGGTCTCTGGCGAGATTCTGC
384	ATGGAGACCGACACCCTCTTGTGTGGGTCTCTCTTGTGGGTGCCGGCAGTAC TGGAGACAAGACGCACACTTGTCCACCTTGCCCTGCGCCGGAAGCTGCTGGAGGCC CCAGTGTCTTTTTGTTCGCCCAAACCGAAGGACACTTTGATGATAAGTCGCACG CCCGAGGTACCTGTGTGGTTGTGATGTCTCACACGAAGATCCGGAGGTGAAGTT TAATTGGTATGTAGATGGCGTGGAGGTTATAACGCCAAAACGAAACCCAGAGAAG ACAATATAACAGTACATATCGAGTAGTATCCGTTCTCACTGTCTGCATCAAGAC TGGTTGAACGGGAAGGAATATAAGTGCAAGGTGAGCAATAAAGCACTCCCGGCCCC AATCGAAAAGACCATCAGCAAAGCGAAGGGGCAACCTCGAGAACCCAGGTATATA CGCTCCCCCTAGTCGGGATGAACTTACTAAAAATCAGGTTAGCCTCACTTGCCTT GTAAAGGGTTCTATCCAGTGATATTGCCGTGCAATGGGAATCAAACGGGCAGCC GGAAAATAACTACAAGACAACCCCTCCTGTGCTCGATAGCGATGGCTCTTTTTTCC TCTACAGCAAACCTTACCGTTGATAAGAGCCGGTGGCAACAAGGTAATGTTTTCTCC TGCTCCGTATGCATGAAGCACTCCATAACCATTATACCCAAAAAAGCCTGTCACCT TAGTCCGGGTAAAGGAGGTAGTGATTCTTGGCAGGAGGAGGTAATCAAACCTTTGTG GGAGGGAGCTGGTACGAGCTCAGATTGCTATATGTGGAAAAAGCACGGGCGGAGGA GAAGGAGGTGGCGAAGGCGGGGTGAAGGTGCGCAACTCTACTCCGCTCTCGCTAA TAAGTGCTGCCACGTGCGGTGTACGAAGCGCTCCCTGGCGCGATTCTGC
385	ATGGAAACAGATACCCTCCTCTTGGGTCTTCTTCTTTGGGTGCCTGGCTCAAC TGGAGATAAAACGCACACGTGTCCGCTTGCCAGCGCCTGAAGCCGCAGGCGGGC CGTCCGTCTTCTCTTCCCTCCAAAACCCAAAGACACACTTATGATCAGTAGGACC

SEQ ID NO:	Sequence
	CCAGAGGTAACCTGCGTCGTGGTTCGACGTTTCCCATGAAGACCCAGAGGTCAAGTT CAACTGGTACGTCGACGGTGTCTGAAGTACATAATGCTAAAACGAAGCCTCGGGAAAG AGCAGTACAACCTCTACCTACCGCGTCGTTTCCGTACTCACCCTACTTCACCAGGAC TGGCTTAACGGTAAAGAGTATAAATGCAAAGTATCTAATAAGGCTCTCGCCGCGCC GATTGAGAAGACAATTTCAAAGGCCAAGGGGCAGCCGCGGGAGCCCCAAGTGTATA CCTTGCCCCCGTCCCGAGATGAGCTGACTAAAAACCAAGTAAGCTTGACTTGCTTG GTCAAAGGCTTCTACCCCTCCGATATAGCTGTGCAATGGGAGTCAAATGGCCAACC AGAGAACAATTTATAAACTACACCCCGGTCTTGGAATCTGATGGCTCATTTTTTTC TCTATTCTAACTGACCGTGGATAAGTCTCGCTGGCAGCAAGGTAACGTGTTTCAGT TGCTCTGTTCTTCACGAAGCACTGCACAGTCATTACACTCAGAAGAGTCTTAGCCT GAGCCCTGGTAAAGGGGGTCTGATTCTTGGCAGGAGGAAGTAATAAACTCTGTG GCCGGGAGTTGGTACGGGCGCAGATTGCGATATGCGGTAAGAGCACCGGCGGAGGC GAAGGCGGTGGGAAGGAGGAGGAGAAGGGAGACAACCTCTATTCCGCATTGGCAAA TAAGTGCTGCCACGTGCGGTGTACCAAACGATCCCTTGACACGGTTCTGT
386	ATGGAGACGGACACCCTCCTTCTCTGGGTTTTGCTCCTTTGGGTCCCTGGTTCCAC TGGAGATAAGACCCATACGTGCCCCCTTGCCCTGCGCCTGAGGCAGCGGGTGGCC CATCAGTCTTTTTGTTCGCCGCCAAGCCAAAGGACACCCTCATGATTAGTAGAACA CCGGAGGTTACGTGCGTCGTAGTGGATGTCAGCCACGAGGATCCCGAGGTTAAGTT TAAGTGGTACGTTGATGGGGTTGAGGTCCATAATGCGAAGACTAAGCCGAGAGAGG AACAGTACAATTCACGTATAGAGTTGTCTCTGTACTGACTGTGCTGCATCAAGAT TGGCTTAACGGTAAGGAGTACAAGTGCAAAGTCTCTAATAAGGCTCTTCCCTGCACC CATTGAGAAAACCTATAAGCAAAGCAAAAGGTCAACCTCGCGAACCTCAGGTGTACA CACTGCCACCCTCTAGGGACGAGCTTACCAAAAATCAAGTATCTCTTACCTGCCTT GTGAAAGGGTTTTATCCCTCAGATATTGCGGTTGAGTGGGAGTCTAACGGACAACC TGAGAACAACCTATAAGACTACTCCCCGGTGCTTGATTGAGACGGGAGTTTTTTTT TGATGACAACTTACCGTCGACAAAAGCCGGTGGCAACAGGGCAATGTATTTCAGT TGTTCTGTAATGCATGAAGCTTTGCATAATCATTACACCCAAAAGAGTCTTTCCCT GTCTCCTGGAAGGGGGGTCAGACTCCTGGATGGAGGAGGTGATCAAACGTGTGTG GGAGAGAGCTCGTCCGGGCTCAGATAGCTATATGCGGCAAGTCTACGGGTGGGGGA GAGGGCGGAGGAGAGGGCGGTGGAGAAGGAGGCGGCCAACTCTACAGCGCTCTGGC CAATAAATGTTGTCTGTCGCGGTGTACTAAGCGCTCACTGGCACGCTTTTGC
387	ATGGAAACCGACACCCTTTTGTGTGGGTATTGCTGTTGTGGGTTCCTCGGTAGCAC GGGGGACAAGACGCATACATGCCC GCCATGCCCCGGCCCCGAAGCTGCTGGGGGAC CATCCGTATTCTCTTCCCTCCCAAAACAAAAGACACGTTGATGATAAGTAGAACA CCAGAGGTAACGTGCGTGGTTGTGATGTTTCCACGAAGATCCGGAGGTAATAAT CAATTGGTATGTAGATGGGGTGGAAGTGCACAATGCCAAAACAAAGCCGCGAGAAG AACAAATACAATAGTACTTACCGGGTTGTGAGCGTGCTCACGGTGTGACCAAGAC TGGCTCAACGGCAAGGAATACAAGTGCAAAGTATCTAATAAAGCTCTGCCTGCGCC GATAGAGAAGACCATCAGTAAGGCCAAAAGGGCAGCCCCGAGAGCCGCAAGTTTACA CTCTTCTCCGAGCAGAGATGAATTGACCAAGAACCAAGTAAGTTTGACGTGCCTG GTGAAGGGCTTCTACCCCTCAGACATTGCGGTGGAGTGGGAAAGTAATGGTCAACC GGAAAACAACCTACAAGACCACGCCGCCGTCTCGACTCCGATGGGTCTTTCTTTC TTTATTCAAAGTTGACAGTAGATAAGTCAAGGTGGCAGCAAGGTAACGTGTTTAGT TGTAAGTGAATGCACGAGGCCCTGCATAATCATTATACCCAAAAGAGTTTGAGCCT CTCACCAGGAAAAGGCGGATCAGACAGCTGGCAGGAGGAGGTAATTAATTTGTGTG GACGGGAGTTGGTCAGGGCGCAAATAGCCATCTGCGGTAAGAGCACGGGTGGAGGA

SEQ ID NO:	Sequence
	GAGGGTGGAGGGGAAGGTGGGGGAGAAGGCGGGCGGGCAGCTCTATTCTGCACTCGC CAACAAGTGTGTGTCACGTCCGATGCACAAAGAGATCTCTTGCTCGATTCTGC
388	ATGGGAGACTGATACTCTTTTGTGTGGGTACTGCTCCTGTGGGTTCAGGCTCCAC AGGAGACAAAACACACACCTGTCCGCCTTGCCCCGGCTCCTGAAGCCGCGGGTGGCC CTAGTGTGTTTTTGTTCGCCGAAACCTAAGGATACCCTCATGATAAGCCGGACG CCCAGGTTACCTGTGTCGTGGTTCGATGTTAGTCATGAGGATCCAGAAGTCAAGTT TAATTGGTACGTGACGGCGTTGAAGTCCACAATGCAAAAACCTAAACCGCGAGAAG AACAGTACAACCTCCACCTACAGAGTTGTCTCAGTTTTGACAGTTCTCCATCAGGAT TGGCTCAATGGAAAGGAATATAAGTGCAAGGTGAGCAATAAAGCGCTTGCCGCCCC TATAGAGAAGACCATTAGCAAGGCGAAAGGACAGCCCCGCGAGCCCCAGGTCTATA CGCTGCCTCCTAGCAGAGATGAGCTCACGAAAAATCAGGTGAGCTTGACATGCTTG GTGAAGGGCTTCTACCCCACTGACATCGCAGTTGAATGGGAGAGCAACGGCCAACC TGAGAACAACTACAAAACAACGCCCCCGGTTCTTGACAGCGATGGGTCTTCTTTT TTTACTCTAAGCTTACAGTTGATAAAAGCAGGTGGCAGCAGGGGAATGTGTTCTCA TGTTCCGTACTGCATGAGGCTCTGCATTCTCCTACACCCAAAAAGCCTTAGCCT GAGCCCCGGTAAGGGAGGTAGTGACTCATGGCAAGAGGAAGTGATTAAGCTCTGCG GCCGGGAGTTGGTGAGAGCCCAAATCGCCATTTGCGGTAAGTACCGGAGGGGGC GAGGGAGGAGGCGAAGGTGGAGGTGAAGGAGGTGGACAGTTGTACTCAGCTCTTGC AAATAAATGTTGTGTCATGTTGGTTGCACGAAAAGATCTCTTGCGAGGTTCTGT
389	ATGGGAGACTGACACTCTTTTGTGTGGGTGCTTCTTCTGTGGGTACCTGGATCCAC TGGGGATAAGACGCATACCTGTCCACCGTGCCCCGCGACCGGAAGCGGCTGGTGGTC CATCAGTTTTTCTGTTCCCACCGAAACCTAAGGACACGTTGATGATATCACGGACA CCAGAGGTTACGTGCGTAGTGGTGGATGTGAGCCACGAGGATCCAGAAGTTAAATT TAATTGGTACGTAGATGGAGTGGAGGTTATAATGCGAAGACAAAGCCTCGCGAGG AACAGTATAAATCCACCTATCGCGTCGTATCTGTGCTTACGGTACTTCACCAAGAC TGTTTGAACGGTAAGGAATATAAATGCAAGGTTTCCAATAAAGCACTTCTGCGCC AATTGAGAAGACAATATCCAAAGCTAAAGGTCAACCCAGGGAACCGCAAGTCTACA CTCTCCCCCGTCTCGCGATGAATTGACGAAGAACCAGGTTAGTCTCACCTGCCTG GTCAAGGGGTTTTTACCCCTCTGACATAGCTGTAGAATGGGAGTCTAATGGACAGCC AGAGAACAATTACAAAACGACCCCCCGGTCCTCGATTCTGATGGGAGTTTTTTTCT TTTATTCAAATTTGACTGTCGATAAGTCAAGATGGCAACAGGGTAACGTATTTTCT TGCAGTGTTATGCATGAAGCATTGCACAACCCTATACACAAAAATCATTGAGTTT GAGTCCCGGTAAAGGGGGAAGCGACTCATGGATGGAAGAAGTAATCAAGCTGTGCG GGCGAGAGCTTGTGCGAGCTCAGATAGCAATCTGTGGTAAGTCTACAGGTGGAGAG GGTGGCGGTGAAGAAGGCGGGGGAGAGGGAGGCCAGCTTTATTCTGCCCTGGCTAA CAAGTGCTGTCACGTTGGATGCACGAAGCGCTCCCTGGCCCGATTCTGC
390	ATGGAAACCGATACATTGCTTTTGTGGGTCTCCTTCTTTGGGTTCTTGGCTCTAC AGGCGATAAGACGCATACCTGTCCCCCATGTCCCGCTCCGGAAGCCGCTGGCGGCC CCTCCGTTTTTCTGTTCCCGCCGAAACCGAAAGACACCCTGATGATATCACGCACT CCCAGGTCACCTGCGTGGTAGTCGATGTTAGTCATGAAGATCCTGAGGTCAAATT CAATTGGTATGTAGATGGCGTTGAGGTACACAACGCGAAGACAAAACCCCGAGAAG AACAGTATAACTCAACCTACCGCGTAGTTTCAGTTCTTACCGTACTGCACCAAGAC TGTTTGAACGGTAAAGAGTACAAATGTAAAGTCAGCAATAAAGCTTTGCCAGCACC TATCGAAAAAACCATCAGTAAGGCCAAGGGTCAACCCAGGGAGCCGCAAGTGTACA CTCTTCCCCCTAGCAGGGATGAATTGACCAAGAATCAGGTCTCTTTGACGTGCCTC GTTAAGGGTTTCTATCCCAGCGATATAGCCGTAGAATGGGAGTCTAACGGTCAGCC AGAAAATAACTATAAGACAACCCCGCCTGTTTTGGATTCCGACGGCTCTTTTTTTC

SEQ ID NO:	Sequence
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391	ATGGAAACCGACACCTTGCTTTTGTGGGTGCTCTTGCTGTGGGTTCGGGGGAGCAC TGGCGACAAGACCCACACATGTCCCCGTGTCCGGCACCAGAAGCAGCGGGGGGAC CGTCAGTATTCTTGTTTCCACCGAAGCCCAAAGACACATTGATGATTTACGAACCT CCTGAAGTTACCTGTGTGGTTGTAGATGTATCACACGAAGACCCAGAAGTCAAAT CAATTGGTATGTCGACGGGGTTGAAGTTCACAATGCGAAGACGAAGCCCCGGGAGG AACAGTACAACAGCACGTACAGGGTTGTGAGCGTTCTTACTGTATTGCACCAGGAT TGGCTCAACGGCAAGGAGTATAAATGTAAAGTTTCTAATAAGGCTCTTCTGCCCC AATTGAAAAGACGATATCTAAAGCGAAGGGCCAACCACGGGAACCTCAGGTGTACA CACTTCCGCTAGCAGGGATGAGTTGACCAAGAATCAAGTCTCTTTGACGTGCCTG GTCAAGGGGTTTTACCCATCAGATATCGCCGTGCAATGGGAGTCAAACGGACAACC CGAAAATAACTATAAACTACTCCACCAGTTCTGGATAGCGACGGCTCATTTTTTTC TGTATTCAAAGCTCACTGTAGACAAGTCTAGGTGGCAGCAGGGTAATGTCTTCTCC TGCTCAGTAATGCATGAGGCTCTTCAACAACCTATACTCAAAGAGCCTTTCCCT GTCACCTGGCGGTGGAAGCGACTCATGGATGGAGGAGGTAATAAAGCTCTGCGGAA GAGAACTGGTACGCGCACAAATCGCAATTTGTGGTAAGAGTACTGGCGGGGAAGGA GGTGGGGAAGAAGGGGGCGGTGAGGGCGGACAGCTCTATTCTGCACTTGCAAACAA ATGTTGCCACGTGGGATGTACTAAGCGAAGCCTTGCAAGATTCTGC
392	ATGGAGACCGACACACTGTTGCTGTGGGTACTCCTCCTGTGGGTGCCAGGAAGCAC GGGCGATAAAACCCACACATGCCCTCCATGCCCTGCTCCAGAGGCCGCCGGTGGGC CATCAGTTTTCTTGTTTCCGCTAAACCAAAGGACACGCTTATGATCTCCAGGACC CCCGAAGTTACGTGTGTGGTGGTTGATGTTAGTCACGAGGACCCGGAAGTCAAGTT CAACTGGTACGTTGATGGTGTAGAGGTGCACAATGCAAAGACGAAGCCACGCGAAG ACAATACAACAGCACATATCGAGTTGTGAGCGTACTCACGGTACTGCATCAGGAC TGGCTGAACGGTAAAGAATACAAATGTAAAGTCTCAATAAGGCACTTCTGCGCC GATAGAAAAACGATCAGTAAGGCCAAGGGCCAACCCCGAGAACCACAGGTATATA CGCTCCCACCGTCACGAGACGAGTTGACAAAAAATCAGGTCTCCCTGACTTGCCCTC GTGAAAGGTTTTTATCCCTCAGATATTGCTGTTGAGTGGGAAAGCAATGGGCAGCC AGAGAATAATTATAAGACGACTCCTCCGGTTTTTGGATTCCGACGGTAGTTTTTCT TGTATAGTAAGCTTACTGTAGACAAGTCAAGATGGCAACAAGGTAATGTGTTCTCT TGCTCAGTTATGCATGAAGCTCTTCATAACCATTACACGCAAAAGAGTCTCAGTCT GAGCCCCGGTGGCGGTAGCGACAGTTGGCAGGAAGAGGTGATTAAGTTGTGCGGTC GCGAGCTCGTTCGGGCCCAAATTGCAATCTGCGGAAAATCTACGGGCGGAGAGGGC GGGGGTGAGGAGGGTGGGGGTGAAGGTGGGCAGCTCTATAGCGCCCTTGCGAATAA ATGTTGTACGTCCGATGCACAAAGAGGTCCCTCGCCAGGTTCTGC
393	ATGGAAACTGACACACTGTTGCTGTGGGTGCTGCTCCTTTGGGTACCCGGATCAAC CGGGGATAAGACCCACACTTGCCCCCTTGCCCTGCCCCCGAAGCGGCCGGAGGTC CTTCAGTATTTTTGTTTCCACCGAAACCCAAAGATACTTTGATGATATCAAGAACT CCTGAAGTACCTGCGTGGTAGTTGACGTATCTCATGAGGATCCCGAGGTGAAGTT CAATTGGTACGTGATGGCGTCGAGGTTCAACGCTAAGACTAAGCCGAGGGAAG AGCAATATAATTCCACTTATAGGGTGGTGTCCGTCTTGACTGTTTTGCACCAGGAT TGTTTGAACGGGAAAGAGTACAAATGTAAAGGTGAGTAATAAAGCTTTGGCTGCTCC

SEQ ID NO:	Sequence
	CATCGAAAAGACAATAAGCAAGGCCAAGGGGCAACCTCGGGAGCCGCAGGTGTACA CCCTTCCCTCCCAGTAGAGACGAACTGACAAAAAACCAGGTGTCCCTGACCTGCCTT GTGAAGGGGTTTTACCCGAGCGACATAGCGGTTGAATGGGAGAGCAACGGGCAACC CGAGAACAACCTACAAAACCTACACCGCCTGTCTGGACTCCGATGGAAGCTTCTTCC TCTACTCCAACTGACCGTGGACAAAAGCAGATGGCAACAAGGAAACGTATTCTCA TGCTCAGTAATGCACGAAGCATTGCACAATCACTACACCCAAAAGTCCCTCTCACT CTCCCCTGGTAAGGGCGGATCAGACTCATGGCAAGAGGAGGTAATTAAGTTGTGCG GGAGGGAGCTCGTCCGCGCGCAAATAGCCATTTGTGGCAAGTCCACTGGAGGAGGC GAGGGTGGAGGAGAGGGTGGTGGGAGGGCAGGCAACTCTACAGTGCCTCGCCAA TAAATGCTGCCATGTTGGGTGCACGAAGCGCAGTCTCGCACAATTCTGC
394	ATGGAGACCGACACTCTGCTGCTCTGGGTACTCTTGCTGTGGGTGCCTGGGTCTAC TGGGGATAAGACCCACACGTGTCTCCATGTCCGGCACCAGGAGGCTGCTGGCGGGC CTTCTGTATTCTCTTCCACCCAAAGCCAAAAGACACATTGATGATATCAAGGACG CCGGAAGTCACCTGTGTTGTGTGGACGTTTCCCATGAAGACCCAGAGGTAAAATT CAATTGGTATGTGGACGGCGTAGAGGTTTACAACGCCAAAACCAACCCCGAGAGG AACAGTATAATAGCACATATCGAGTAGTATCTGTTCTCACAGTGCTCCATCAAGAC TGGCTTAATGGTAAAGAGTATAAATGCAAAGTTTCCAATAAAGCCCTCGCTGCACC GATCGAGAAGACAATCAGTAAAGCGAAGGGCCAGCCTCGGGAACCGCAGGTGTATA CTCTTCCACCCCTCAAGAGACGAGCTCACTAAAAACCAAGTTTCATTGACATGCCTC GTCAAAGGTTTCTACCCATCAGACATCGCGGTGCAATGGGAAAGTAATGGGCAGCC GGAAAACAACCTATAAAACGACGCCGCCCGTCTTGATTCTGATGGTTTCATTTTTTC TTTACTCTAAATTGACCGTCGATAAAAAGTAGGTGGCAACAAGGAAATGTTTTTTCC TGCTCCGTCTGTCATGAAGCGTTGCACAGTCACTATAACCCAGAAGAGTCTTTCCTT GTCACCCGGAAAAGGCGGTTTCAAGTTCATGGCAGGAAGAAGTAATTAACCTCTGTG GCCGCGAGCTTGTAGGGCGCAGATAGCCATATGTGGTAAAAGCACCGGAGGAGGT GAAGGCGGAGGCGAAGGAGGTGGGGAAGGAAGACAATTGTATTCTGCATGCAAA TAAATGCTGTCATGTGGGTGCACGAAACGCAGTCTTGCACAATTTTGT
395	ATGGAAACCGATACGCTGCTTCTTTGGGTCTTCTCCTCTGGGTTCAGGGTCCAC CGGCGACAAAACCCATACCTGCCCCCTTGCCCTGCACCAGAAGCGGCGGGAGGAC CTAGCGTTTTTTCTTTTCCCTCCGAAACCGAAAGATACCCTCATGATATCAAGAACA CCTGAGGTTACTTGCGTTGTCTGGACGTGAGTCACGAAGACCCGAGGTGAAGTT CAACTGGTATGTAGATGGAGTGGAGGTCCATAATGCAAAAACGAAACCGAGAGAAG ACAATACAACCTCTACATATCGAGTCGTGTGAGTACTCACGGTTTTGCATCAAGAT TGGCTGAACGGTAAGGAGTACAAGTGTAAAGTTAGCAACAAGGCTCTCGCGGCGCC GATAGAAAAGACTATAAGTAAAGCAAAAGGCCAGCCAGAGAACCTCAAGTTTACA CTCTGCCTCCAGCAGAGATGAACTGACTAAAAATCAGGTTTCATTGACCTGTCTC GTCAAGGGTTTTTATCCAAGCGACATAGCAGTTGAATGGGAAAGCAACGGTCAACC AGAAAATAAATTACAAAACCACTCCACCAGTCTTGACTCTGACGGATCCTTCTTTTC TCTATTCAAAATTGACGGTGGATAAATCTAGGTGGCAGCAAGGCAACGTCTTCTCT TGTAGCGTTATGCATGAGGCGCTGCACAACCACTACACACAAAAGTCTCTTAGTTT GAGCCCGGGCGGCGGAAGCGACTCTTGGCAAGAGGAAGTGATAAACTCTGTGGTC GAGAATTGGTACGCGCGCAGATCGCTATCTGCGGCAAGTCCACAGGGGGAGGGGAA GGTGGCGGGGAAGGTGGTGGCGAGGGCAGGCAGTTGTATAGTGCCTTGCCACAA GTGCTGCCATGTGGGGTGCACCAAGCGCAGTTTGGCACGGTTCTGC
396	ATGGAAACGGACACCCTTCTGCTCTGGGTACTGCTGCTCTGGGTTCCCTGGTTCTAC CGGTGATAAACTCACACTTGTCCCCGTGTCCGGCACCAGAAGCCGCAGGAGGGC CATCTGTCTTTCTTTTCCCCCAAAACCAAGGATACACTGATGATCTCCGCACT

SEQ ID NO:	Sequence
	CCCGAAGTTACTTGTGTCGTAGTAGACGTTTCTCACGAGGACCCAGAGGTGAAATT CAATTGGTATGTTGACGGAGTAGAGGTGCATAATGCCAAGACAAAGCCCCGAGAGG AACAAATACAATTCAACCTACAGAGTAGTGTCCGTTCTTACGGTTCTCCATCAGGAT TGGCTCAACGGTAAGGAATATAAGTGCAAGGTAAGCAACAAAGCGCTGGCCGCACC CATTGAGAAAACCATTTCAAAGCTAAAGGCCAACCCCGCGAACCACAAGTTTATA CTCTCCCCCAAGTCGCGATGAACTTACAAAAAATCAAGTCTCATTGACGTGCTTG GTCAAAGGCTTCTACCCGAGCGATATCGCTGTTGAATGGGAGTCTAATGGACAACC GGAAAATAACTATAAAACTACACCCCAAGTCTCGATTGAGACGGCAGCTTCTTCC TGTATTCAAACTGACGGTTGACAAATCACGCTGGCAACAGGGTAACGTTTTTTTCC TGTAGCGTTCTTCATGAAGCCTTGACAGTCACTACACCCAGAAGTCCCTTAGCTT GTCACCTGGCGGGGGTTCAGACTCTTGGCAGGAGGAGGTAATCAAACGTGTGCGGAA GAGAACTGGTGAGGGCTCAGATTGCAATTTGTGGGAAGAGCACGGGTGGCGGTGAA GGAGGTGGCGAGGGCGGAGGAGAGGGGAGGCAACTCTACAGTGCCTTGGCTAATAA ATGCTGTACGTCGGCTGTACTAAGAGAAGCCTCGCCAGATTTTGC
397	ATGGAAACAGATACTTTGTTGCTGTGGGTACTCCTCCTCTGGGTACCTGGGAGCAC CGGGGACAAGACGCATACCTTGCCCTCCGTGCCCTGCACCAGAAGCCGCTGGTGGCC CATCTGTGTTTTTTGTTCCCCCTAAGCCAAAAGACACATTGATGATTTACGAACT CCAGAAGTGACTTGCGTAGTTGTTGACGTATCACACGAAGACCCCGAGGTTAAATT TAATTGGTATGTGGACGGGGTCGAGGTGCATAACGCCAAAACCAAACCCCGGGAGG AACAATATAACTCTACGTATCGGGTCGTATCTGTGTTGACCGTCCTTACCAAGAT TGGTTGAACGGCAAGGAATATAAGTGTAAGTGTCTAATAAAGCATTGGCTGCCCC GATAGAAAAGACGATCTCTAAAGCCAAGGGCCAACCCAGAGAGCCTCAAGTATATA CTCTCCCACCGAGTCGAGATGAGCTCACTAAGAACCAGGTGTCACTCACGTGTCTG GTTAAAGGATTTTACCCTAGTGATATAGCCGTGAGTGGGAATCAAATGGGCAGCC GGAGAATAACTATAAGACCACGCCTCCAGTTCTCGATTCCGATGGTAGCTTTTTTCC TTTACTCTAAACTTACGGTCGACAAGTCCAGGTGGCAACAGGGCAATGATTTTTCT TGCTCCGTGATGCACGAGGCTTTGCACAACCATTACACGCAAAAGTCACTGTCCCT GTCTCCTGGAGGCGGTTCTGACAGTTGGCAGGAGGAGGTAATCAAATTGTGTGGGC GGGAGTTGGTTAGGGCGCAAATGCTATTTGCGGCAAAAGTACTGGGGCGGTGAA GCGGGAGGCGAGGGAGGAGGAGAAGGTGCACTGTATTCTGCCTTGGCGAACAA ATGCTGTACGTCGGCTGTACGAAACGGTCTTTGGCCAGTTTTTGT
398	ATGGAAACTGACACTCTTCTGTTGTGGGTCTTCTGCTGTGGGTTCTTGGCTCTAC TGGAGATAAGACACACACTTGTCGCCATGCCCTGCGCCGGAAGCGGCGGGAGGAC CGTCCGTTTTTCTGTTCCCTCCCAAACCCAAAGACACGTTGATGATTAGTCGCACG CCAGAAGTTACGTGCGTTGTCGTAGATGTATCCACGAAGACCCCGAGGTGAAGTT CAATTGGTATGTAGATGGGGTGGAGGTCCATAACGCTAAGACCAAACACGCGAGG AACAATATAATTCTACGTACCGGTAGTGAGCGTTCTCACAGTTCTTCAACAGGAT TGGCTTAACGGCAAGGAGTATAAGTGTAAGGTGTCTAATAAAGCCTTGGCTGCCCC GATCGAAAAACGATAAGTAAAGCAAAGGGTCAACCTAGAGAACCCCAAGTGTACA CTCTCCCGCCATCACGGGATGAATTGACTAAGAACCAAGTGTCACTCACGTGTCTT GTAAAGGGCTTCTACCCATCCGATATAGCCGTTGAGTGGGAATCAAATGGTCAGCC AGAGAACAACATAAGACAACCTCCGCGGTACTTGATAGTGACGGTTCTTTTTTCC TTTACAGTAAATTGACGGTAGATAAGTCTCGCTGGCAGCAAGGAAACGTCTTTTCT TGTTCAAGTGCTTCATGAGGCGTTCACTCACACTATACTCAGAAGAGTTTGAGTTT GTCTCCAGGTGGAGGCAGCGACTCATGGCAAGAGGAAGTAATCAAACGTGTGTGGTC GCGAATTGGTACGAGCACAGATCGCGATCTGCGGGAAATCAACAGGTGGCGGCGAA

SEQ ID NO:	Sequence
	GGCGGCGGGGAAGGCGGCGGCGAAGGTAGGCAACTTTACTCAGCCCTTGCGAACAA ATGTTGCCACGTAGGCTGTACTAAGAGAAGTCTCGCCAGTTTTGC
399	ATGGAGACAGATACCCTTCTGTGTGGGTCCTTCTGCTTTGGGTGCCGGGAAGTAC AGGCGACAAGACTCATACCTGCCCCCTTGTCCAGCACCAGAAGCAGCTGGCGGGC CAAGCGTGTTCCTGTTTCCACCTAAGCCCCAAAGATACGTTGATGATCAGCCGCACC CCGGAAGTAACCTGTGTAGTAGTAGATGTGTCCCACGAAGACCCCGAAGTAAAGTT TAATTGGTACGTGATGGTGTGGAAGTACATAACGCTAAAACGAAGCCCCGAGAAG AGCAGTACAACAGTACTTACAGAGTAGTTTCTGTTCTTACAGTGTGTCATCAGGAT TGGCTGAACGGGAAGGAGTATAAATGTAAAGTCTCAAACAAGGCACTTGCGGCACC AATAGAGAAGACAATATCTAAGGCCAAAGGGCAGCCTAGAGAGCCACAAGTATATA CGCTGCCCCCAGCAGGGACGAGCTGACAAAGAACCAAGTGTCACTGACCTGCCTT GTTAAGGGCTTCTATCCGAGTGATATTGCTGTTGAATGGGAAAGTAACGGACAGCC GGAGAACAACATAAACTACTCCACCCGTGTTGGATAGTGACGGTAGCTTTTTTC TGTACTCCAAGTTGACGGTAGACAAAAGTCGGTGGCAGCAGGGGAACGTATTTTCT TGTTCTGTGTCATGCACGAAGCTCTTCACAATCACTATACGAGAAGTCCCTCTCTCT CTCTCCTGGGAAGGGTGGTTCCGACAGCTGGCAGGAGGAGGTATTAACTGTGTG GTAGAGAGCTGGTACGGGCTCAAATTGCAATTTGTGGTAAGAGTACTGGCGGTGGC GAGGAAGGGGTGGGGAGGAGGGCGGAGGTAGGCAGCTCTACTCTGCTCTCGCCAA CAAGTGTTGTACGTCGGGTGTACTAAAAGATCACTTGCCCGCTTTTGT
400	ATGGAAACCGATACCCTGCTCTTGTGGGTCCTCCTGCTTTGGGTCCCAGGTTCCAC AGGCGACAAAACACATACATGCCCGCGGTGTCCGGCGCCTGAAGCAGCAGGAGGCC CCAGTGATATTCCTTTTCCCTCCAAAGCCAAAAGATACGTTGATGATATCTAGGACA CCTGAGGTTACCTGCGTCGTAGTGACGTATCCCACGAAGACCCAGAAGTCAAGTT TAACTGGTATGTGGACGGAGTGAGGTTACACAATGCAAAGACAAAGCCGCGAGAGG AACAATATAAATCCACCTATAGAGTCGTGTCAGTCCTTACGGTCTTGCACCAGGAC TGGCTCAATGGTAAGGAGTATAAGTGCAAAGTATCAAACAAGCTCTCGCAGCGCC CATCGAAAAGACCATCAGCAAAGCTAAGGGCCAGCCAAGAGAGCCTCAAGTGTACA CGTTGCCGCCTTCAAGGGACGAGCTCACTAAAAATCAGGTATCACTTACGTGTCTT GTCAAAGGGTTTTATCCTTCCGACATCGCGGTTGAATGGGAGAGCAATGGACAGCC GGAGAATAATTATAAACGACGCCGCGGTCTTGACAGCGATGGTTCATTTTTCC TTTACTCAAAGCTGACGGTTGATAAGTCTAGGTGGCAGCAGGGGAACGTCTTTTCC TGTAAGTGTACTTCATGAGGCGCTCCATTCTCATTACACTCAGAAGTCACTGAGCCT TTCACCCGGCAAAGGTGGATCAGACTCCTGGCAAGAAGAGGTAATCAAACCTCTGTG GGAGGGAACTCGTTCGAGCCAGATTGCAATCTGTGGGAAAAGCACAGGCGGAGGG GAAGAAGGGGTGGCGAAGAAGGTGGGGGCAGGCAGCTCTATTAGCTCTTGCCAA CAAATGCTGTGATGAGGCTGCACAAAGCGATCACTGGCGAGATTCTGT
401	ATGGAAACCGACACCCTGCTGCTCTGGGTTCTTCTCCTCTGGGTTCCCGGCTCAAC CGGAGATAAAACTCATACTTGCCCACCCTGCCCAGGCTCCCGAGGCAGCAGGTGGAC CCTCAGTATTTTTGTTCCCTCCGAAACCTAAAGATACACTTATGATTAGCCGGACC CCTGAGGTAACGTGTGTGGTGGTTGACGTAAGTCATGAAGATCCAGAAGTAAAGTT TAACTGGTACGTAGACGGTGTGGAGGTACATAATGCGAAGACAAAACACGAGAGG AACAGTATAACTCTACCTACCGCGTAGTAAGCGTACTTACTGTGCTCCACCAAGAC TGGCTTAACGGGAAAGAGTATAAGTGTAAAGTCAGTAATAAAGCACTGGCCGCCCC GATCGAAAAACAATCAGCAAAGGCCAAAGGACAACCAAGGGAGCCTCAGGTCTATA CTCTTCCCCGAGTAGGGATGAGCTTACCAAGAACCAGGTGTCTCTGACATGCCTT GTCAAAGGATTTTACCCGAGTGACATAGCCGTAGAATGGGAGTCAAACGGCCAACC TGAAAACAACATAAGACCACGCTCCCGTACTCGACTCAGATGGAAGCTTTTTCC

SEQ ID NO:	Sequence
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402	ATGGAACTGATACTCTTCTCCTTTGGGTGCTCCTCCTCTGGGTCCCGGGTCCAC AGGCGATAAGACACATACCTGTCCACCCTGCCCAGCACCTGAAGCTGCAGGCGGCC CCAGCGTATTCTGTTTCTCCGAAGCCGAAAGACACACTTATGATTTCCCGGACG CCTGAGGTAACCTGCGTCGTAGTAGATGTGTCTCACGAAGACCCCGAGGTGAAAT CAACTGGTACGTTGATGGTGTGGAAGTTCATAATGCGAAAACTAAACCACGAGAGG AGCAATATAACTCAACTTATAGAGTTGTGAGCGTCTTGACGGTACTGCACCAGGAC TGGCTGAATGGCAAAGAGTACAAATGCAAAGTCTCAAATAAGGCGTTGGCGGCTCC CATAGAAAACTATCAGCAAAGCCAAGGGTCAACCTCGGGAGCCACAAGTGTATA CTCTTCCGCCCTAGTCGCGACGAGCTCACAAAGAATCAGGTGAGTCTTACTGTTTG GTTAAGGGTTTCTACCCAGTGACATTGCGGTGCGGTGAGTGGGAAAGTAACGGACAGCC TGAAAACAACATAAAACAACGCCTCCAGTACTCGATTGAGTGGTTCATTCTTTTC TTTATTCCAACTCACAGTCGACAAGAGTAGATGGCAACAAGGGAACGTGTTTAGC TGTAGCGTACTCCATGAGGCACTCCACTCTCACTATACCCAAAAGTCTCTCAGCTT GTCACCCGGAAGAGGCGGTTCTGACAGTTGGCAAGAGGAAGTGATTAAATTGTGTG GGCGGGAACCTGTGAGGGCTCAAATCGCGATTTGCGGCAAGTCCACTGGTGGCGGC GAGGAAGGAGGAGGTGAAGAAGGAGGAGGTAGGCAACTGTATTGAGCGTTGGCGAA TAAATGCTGCCATGTTGGATGTACTAAACGGAGCCTTGCTCAGTTCTGC
403	ATGGAACTGACACCTTGTGCTTTGGGTATTGCTTCTGTGGGTCCCGGTAGCAC GGGTGATAAAACGCATACCTGCCCCCTTGCCCGGCACCTGAAGCTGCCGGAGGTC CTTCCGTGTTTCTGTTCCCACTAAGCCAAAAGACACACTTATGATTTCTCGCACA CCAGAAGTAACGTGCGTCGTAGTTGACGTCTCCCATGAAGACCCGGAGGTAAAT TAATTGGTACGTCGACGGGGTAGAAGTTCATAACGCAAAGACTAAACCACGAGAAG AGCAATACAACCTCTACATACAGAGTAGTAAGCGTTCTCACCGTTCTTCATCAAGAT TGGCTCAACGGAAGGAGTATAAGTGTAAAGGTGTCCAATAAAGCGTTGGCCGCACC AATCGAAAAGACCATAAGCAAAGCCAAAGGCCAACCCCGCGAACCAGGAGGTGTACA CACTTCCCCCGTCCAGGGATGAATTGACAAAAACCAAGTTTCCCTCACGTGTCTC GTCAAGGGATTCTACCCGAGTGATATCGCAGTTGAATGGGAAAGCAATGGTCAGCC CGAGAATAACTACAAGACTACTCCCCCTGTGTTGGACTCAGACGGCTCATTTCTTCC TCTACAGTAAGTTGACTGTGGACAAAAGTCCGTGGCAGCAAGGCAATGTCTTCAGT TGTAAGTGAATGCATGAAGCACTCCACAATCATTACACCCAAAAATCCCTGAGCCT GTCCCCGGGCGGAGGTTGAGATTGATGGCAGGAGGAAGTTATAAACTGTGCGGGC GCGAGTTGGTGAGGGCGCAGATCGCAATCTGTGAAAAGAGTACGGGAGGTGGCGAA GAGGGTGGTGGAGAAGAGGGAGGAGGTGACAACTGTATTCCGCGCTCGCGAACAA GTGTTGCCACGTTGGCTGCACCAACGAAGCCTGGCTCGATTTTGC
404	ATGGAGACTGACACCCTTCTCCTCTGGGTCTCCTTGCTTTGGGTCCCTGGCTCTAC TGTTGACAAGACACACACTTGTCCACCTTGCCCGGCTCCCGAGGCGGCAGGAGGAC CAAGCGTTTTTCTGTTCCCTCCCAAACCAAGGATACGCTTATGATCTCTCGAACG CCGGAAGTTACTTGCCTAGTAGTTGATGTCTCCCATGAAGATCCCGAAGTGAAGTT CAACTGGTATGTAGATGGTGTGGAAGTTCATAACGCGAAAAACCAACCACGCGAAG AACAGTATAACAGTACTTATCGGGTGTTCAGTACTCACGGTGTCTCATCAAGAC TGGCTTAATGGAAGGAGTATAAATGTAAGGTAAAGTAACAAGGCATTGGCGGCTCC

SEQ ID NO:	Sequence
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405	ATGGAAACTGACACACTTCTTCTGTGGGTACTCTTGTGTGGGTTCCGGGCTCAAC GGGTGACAAGACACATACTTGTCCACCATGTCCCGCCCCAGAAGCTGCGGGAGGAC CATCAGTTTTTTTTGTTCCCCCGAAACCGAAGGATACCCCTCATGATAAGTCGAACG CCCGAAGTCACTTGCGTGGTGGTTGATGTTAGCCACGAGGACCCAGAAGTGAAGTT CAACTGGTACGTGGACGGGGTCGAAGTTTATAATGCGAAAACAAGCCTCGCGAGG AACAGTACAACCTACATACAGGGTTGTGTCTGTTTTGACAGTCTTGACCAAGAT TGGCTCAACGGGAAGGAATATAAGTGTAAGGTAAGCAATAAAGCACTGGCGGCCCC GATCGAAAAACGATATCCAAGGCCAAGGGCCAGCCCCGAGAGCCTCAGGTATATA CTCTGCCGCCAAGCCGGGATGAACTGACTAAAAACCAGGTCTCTTTGACTTGTCTT GTCAAGGGATTTTACCCAAGTGACATTGCGGTAGAGTGGGAAAGCAACGGTCAACC AGAAAACAATTACAAGACGACACCGCCGGTACTCGACTCAGATGGATCCTTTTTTCC TGTATAGCAAGCTGACAGTGGACAAGTCCCCTGGCAGCAAGGGAACGTATTTTCA TGCAGCGTGATGCATGAGGCTCTTCAACAACCATACACACAGAAAAGTCTGTCTAT GAGCCCTGGCGGCGGGAGCGATTCTTGGCAAGAAGAAGTTATAAACTTTGCGGTC GAGAGCTGGTTCGGGCACAAATTGCTATCTGCGGAAAATCTACAGGAGGAGGCGAG GAGGGAGGGGGCGAAGAAGGCGGGGGGAGACAGTTGTACAGTGCCTCGCTAACAA GTGTTGCCACGTGCGTTGCACAAAGAGATCCCTGGCTCAATTCTGT
406	ATGGAGACAGATACTCTCTTGTCTGTGGGTGCTGCTCTTGTGGGTTCCCTGGAAGTAC CGGTGATAAACTCACACCTGTCCCCCGTGTCCCGCACCAGAAGCGGCCGGTGGTC CCTCCGTTTTTCTCTTCCCTCCTAAACCTAAGGACACACTTATGATTAGCAGAACT CCAGAAGTTACGTGCGTAGTCGTTGACGTTAGTCATGAAGATCCTGAGGTTAAGTT CAACTGGTACGTAGACGGAGTAGAGGTCCACAACGCCAAGACGAAACCCCGAGAAG AGCAGTATAATTCTACCTATCGAGTTGTTTCAGTATTGACGGTGCTTACCAAGAT TGGCTGAATGGCAAAGAGTATAAGTGCAAGGTAAGCAACAAAGCACTCGCGGCTCC TATCGAGAAAATATTTCCAAAGCTAAGGGCCAGCCTCGCGAACCACAAGTCTATA CCCTGCCACCGAGTCGGGACGAACTACCAAGAACCAAGTGTCTCTTACTTGCCCTC GTTAAAGGTTTTTATCCCAGCGACATAGCCGTGCAATGGGAGTCCAATGGCCAACC TGAGAACAACATATAAACTACCCCTCCTGTACTTGATAGCGACGGAAGTTTTTTCC TCTATTCAAACTCACAGTTGATAAGTCTCGATGGCAACAGGGCAACGTCTTCTCT TGCAGTGTGTGTCATGAAGCTCTGCACTCTCATTACACACAGAAGAGTTTGTCTCT CAGTCCAGGTGGCGGCTCAGATAGCTGGCAGGAAGAAGTAATCAAGTTGTGCGGCA GGGAACTGGTAAGGGCACAGATAGCCATTTGTGGAATACTACGGGTGGCGGTGAG GAAGGCGGCGGAGAAGAAGGGGGAGGTGCGGCAGCTGTATAGTGCCTCGCAAACAA GTGCTGCCATGTGCGGTGCACCAAGCGATCCCTTGCCCAGTTTTGC
407	ATGGAGACGGACACTCTTCTCCTGTGGGTTCTCCTCTTGTGGGTTCCAGGATCTAC CGGCGATAAGACGCACACATGCCACCCCTGTCTGCGCCTGAAGCCGCGGGGGGAC CCAGCGTTTTTCTCTTCCCGCCGAAACCGAAAGACACACTTATGATCAGCCGACT

SEQ ID NO:	Sequence
	CCCGAGGTTACCTGCGTGGTGGTAGATGTATCTCACGAGGATCCCGAGGTCAAATT CAACTGGTACGTTGATGGGGTTGAAGTTCATAATGCCAAAACGAAGCCAAGAGAAG AGCAGTATAACTCCACATATAGAGTTGTTTCCGTCTTGACTGTTCTTCACCAAGAT TGGCTGAATGGGAAGGAGTACAAATGTAAAGTTAGCAACAAGGCACTCGCCGCTCC CATTGAAAAAACTATAAGCAAAGCTAAGGGCCAACCGCGCGAACCACAGGTCTACA CGTTGCCGCCCTCTAGGGACGAACTCACGAAGAATCAGGTTTCCCTTACCTGCCTC GTTAAAGGATTCTACCCCTCTGACATAGCGGTTGAATGGGAGAGCAACGGTCAGCC TGAGAACAACCTACAAAACGACGCCCTCCGGTGTGGATTCCGACGGTAGTTTTTTTCC TCTATAGTAAGCTGACAGTGGATAAATCTCGGTGGCAGCAAGGGAATGTATTCTCC TGTTTCAGTCCTGCATGAAGCCCTCCACTCCCATTATACACAGAAATCTCTTTCTCT GAGTCCCGGTAAAGGTGGGAGTGACTCTTGGCAGGAAGAGGTAATTAAGTTGTGTG GAAGGGAGCTGGTAAGAGCACAGATTGCCATCTGTGGCAAATCCACGGGCGGCGAA GTTGAGGGGGGTGAGGGGGAAGGGGGGTCCAGACAACGTATTCTGCTCTGGCGAA TAAGTGTTGCCATGTAGGGTGCACTAAACGGTCCTTGGCGCAGTTCTGT
408	ATGGAGACTGACACACTGCTCCTCTGGGTCCCTTTGCTCTGGGTTCCGGGGTCCAC CGGTGATAAAACTCATACGTGCCACCTTGCCCCGACCGGAGGCTGCTGGAGGAC CCTCTGTCTTCTGTTCCTGTTCCCGCCGAAGCCTAAAGACACATTGATGATCAGTCGAACA CCGGAAGTCACCTGTGTAGTGGTTGATGTGAGCCATGAGGACCCTGAAGTAAATTT TAACTGGTATGTTGATGGCGTAGAAGTACACAACGCGAAGACTAAACCAAGGGAAG AGCAATACAACCTCTACCTATAGGGTCGTTAGCGTACTGACTGTGCTTCACCAAGAC TGGCTTAACGGGAAGGAGTACAAGTGCAAAGTGAGCAATAAGGCCCTCGCCGCGCC TATCGAGAAAACCATTTCCAAAGCCAAGGGTCAACCAAGGGAGCCTCAGGTTTACA CCCTGCCCCCTTCAAGGGATGAGTTGACAAAAAACAGGTAAGTCTGACGTGTCTC GTTAAGGGATTCTACCCGTGAGATATCGCGGTAGAGTGGGAGAGCAACGGTCAGCC AGAAAATAATTACAAAACAACACCTCCAGTTTTGGACTCTGATGGGAGTTTTTTTC TTTATTCTAAGTTGACAGTGGATAAGTCACGCTGGCAACAGGGGAACGTATTTAGC TGCTCAGTACTTCATGAAGCGTTGCATTCTCACTACACACAGAAGAGCCTCTCCTT GAGTCCCGGAGGTGGCTCTGATTCTTGGCAGGAGGAGGTAATAAACTTTGTGGTA GAGAACTGGTTCGCGCTCAGATAGCTATTTGTGGAAAATCCACTGGCGGTGAAGGT GAAGGTGGAGAAGGAGAGGGCGGAAGCCGGCAGTTGTACTCTGCCCTGGCTAATAA GTGCTGTCTACGTGGGCTGCACTAAGCGGAGCTTGGCAAGATTTTGC
409	ATGGAAACCGACACGCTGCTGCTGTGGGTGCTGTTGTTGTGGGTTCCAGGCTCAAC TGGCGATAAAACTCATACCTGTCCACCTTGTCCTGCGCCTGAGGCAGCTGGAGGGC CTAGCGTGTTCCCTGTTCCCCCCCCAAACCCAAAGACACGCTCATGATTAGCCGAACC CCTGAAGTGACCTGCGTTGTTGTGGACGTAAGCCACGAAGACCCCGAAGTTAAGTT TAATTGGTACGTCGACGGTGTTGAGGTTCATAACGCGAAGACTAAGCCGAGAGAGG AGCAATATAACAGCACCTACCGCTAGTCTCAGTCTTACCCTGCTCCACCAGGAC TGGCTTAACGGGAAGGAATACAAATGCAAAGTTTCCAACAAAGCCTTGGCAGCCCC AATAGAGAAGACAATATCTAAGGCGAAAAGGCCAACCGCGGGAACCGCAAGTTTATA CCCTCCCACCGAGCAGGGATGAGCTGACAAAAAATCAGGTTTCCCTCACTTGTCTG GTCAAGGGATTTTATCCTTCAGACATAGCCGTTGAATGGGAGAGTAATGGGCAGCC GGAGAATAATTACAAGACCACCCCCCGGTGTTGGACAGCGACGGTTCCTTCTTTTC TCTATTCTAACTTACCGTCGACAAATCACGGTGGCAACAAGGAAATGTATTCTCA TGCAGTGTATTGCACGAAGCTCTGCACTCTCATTACACCCAAAAATCCCTCTCTCT CAGCCCTGGCGGTGGATCTGATTCTTGGCAGGAAGAGGTGATTAACTGTGTGGGC GAGAGCTTGTCCGAGCTCAGATCGCTATTTGTGGCAAGAGTACCGGAGGCGAGGGT

SEQ ID NO:	Sequence
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500	ATGGAAACTGATACCTGTTGTTGTGGGTCCTTTTGCTTTGGGTTCCAGGCAGCAC CGGAGATAAAACCCATACGTGTCTCCATGCCCAGCTCCCGAGCTGCTCGGTGGTC CTTCAGTGTTCTCTTCCCCCAAAGCCGAAGGACACGCTCATGATTAGTCGAACG CCAGAGGTGACATGTGTGGTCGTTGATGTTTCCCATGAGGATCCGGAAGTTAAGTT CAACTGGTACGTAGATGGCGTGGAGGTTACAATGCAAAAACCAAGCCCCGCGAGG AGCAGTATAACTCAACCTACAGAGTAGTATCTGTGCTCACGGTCTTGCATCAGGAT TGGTTGAACGGGAAGGAATACAAGTGTAAGTAAGTAATAAGGCACTGCCGGCCCC CATAGAAAAAACTATCAGCAAAGCTAAAGGTGAGCCGCGGGAGCCACAAGTTTACA CTCTTCCTCCTAGTAGAGACGAGCTGACGAAGAATCAAGTTTCTTTGACTTGTCTC GTGAAGGGATTCTACCCAAGCGATATAGCTGTAGAGTGGGAAAGCAACGGACAACC AGAAAATAACTACAAGACTACACCCCCGTTCTCGATTCTGATGGCTCATTCTTCT TGTACTCAAAATTGACAGTTGACAAATCTCGATGGCAGCAGGGTAACGTATTTAGT TGCTCTGTTATGCACGAAGCGTTGCATAACCACTACACACAGAAGTCATTGTCAC GAGCCAGGAAAAGGTGGTGGCGGGTCCGGCGGTGGAGGTAGCGGTGGCGGGGGCT CCCAGCTTTATAGTGCCCTTGCAAAACAAATGTTGCCACGTCGGATGTACGAAGCGC AGTTTGGCGAGATTCTGTGGAGGGGGCGGATCCGGAGGCGGGGGTCCGGAGGAGG AGGTAGCTCATGGATGGAAGAGGTAATAAACTGTGCGGACGCGAGCTTGTGAGGG CCCAAATCGCAATTTGTGGCATGAGCACATGGAGT
540	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAAGGCGAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTAAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCTATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTCACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
541	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAAGGCGAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTTTG GTAAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC

SEQ ID NO:	Sequence
	TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCAAT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTCAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
542	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTAAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCAAT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTCAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
543	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTAAAGGGTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCAAT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGAGAAGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTCAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
544	ATGGAAACGGATACGCTGTTGTTGTGGGTTCTGCTCTTGTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT

SEQ ID NO:	Sequence
	TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTTC TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGATCTGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTACGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
545	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTTC TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGATCTGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTCAAGTTGGGTGTACCAAGCGGTCCCTTGCGCAATTCTGC
546	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGCGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTTC TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGATCTGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTACGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC
547	ATGGAAACGGATACGCTGTTGTTGTGGGTCTGCTCTTGTTGGGTGCCAGGGAGCAC AGGTGATAAAACCCACACTTGCCACCTTGCCCTGCGCCGGAAGCCGCCGGAGGAC

SEQ ID NO:	Sequence
	CTAGTGTTTTCTCTTTCCCCCTAAGCCCAAAGACACGTTGATGATCTCTCGGACA CCGGAAGTAACCTTGTGTCGTTGTGGATGTGTCACATGAGGATCCCGAGGTGAAATT TAATTGGTACGTTGACGGCGTGGAGGTGCATAACGCAAAGACTAAACCACGCGAGG AGCAGTATAATTCTACATACCGGGTTGTCTCAGTTCTCACAGTTCTTCATCAGGAT TGGTTGAATGGAAAGGAGTACAAATGCAAAGTGTCCAACAAAGCGCTTGCTGCGCC GATTGAAAAGACGATTTCAAAGGCAAAAGGGCAGCCCCGGAACCCCAAGTATATA CTTTGCCTCCCTCACGCGATGAACTGACTAAGAACCAGGTGAGCCTGACTTGTGTTG GTTAAGGGTTTTTATCCAAGTGACATTGCTGTTGAATGGGAGTCCAATGGCCAGCC TGAGAATAACTACAAAACGACACCTCCTGTACTTGACAGCGACGGCTCCTTTTTTCT TTTATTCAAACTCACAGTGGACAAATCCAGGTGGCAGCAGGGTAACGTCTTTTCT TGCAGCGTGCTCCACGAAGCTTTGCATTACATTATACGCAAAAATCCTTGTCATT GTCCCCAGGTAAGGGCGGAAGCGACTCATACCAAGAAGAAGTCATTAACTTTGTG GACGGGAGCTGGTTAGGGCACAGATTGCTATTTGTGGTAAGTCTACGGGAGGAGAA GGCTCTGGAGGCGAAGGATCTGGGGGCGGAAGGCAGCTTTACTCTGCTCTGGCTAA CAAGTGTTGTCAAGTTGGGTGTACCAAGCAATCCCTTGCGCAATTCTGC

- [0192] In some embodiments, any of the nucleotide sequences shown in Table 10 further comprise additional nucleotide sequence on their 5' and/or 3' ends. In some embodiments, any of the nucleotide sequences shown in Table 10 further comprise the nucleotide sequence
- 5 ACGGGACCGATCCAGCCTCCGGACTCTAGAGCCACC (SEQ ID NO: 494) on their 5' ends and/or any of the nucleotide sequences shown in Table 10 further comprise the nucleotide sequence TGATAAACCGGTTAGTAATGAGTTTGATATCTCGAC (SEQ ID NO: 495) on their 3' ends.
- [0193] A variety of host cells and expression vector systems can be utilized to express the
- 10 fusion proteins described herein. Such expression systems represent vehicles by which the coding sequences of interest can be produced and subsequently purified, but also represent cells which can, when transformed or transfected with the appropriate nucleotide coding sequences, express a fusion protein described herein *in situ*. These include but are not limited to microorganisms such as bacteria (*e.g.*, *E. coli* and *B. subtilis*) transformed with, *e.g.*,
- 15 recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing fusion protein coding sequences; yeast (*e.g.*, *Saccharomyces Pichia*) transformed with, *e.g.*, recombinant yeast expression vectors containing fusion protein coding sequences; insect cell systems infected with, *e.g.*, recombinant virus expression vectors (*e.g.*, baculovirus) containing fusion protein coding sequences; plant cell systems (*e.g.*, green algae such as *Chlamydomonas reinhardtii*) infected with, *e.g.*, recombinant virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with, *e.g.*, recombinant plasmid
- 20

- expression vectors (e.g., Ti plasmid) containing fusion protein coding sequences; or mammalian cell systems (e.g., COS (e.g., COS1 or COS), CHO, BHK, MDCK, HEK 293, NS0, PER.C6, VERO, CRL7030, HsS78Bst, HeLa, and NIH 3T3, HEK-293T, HepG2, SP210, R1.1, B-W, L-M, BSC1, BSC40, YB/20, and BMT10 cells) harboring, e.g.,
- 5 recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). In certain embodiments, cells for expressing the fusion proteins described herein are human cells, e.g., human cell lines. In certain embodiments, a mammalian expression vector is pOptiVEC™ or pcDNA3.3. In certain
- 10 embodiments, bacterial cells such as *Escherichia coli*, or eukaryotic cells (e.g., mammalian cells), are used for the expression of a fusion protein. For example, mammalian cells such as CHO or HEK293 cells, in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for fusion proteins disclosed herein.
- 15 **[0194]** In bacterial systems, a number of expression vectors can be advantageously selected depending upon the use intended for the fusion protein being expressed. For example, when a large quantity of a fusion protein is to be produced, vectors which direct the expression of high levels of fusion protein products that are readily purified can be desirable. Such vectors include, but are not limited to, the *E. coli* expression vector pUR278 (Ruether U & Mueller-
- 20 Hill B (1983) EMBO J 2:1791-1794), in which the fusion protein coding sequence can be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye S & Inouye M (1985) Nuc Acids Res 13:3101-3109; Van Heeke G & Schuster SM (1989) J Biol Chem 24:5503-5509); and the like, all of which are herein incorporated by reference in their entireties. For example, pGEX vectors can also be
- 25 used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.
- 30 **[0195]** In an insect system, *Autographa californica* nuclear polyhedrosis virus (AcNPV), for example, can be used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The fusion protein coding sequence can be cloned individually into non-

essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

[0196] In mammalian host cells, a number of viral-based expression systems can be utilized. In cases where an adenovirus is used as an expression vector, the fusion protein coding sequence of interest can be ligated to an adenovirus transcription/translation control complex, *e.g.*, the late promoter and tripartite leader sequence. This chimeric gene can then be inserted in the adenovirus genome by *in vitro* or *in vivo* recombination. Insertion in a non-essential region of the viral genome (*e.g.*, region EI or E3) will result in a recombinant virus that is viable and capable of expressing the fusion protein molecule in infected hosts (*see, e.g.*, Logan J & Shenk T (1984) PNAS 81(12):3655-9, which is herein incorporated by reference in its entirety). Specific initiation signals can also be required for efficient translation of inserted fusion protein coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression can be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, *etc.* (*see, e.g.*, Bitter G *et al.* (1987) Methods Enzymol. 153:516-544, which is herein incorporated by reference in its entirety).

[0197] In addition, a host cell strain can be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (*e.g.*, glycosylation) and processing (*e.g.*, cleavage) of protein products can be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product can be used. Such mammalian host cells include but are not limited to CHO, VERO, BHK, Hela, MDCK, HEK 293, NIH 3T3, W138, BT483, Hs578T, HTB2, BT20 and T47D, NS0 (a murine myeloma cell line that does not endogenously produce any immunoglobulin chains), CRL7030, COS (*e.g.*, COS1 or COS), PER.C6, VERO, HsS78Bst, HEK-293T, HepG2, SP210, R1.1, B-W, L-M, BSC1, BSC40, YB/20, BMT10, and HsS78Bst cells.

[0198] For long-term, high-yield production of recombinant proteins, stable expression cells can be generated. For example, cell lines which stably express a fusion protein described herein can be engineered.

[0199] In certain embodiments, rather than using expression vectors which contain viral origins of replication, host cells can be transformed with a polynucleotide (*e.g.*, DNA or RNA) controlled by appropriate transcriptional regulatory elements (*e.g.*, promoter, enhancer, sequences, transcription terminators, polyadenylation sites, *etc.*), and a selectable marker. Following the introduction of polynucleotide, engineered cells can be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method can advantageously be used to engineer cell lines which express a fusion protein described herein or a fragment thereof.

[0200] A number of selection systems can be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler M *et al.* (1977) Cell 11(1):223-32), hypoxanthineguanine phosphoribosyltransferase (Szybalska EH & Szybalski W (1962) PNAS 48(12):2026-2034) and adenine phosphoribosyltransferase (Lowy I *et al.* (1980) Cell 22(3):817-23) genes in tk-, hgp^{rt}- or ap^{rt}-cells, respectively, all of which are herein incorporated by reference in their entireties. Also, antimetabolite resistance can be used as the basis of selection for the following genes: *dhfr*, which confers resistance to methotrexate (Wigler M *et al.* (1980) PNAS 77(6):3567-70; O'Hare K *et al.* (1981) PNAS 78:1527-31); *gpt*, which confers resistance to mycophenolic acid (Mulligan RC & Berg P (1981) PNAS 78(4):2072-6); neo, which confers resistance to the aminoglycoside G-418 (Wu GY & Wu CH (1991) Biotherapy 3:87-95; Tolstoshev P (1993) Ann Rev Pharmacol Toxicol 32:573-596; Mulligan RC (1993) Science 260:926-932; Morgan RA & Anderson WF (1993) Ann Rev Biochem 62:191-217; Nabel GJ & Felgner PL (1993) Trends Biotechnol 11(5):211-5); and *hygro*, which confers resistance to hygromycin (Santerre RF *et al.* (1984) Gene 30(1-3):147-56), all of which are herein incorporated by reference in their entireties. Methods commonly known in the art of recombinant DNA technology can be routinely applied to select the desired recombinant clone and such methods are described, for example, in Ausubel FM *et al.* (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler M, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli NC *et al.* (eds.), Current Protocols in Human Genetics, John Wiley &

Sons, NY (1994); Colbère-Garapin F *et al.* (1981) J Mol Biol 150:1-14, all of which are herein incorporated by reference in their entireties.

Pharmaceutical Compositions

[0201] The present disclosure provides pharmaceutical compositions comprising the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them. The pharmaceutical compositions described herein are formulated with suitable carriers, excipients, and other agents that provide improved transfer, delivery, tolerance, and the like. A multitude of appropriate formulations can be found in the formulary known to all pharmaceutical chemists: *Remington's Pharmaceutical Sciences*, Mack Publishing Company, Easton, PA. These formulations include, for example, powders, pastes, ointments, jellies, waxes, oils, lipids, lipid (cationic or anionic) containing vesicles (such as LIPOFECTINTM, Life Technologies, Carlsbad, CA), DNA conjugates, anhydrous absorption pastes, oil-in-water and water-in-oil emulsions, emulsions carbowax (polyethylene glycols of various molecular weights), semi-solid gels, and semi-solid mixtures containing carbowax. *See also*, Powell *et al.*, "Compendium of excipients for parenteral formulations" PDA (1998) *J Pharm Sci Technol* 52:238-311.

[0202] The dose of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them administered to a patient may vary depending upon the age and the size of the patient, target disease, conditions, route of administration, and the like. The preferred dose is typically calculated according to body weight or body surface area. Depending on the severity of the condition, the frequency and the duration of the treatment can be adjusted. Effective dosages and schedules for administering the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them may be determined empirically; for example, patient progress can be monitored by periodic assessment, and the dose adjusted accordingly. Moreover, interspecies scaling of dosages can be performed using well-known methods in the art (*e.g.*, Mordenti *et al.*, 1991, *Pharmaceut. Res.* 8:1351).

[0203] Various delivery systems are known and can be used to administer the pharmaceutical composition disclosed herein, *e.g.*, encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the mutant viruses, receptor mediated endocytosis (*see, e.g.*, Wu *et al.*, 1987, *J. Biol. Chem.* 262:4429-4432). Methods of introduction include, but are not limited to, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The composition may be administered by any convenient

route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (*e.g.*, oral mucosa, rectal and intestinal mucosa, *etc.*) and may be administered together with other biologically active agents. Administration can be systemic or local.

5 [0204] Any pharmaceutical composition described herein can be delivered subcutaneously or intravenously with a standard needle and syringe. In addition, with respect to subcutaneous delivery, a pen delivery device readily has applications in delivering a pharmaceutical composition disclosed herein. Such a pen delivery device can be reusable or disposable. A reusable pen delivery device generally utilizes a replaceable cartridge that contains a
10 pharmaceutical composition. Once all of the pharmaceutical composition within the cartridge has been administered and the cartridge is empty, the empty cartridge can readily be discarded and replaced with a new cartridge that contains the pharmaceutical composition. The pen delivery device can then be reused. In a disposable pen delivery device, there is no replaceable cartridge. Rather, the disposable pen delivery device comes prefilled with the pharmaceutical
15 composition held in a reservoir within the device. Once the reservoir is emptied of the pharmaceutical composition, the entire device is discarded.

[0205] In certain situations, the pharmaceutical composition can be delivered in a controlled release system. In one embodiment, a pump may be used (*see*, Langer, *supra*; Sefton, 1987, *CRC Crit. Ref. Biomed. Eng.* 14:201). In another embodiment, polymeric materials can be
20 used; *see*, *Medical Applications of Controlled Release*, Langer and Wise (eds.), 1974, CRC Pres., Boca Raton, Florida. In yet another embodiment, a controlled release system can be placed in proximity of the composition's target, thus requiring only a fraction of the systemic dose (*see, e.g.*, Goodson, 1984, in *Medical Applications of Controlled Release, supra*, vol. 2, pp. 115-138). Other controlled release systems are discussed in the review by Langer, 1990,
25 *Science* 249:1527-1533.

[0206] The injectable preparations may include dosage forms for intravenous, subcutaneous, intracutaneous and intramuscular injections, drip infusions, *etc.* These injectable preparations may be prepared by methods publicly known. For example, the injectable preparations may be prepared, *e.g.*, by dissolving, suspending, or emulsifying any of the fusion proteins described
30 herein in a sterile aqueous medium or an oily medium conventionally used for injections. As the aqueous medium for injections, there are, for example, physiological saline, an isotonic solution containing glucose and other auxiliary agents, *etc.*, which may be used in combination with an appropriate solubilizing agent such as an alcohol (*e.g.*, ethanol), a polyalcohol (*e.g.*,

propylene glycol, polyethylene glycol), a nonionic surfactant [*e.g.*, polysorbate 80, HCO-50 (polyoxyethylene (50 mol) adduct of hydrogenated castor oil)], *etc.* As the oily medium, there are employed, *e.g.*, sesame oil, soybean oil, *etc.*, which may be used in combination with a solubilizing agent such as benzyl benzoate, benzyl alcohol, *etc.* The injection thus prepared is preferably filled in an appropriate ampoule.

[0207] Advantageously, the pharmaceutical compositions for oral or parenteral use described above are prepared into dosage forms in a unit dose suited to fit a dose of the active ingredients. Such dosage forms in a unit dose include, for example, tablets, pills, capsules, injections (ampoules), suppositories, *etc.* The amount of the aforesaid fusion protein contained is generally about 5 to about 500 mg per dosage form in a unit dose; especially in the form of injection, it is preferred that the aforesaid fusion protein is contained in about 5 to about 100 mg and in about 10 to about 250 mg for the other dosage forms.

Therapeutic uses

Monotherapy

[0208] The present disclosure provides methods of enhancing a relaxin-2-related activity in a primary cell, comprising contacting the primary cell with a fusion protein or component peptide described herein. In some embodiments, contacting the primary cell with the fusion protein or component peptide results in enhanced relaxin-2 activity in the cell, *e.g.*, as described above. In some embodiments, contacting the primary cell with the fusion protein or component peptide results in activation of the relaxin-2 receptor (RXFP1) on a cell surface. Activation of RXFP1 on the cell surface can lead to cellular responses, including but not limited to, the elevation of cAMP levels, vasodilation, the expression of angiogenic factors, including VEGF, the expression of MMPs, and collagen degradation. In some embodiments, the cell is selected from the group consisting of endothelial cells, vascular smooth muscle cells, other vascular cells, cardiomyocytes, other cardiac cells, and fibroblasts. In some embodiments, the primary cell is within a subject, as described below.

[0209] In certain embodiments, the present disclosure provides methods for activating RXFP1 on a cell surface, comprising administering an effective amount of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them to a subject in need thereof, thereby activating RXFP1 on the surface of the cell. Activation of RXFP1 on the cell surface can lead to cellular responses, including but not limited to, the elevation of cAMP levels, vasodilation, the expression of angiogenic factors, including VEGF, the expression of MMPs, and collagen degradation. In some embodiments,

the cell is selected from the group consisting of endothelial cells, vascular smooth muscle cells, other vascular cells, cardiomyocytes, other cardiac cells, and fibroblasts.

[0210] This disclosure also provides methods for treating various relaxin-2 associated diseases. As used herein, the term “relaxin-2-associated disease,” is a disease or disorder that is caused by, or associated with, relaxin-2 protein production or relaxin-2 protein activity. The term “relaxin-2-associated disease” includes a disease, disorder or condition that would benefit from an increase in relaxin-2 protein activity. As used herein, the term “relaxin-2-associated disorder” has the same meaning as “relaxin-2-associated disease.”

[0211] In certain embodiments, the relaxin-2-associated disease or disorder is selected from the group consisting of kidney diseases, fibrotic diseases, and cardiovascular diseases. In certain embodiments, the relaxin-2-associated disease or disorder is pulmonary hypertension.

[0212] There are five groups of pulmonary hypertension as defined by the World Health Organization (WHO). Group 1 is pulmonary arterial hypertension (PAH), the diagnosis of which requires right heart catheterization (RHC) to demonstrate a mean pulmonary arterial (PA) pressure (mPAP) ≥ 20 mm Hg at rest and a pulmonary vascular resistance (PVR) of ≥ 2 Wood units. Additional criteria to meet Group 1 PAH includes: a mean pulmonary capillary wedge pressure (PCWP) ≤ 15 mm Hg, chronic lung diseases (CLDs) and other causes of hypoxemia are mild or absent; venous thromboembolic disease and PA obstructions are absent; and certain miscellaneous disorders are absent, including systemic disorders (*e.g.*, sarcoidosis, chronic renal insufficiency), hematologic disorders (*e.g.*, myeloproliferative diseases and chronic hemolytic anemias), and metabolic disorders (*e.g.*, glycogen storage disease). Group 1 also includes PAH due to an unknown mechanism (idiopathic PAH) and heritable genetic defects (heritable PAH); PAH developed from drugs and toxins; PAH associated with systemic disorders such as connective tissue diseases, human immuno-deficiency virus (HIV) infection, congenital heart disease, and schistosomiasis; PAH with overt features of venous/capillary involvement; and persistent PH of the newborn.

[0213] Group 2 is PH due to left heart disease (PH-LHD), which may be diagnosed clinically when there is sufficient LHD on echocardiography (with or without other confirmatory testing) to explain PH. For patients in whom RHC is performed, an mPAP ≥ 20 mmHg, PCWP ≥ 15 mmHg, and a normal or reduced cardiac output is consistent with a hemodynamic diagnosis of LHD-PH. Important adjunct information is the presence of left atrial (LA) enlargement on an echocardiogram and a left heart catheterization (LHC) to confirm an elevated left ventricular end-diastolic pressure. Once PH-LHD is confirmed, patients should be allocated into one of

the following categories: PH-LHD due to heart failure with preserved or reduced ejection fraction (group 2.1), heart failure with reduced ejection fraction (group 2.2), valvular heart disease, or congenital or acquired conditions leading to postcapillary PH (group 2.3; *e.g.*, restrictive cardiomyopathy, constrictive pericarditis, LA myxoma, congenital or acquired inflow/outflow tract obstruction, and congenital cardiomyopathies). There are two subgroups of Group 2 PH that patients can be distinguished into: those who have combined pre- and postcapillary PH (CpcPH) and those who have isolated postcapillary hypertension (IpcPH).

[0214] Group 3 is PH due to chronic lung disease and/or hypoxemia, which is the diagnosis of PH due to CLD and/or hypoxemia made by demonstration of PH on RHC or echocardiogram and evidence of moderate to severe lung dysfunction and/or hypoxemia. Patients are allocated into PH due to obstructive lung disease (group 3.1), restrictive lung disease (group 3.2), mixed obstructive and restrictive lung disease (group 3.3), PH associated with hypoventilation (group 3.4) hypoxia without lung disease (group 3.5), or PH due to developmental disorders (group 3.6). In some cases, Group 3 PH may be due to COPD, interstitial lung disease, or obstructive sleep apnea.

[0215] Group 4 is PH due to pulmonary artery obstructions and includes mostly patients with chronic thromboembolic PH (CTEPH; group 4.1) as well as PH due to PA obstructions (group 4.2, *e.g.*, benign or malignant tumors, arteritis in the absence of CTD, congenital PA stenosis, parasites).

[0216] Group 5 is PH due to multifactorial mechanisms and include patients with PH who do not clearly fit into Group 1 through 4. Group 5 PH can be further classified into those that have: hematologic disorders such as chronic hemolytic anemia (*e.g.*, sickle cell disease, beta thalassemia, or spherocytosis) and myeloproliferative disorders; systemic or metabolic disorders including sarcoidosis, pulmonary Langerhans histiocytosis X, and neurofibromatosis; metabolic disorders including Gaucher disease and glycogen storage disease; chronic renal failure and PH associated with hemodialysis; pulmonary tumor thrombotic microangiopathy; and fibrosing mediastinitis.

[0217] In certain embodiments, the relaxin-2-associated disease or disorder is pulmonary hypertension, including, any of the WHO defined Group 1, Group 2, Group 3, Group 4, and Group 5 PH.

[0218] In certain embodiments, the relaxin-2-associated disease or disorder is pulmonary hypertension, including, but not limited to, pulmonary arterial hypertension (PAH), pulmonary hypertension due to left heart disease (PH-LHD), combined precapillary and postcapillary

pulmonary hypertension (CpcPH), and isolated postcapillary pulmonary hypertension (IpcPH). In certain embodiments, the relaxin-2-associated disease or disorder is pulmonary arterial hypertension (PAH). In certain embodiments, the relaxin-2-associated disease or disorder is pulmonary hypertension due to left heart disease (PH-LHD). In certain embodiments, the
5 relaxin-2-associated disease or disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH). In certain embodiments, the relaxin-2-associated disease or disorder is isolated postcapillary pulmonary hypertension (IpcPH).

[0219] In certain embodiments, the relaxin-2-associated disease or disorder is a Group 2 pulmonary hypertension. In certain embodiments, the relaxin-2-associated disease or disorder
10 is isolated postcapillary pulmonary hypertension (IpcPH). IpcPH includes characteristics such as right ventricular dysfunction; thickening and stiffening of left ventricle (LHD); and compromised kidney function. In certain embodiments, the relaxin-2-associated disease or disorder is selected from the group consisting of right ventricular dysfunction; thickening and stiffening of left ventricle (LHD); and compromised kidney function. In certain embodiments,
15 the relaxin-2-associated disease or disorder is combined pre- and postcapillary pulmonary hypertension (CpcPH). CpcPH includes characteristics such as pulmonary artery narrowing, thickening, stiffening, and/or fibrotic remodeling; right ventricular dysfunction; thickening and stiffening of left ventricle (LHD); and compromised kidney function. In certain embodiments, the relaxin-2-associated disease or disorder is selected from the group consisting of pulmonary
20 artery narrowing, thickening, stiffening, and/or fibrotic remodeling; right ventricular dysfunction; thickening and stiffening of left ventricle (LHD); and compromised kidney function.

[0220] In certain embodiments, the relaxin-2-associated disease or disorder is heart failure, including, but not limited to, heart failure with preserved ejection fraction (HFpEF), and heart
25 failure with reduced ejection fraction (HFrEF). In certain embodiments, the relaxin-2-associated disease or disorder is heart failure with preserved ejection fraction (HFpEF). In certain embodiments, the relaxin-2-associated disease or disorder is heart failure with reduced ejection fraction (HFrEF).

[0221] In certain embodiments, the relaxin-2-associated disease or disorder is heart disease,
30 including, but not limited to, valvular heart disease.

[0222] In certain embodiments, the relaxin-2-associated disease or disorder is Group 2 PH (CpcPH or IpcPH) with heart failure with preserved ejection fraction (HFpEF). In certain
embodiments, the relaxin-2-associated disease or disorder is CpcPH with HFpEF. In certain

embodiments, the relaxin-2-associated disease or disorder is IpcPH with HFpEF. In certain embodiments, the HFpEF is defined as signs and symptoms of New York Heart Association (NYHA) class II-III heart failure and LVEF $\geq 50\%$ and at least one of (i) Heart Failure Association-Pre-test assessment, Echocardiography and natriuretic peptide score, Functional testing in cases of uncertainty, Final etiology (HFA-PEFF) score ≥ 5 points; and/or (ii) HFA-PEFF score 2-4 points and abnormal diastolic stress testing or invasive hemodynamic measurements. In certain embodiments, the relaxin-2-associated disease or disorder is CpcPH with NYHA class II-III heart failure and LVEF $\geq 50\%$ and at least one of (i) HFA-PEFF score ≥ 5 points; and/or (ii) HFA-PEFF score 2-4 points and abnormal diastolic stress testing or invasive hemodynamic measurements. In certain embodiments, the relaxin-2-associated disease or disorder is IpcPH with NYHA class II-III heart failure and LVEF $\geq 50\%$ and at least one of (i) HFA-PEFF score ≥ 5 points; and/or (ii) HFA-PEFF score 2-4 points and abnormal diastolic stress testing or invasive hemodynamic measurements.

[0223] In certain embodiments, the relaxin-2-associated disease or disorder is Group 2 PH (CpcPH or IpcPH) with heart failure with mid-range ejection fraction (HFmrEF). In certain embodiments, the relaxin-2-associated disease or disorder is CpcPH with HFmrEF. In certain embodiments, the relaxin-2-associated disease or disorder is IpcPH with HFmrEF. In certain embodiments, HFmrEF is defined as signs and symptoms of New York Heart Association (NYHA) class II-III heart failure and LVEF 40% to 49%. In certain embodiments, the relaxin-2-associated disease or disorder is CpcPH with NYHA class II-III heart failure and LVEF 40% to 49%. In certain embodiments, the relaxin-2-associated disease or disorder is IpcPH with NYHA class II-III heart failure and LVEF 40% to 49%.

[0224] In certain embodiments, the relaxin-2-associated disease or disorder is Group 2 PH (CpcPH or IpcPH) with heart failure with reduced ejection fraction (HFrEF). In certain embodiments, the relaxin-2-associated disease or disorder is CpcPH with HFrEF. In certain embodiments, the relaxin-2-associated disease or disorder is IpcPH with HFrEF.

[0225] In certain embodiments, CpcPH is based on right heart catheterization (RHC) performed showing pulmonary vascular resistance (PVR) ≥ 3 Wood units, mPAP of > 20 mm Hg, PCWP > 15 mm Hg or PCWP > 12 mm Hg and ≤ 14 mm Hg with evidence on left atrial volume index (LAVI) on echocardiography of ≥ 34 mL/m². In certain embodiments, IpcPH is based on RHC performed showing PVR < 3 Wood units, mPAP of > 20 mm Hg, PCWP > 15 mm Hg or PCWP > 12 mm Hg and ≤ 14 mm Hg with evidence on left atrial volume index (LAVI) on echocardiography of ≥ 34 mL/m².

[0226] In certain embodiments, the relaxin-2-associated disease or disorder is a cardiovascular disease associated with pregnancy, including, but not limited to, preeclampsia, post-partum hypertension, post-partum cardiomyopathy, pregnancy induced heart failure, and maternal hypertension complicating the puerperium.

5 [0227] In certain embodiments, the relaxin-2-associated disease or disorder is kidney disease. In certain embodiments, the relaxin-2-associated disease or disorder is chronic kidney disease. In certain embodiments, the relaxin-2-associated disease or disorder is hypertensive kidney disease.

[0228] In certain embodiments, the relaxin-2-associated disease or disorder is joint disease. In
10 certain embodiments, the relaxin-2-associated disease or disorder is frozen shoulder (also known as adhesive capsulitis).

[0229] Administration of the compositions according to the methods described herein may result in a reduction of the severity, signs, symptoms, or markers of a relaxin-2-associated disease or disorder in a patient with a relaxin-2-associated disease or disorder. By “reduction”
15 in this context is meant a statistically significant decrease in such level. The reduction (absolute reduction or reduction of the difference between the elevated level in the subject and a normal level) can be, for example, at least about 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or to below the level of detection of the assay used.

[0230] In certain embodiments, administration of the compositions according to the methods
20 described herein results in pulmonary vasodilation in the patient. In certain embodiments, administration of the compositions according to the methods described herein results in an anti-inflammatory effect in the patient. In certain embodiments, administration of the compositions according to the methods described herein results in an anti-fibrotic effect in the patient. In certain embodiments, administration of the compositions according to the methods described
25 herein results in right ventricular remodeling in the patient. In certain embodiments, administration of the compositions according to the methods described herein results in peripheral vasodilation in the patient. In certain embodiments, administration of the compositions according to the methods described herein results in cardiac relaxation in the patient. In certain embodiments, administration of the compositions according to the methods described
30 described herein results in left ventricular remodeling in the patient. In certain embodiments, administration of the compositions according to the methods described herein results in improvement in kidney function in the patient.

[0231] In certain embodiments, administration of the compositions according to the methods described herein results in increased renal plasma flow. In certain embodiments, administration of the compositions according to the methods described herein results in increased renal plasma flow that persists after 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 1 month, after a single administration. In certain embodiments, the increase in the renal plasma flow in the subject is maintained by at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95% 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 1 month after a single administration. In certain embodiments, administration of the compositions according to the methods described herein results in increased renal plasma flow that persists after 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 1 month, after a single administration to a human. In certain embodiments, the increase in the renal plasma flow in the subject is maintained by at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, or at least about 95% 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 1 month after a single administration to a human.

Combination Therapies and Formulations

[0232] The present disclosure also provides compositions and therapeutic formulations comprising the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them in combination with one or more additional therapeutically active components (*i.e.*, therapeutic agents), and methods of treatment comprising administering such combinations to subjects in need thereof.

[0233] Exemplary additional therapeutic agents include any therapeutic agents that may be used for the treatment of any relaxin-2-related disorders described herein. Exemplary additional therapeutic agents that may be combined with or administered in combination with the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them include, but are not limited to any one or more of: angiotensin II receptor blockers, *e.g.*, azilsartan, candesartan, eprosartan, losartan; ACE inhibitors, *e.g.*, lisinopril, benazepril, captopril, enalapril, moexipril, perindopril, quinapril, trandolapril; calcium channel blockers, *e.g.*, amlodipine, amlodipine and benazepril, amlodipine and valsartan, sacubitril and valsartan, diltiazem, felodipine, isradipine, nicardipine, nimodipine, nisoldipine, verapamil; diuretics, *e.g.*, chlorthalidone, hydrochlorothiazide, metolazone, indapamide, torsemide, furosemide, bumetanide, amiloride,

triamterene, spironolactone, eplerenone; aldosterone antagonists, *e.g.*, spironolactone, eplerenone; digoxin, *e.g.*, lanoxin; beta blockers, *e.g.*, carvedilol, metoprolol, bisoprolol; activin signaling inhibitors, *e.g.*, sotatercept; sodium/glucose cotransporter 2 (SGLT2) inhibitors, *e.g.*, empagliflozin, dapagliflozin, bexagliflozin, canagliflozin, ertugliflozin, 5 ipragliflozin, luseogliflozin, remogliflozin etabonate, sergliflozin etabonate, sotagliflozin, tofogliflozin, henagliflozin, janagliflozin, mizagliflozin, velagliflozin proline hydrate, enavogliflozin; and glucagon-like peptide-1 (GLP-1) receptor agonists, *e.g.*, exenatide, liraglutide, albiglutide, dulaglutide, lixisenatide, semaglutide, and tirzepatide.

[0234] In some embodiments, the additional therapeutic agents that may be combined with or 10 administered in combination with the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them include, but are not limited to any one or more of: sotatercept, empagliflozin, dapagliflozin, sacubitril, valsartan, semaglutide, dulaglutide, and tirzepatide.

[0235] In some embodiments, the additional therapeutic agents are drugs effective in treating 15 fibrosis, including but not limited to, small molecule drugs and antibodies. Exemplary anti-fibrosis drugs include, but are not limited to, TGF- β inhibitors, *e.g.*, small molecules such as hydronidone, distiartide, or antibodies such as fresolimumab, PDGF or VEGF antagonist, *e.g.*, small molecules such as imatinib, nilotinib, or any drugs that target extracellular factors that are involved in the pathogenesis of fibrosis. The description of exemplary drugs for fibrosis 20 can be found, *e.g.*, Li *et al.*, “Drugs and Targets in Fibrosis, *Frontiers in Pharm.*” 8: Article 855 (2007), incorporated herein by reference.

[0236] The additional therapeutically active component(s) may be administered just prior to, concurrent with, or shortly after the administration of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them.

25 [0237] The present disclosure provides pharmaceutical compositions in which the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them is co-formulated with one or more of the additional therapeutically active component(s) as described elsewhere herein.

Administration Regimens

30 [0238] In some embodiments, multiple doses of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them may be administered to a subject over a defined time course. The methods according to this aspect of the disclosure comprise sequentially administering to a subject multiple doses of the fusion

proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them. As used herein, “sequentially administering” means that each dose of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them is administered to the subject at a different point in time, *e.g.*, on different days separated by a predetermined interval (*e.g.*, hours, days, weeks, or months). The present disclosure provides methods which comprise sequentially administering to the patient a single initial dose of a fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them, followed by one or more secondary doses of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them, and optionally followed by one or more tertiary doses of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them.

[0239] The terms “initial dose,” “secondary doses,” and “tertiary doses,” refer to the temporal sequence of administration of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them. Thus, the “initial dose” is the dose which is administered at the beginning of the treatment regimen (also referred to as the “baseline dose”); the “secondary doses” are the doses which are administered after the initial dose; and the “tertiary doses” are the doses which are administered after the secondary doses. The initial, secondary, and tertiary doses may all contain the same amount of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them, but generally may differ from one another in terms of frequency of administration. In certain embodiments, however, the amounts of fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them contained in the initial, secondary and/or tertiary doses varies from one another (*e.g.*, adjusted up or down as appropriate) during the course of treatment. In certain embodiments, two or more (*e.g.*, 2, 3, 4, or 5) doses are administered at the beginning of the treatment regimen as “loading doses” followed by subsequent doses that are administered on a less frequent basis (*e.g.*, “maintenance doses”).

[0240] In one exemplary embodiment, each secondary and/or tertiary dose is administered 1 to 26 (*e.g.*, 1, 1½, 2, 2½, 3, 3½, 4, 4½, 5, 5½, 6, 6½, 7, 7½, 8, 8½, 9, 9½, 10, 10½, 11, 11½, 12, 12½, 13, 13½, 14, 14½, 15, 15½, 16, 16½, 17, 17½, 18, 18½, 19, 19½, 20, 20½, 21, 21½, 22, 22½, 23, 23½, 24, 24½, 25, 25½, 26, 26½, or more) weeks after the immediately preceding dose. The phrase “the immediately preceding dose,” as used herein, means, in a sequence of

multiple administrations, the dose of fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them, which is administered to a patient prior to the administration of the very next dose in the sequence with no intervening doses.

5 [0241] In one embodiment, each secondary and/or tertiary dose is administered 4 weeks after the immediately preceding dose. In one embodiment, a dose of the fusion protein or component peptide described herein, or the nucleic acid molecules, or the expression vectors that encode them, is administered to a patient once every 4 weeks (Q4W).

[0242] The methods according to this aspect of the disclosure may comprise administering to
10 a patient any number of secondary and/or tertiary doses of fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them. For example, in certain embodiments, only a single secondary dose is administered to the patient. In other embodiments, two or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, or more) secondary doses are administered to the patient. Likewise, in certain embodiments, only a single tertiary
15 dose is administered to the patient. In other embodiments, two or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, or more) tertiary doses are administered to the patient.

[0243] In embodiments involving multiple secondary doses, each secondary dose may be administered at the same frequency as the other secondary doses. For example, each secondary dose may be administered to the patient 1 to 2 weeks after the immediately preceding dose.
20 Similarly, in embodiments involving multiple tertiary doses, each tertiary dose may be administered at the same frequency as the other tertiary doses. For example, each tertiary dose may be administered to the patient 2 to 4 weeks after the immediately preceding dose. Alternatively, the frequency at which the secondary and/or tertiary doses are administered to a patient can vary over the course of the treatment regimen. The frequency of administration
25 may also be adjusted during the course of treatment by a physician depending on the needs of the individual patient following clinical examination.

[0244] In one embodiment, one or more of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered to a subject as a weight-based dose. A “weight-based dose” (*e.g.*, a dose in
30 mg/kg) is a dose of the protein or peptides that will change depending on the subject’s weight.

[0245] In another embodiment, one or more of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them, is administered to a subject as a fixed dose. A “fixed dose” (*e.g.*, a dose in mg) means that one

dose of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them is used for all subjects regardless of any specific subject-related factors, such as weight. In one particular embodiment, a fixed dose of fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them is based on a predetermined weight or age.

[0246] In general, a suitable dose of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them can be in the range of about 0.001 to about 200.0 milligram per kilogram body weight of the recipient, generally in the range of about 1 to 50 mg per kilogram body weight. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered in the range of about 0.001 mg/kg to about 200 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered in the range of 0.001 mg/kg to 200 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered in the range of about 0.01 mg/kg to about 100 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered in the range of 0.01 mg/kg to 100 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered in the range of about 0.1 mg/kg to about 20 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered in the range of 0.1 mg/kg to 20 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered in the range of about 1 mg/kg to about 50 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered in the range of 1 mg/kg to 50 mg/kg. For example, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them can be administered at about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.5 mg/kg, about 1 mg/kg, about 1.5 mg/kg, about 2 mg/kg, about 3 mg/kg, about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 40 mg/kg, about 50 mg/kg per single dose.

In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them can be administered at 0.1 mg/kg, 0.2 mg/kg, 0.3 mg/kg, 0.5 mg/kg, 1 mg/kg, 1.5 mg/kg, 2 mg/kg, 3 mg/kg, 5 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, 30 mg/kg, 40 mg/kg, 50 mg/kg per single dose. Values and ranges intermediate to the recited values are also intended to be part of this disclosure.

[0247] In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 0.3 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 0.3 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 1 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 1 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 3 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 3 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 10 mg/kg. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 10 mg/kg.

[0248] In some embodiments, one or more of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them is administered as a fixed dose of between about 10 mg to about 2500 mg. In some embodiments, one or more of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them is administered as a fixed dose of between 10 mg to 2500 mg. In some embodiments, one or more of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them is administered as a fixed dose of between about 100 mg to about 1500 mg. In some embodiments, one or more of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them is administered as a fixed dose of between 100 mg to 1500 mg. In some embodiments, the fusion proteins or

component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of about 10 mg, about 15 mg, about 20 mg, 25 mg, about 30 mg, about 50 mg, about 75 mg, about 100 mg, about 125 mg, about 150 mg, about 175 mg, 200 mg, about 225 mg, about 250 mg, about 275 mg, about 300 mg, about 325
5 mg, about 350 mg, about 375 mg, about 400 mg, about 425 mg, about 450 mg, about 475 mg, about 500 mg, about 525 mg, about 550 mg, about 575 mg, about 600 mg, about 625 mg, about 650 mg, about 675 mg, about 700 mg, about 725 mg, about 750 mg, about 775 mg, about 800 mg, about 825 mg, about 850 mg, about 875 mg, about 900 mg, about 925 mg, about 950 mg, about 975 mg, about 1000 mg, about 1500 mg, about 2000 mg, or about 2500 mg. In some
10 embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 50 mg, 75 mg, 100 mg, 125 mg, 150 mg, 175 mg, 200 mg, 225 mg, 250 mg, 275 mg, 300 mg, 325 mg, 350 mg, 375 mg, 400 mg, 425 mg, 450 mg, 475 mg, 500 mg, 525 mg, 550 mg, 575 mg, 600 mg, 625 mg, 650 mg, 675 mg, 700 mg, 725 mg,
15 750 mg, 775 mg, 800 mg, 825 mg, 850 mg, 875 mg, 900 mg, 925 mg, 950 mg, 975 mg, 1000 mg, 1500 mg, 2000 mg, or 2500 mg. Values and ranges intermediate to the recited values are also intended to be part of this disclosure.

[0249] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a
20 fixed dose of about 150 mg. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of 150 mg. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of at least 150 mg. In some embodiments,
25 the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of about 300 mg. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of 300 mg. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of
30 about 600 mg. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of about 600 mg.

[0250] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered by intravenous administration. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered by subcutaneous administration.

[0251] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered by intravenous infusion. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered by intravenous infusion over a duration of 1 minute, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 minutes, 2 hours, 3 hours, 4 hours, or more. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered by intravenous infusion over 30 minutes. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered by intravenous infusion over 60 minutes. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered by intravenous infusion over 30 to 60 minutes.

[0252] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered intravenously at a dose of about 0.3 mg/kg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered intravenously at a dose of 0.3 mg/kg once every 4 weeks. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 0.3 mg/kg once every 4 weeks. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 0.3 mg/kg once every 4 weeks. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 1 mg/kg

once every 4 weeks. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 1 mg/kg once every 4 weeks. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 3 mg/kg once every 4 weeks. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 3 mg/kg once every 4 weeks. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 10 mg/kg once every 4 weeks. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 10 mg/kg once every 4 weeks.

[0253] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at a dose of about 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at a dose of 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at a dose of at least 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of about 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of at least 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of about 300 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of 300 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are

administered as a fixed dose of about 600 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of 600 mg once every 4 weeks.

- 5 [0254] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered subcutaneously at a dose of about 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered subcutaneously at a dose of 150 mg once
- 10 every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered subcutaneously at a dose of at least 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose
- 15 subcutaneously of about 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are
- 20 administered as a fixed dose subcutaneously of at least 150 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of about 300 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the
- 25 expression vectors that encode them are administered as a fixed dose subcutaneously of 300 mg once every 4 weeks. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of about 600 mg once every 4 weeks. In some
- 30 embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of 600 mg once every 4 weeks.

[0255] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered

intravenously at a dose of about 0.3 mg/kg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered intravenously at a dose of 0.3 mg/kg once every 1 month. In certain embodiments, the fusion proteins or component peptides described
5 herein or the nucleic acid molecules, or the expression vectors that encode them are administered at about 0.3 mg/kg once every 1 month. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 0.3 mg/kg once every 1 month. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic
10 acid molecules, or the expression vectors that encode them are administered at about 1 mg/kg once every 1 month. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 1 mg/kg once every 1 month. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors
15 that encode them are administered at about 3 mg/kg once every 1 month. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 3 mg/kg once every 1 month. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at
20 about 10 mg/kg once every 1 month. In certain embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at 10 mg/kg once every 1 month.

[0256] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at a
25 dose of about 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at a dose of 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered at a dose of at least 150
30 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of about 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the

expression vectors that encode them are administered as a fixed dose of 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of at least 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of about 300 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of 300 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of about 600 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose of 600 mg once every 1 month.

15 [0257] In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered subcutaneously at a dose of about 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered subcutaneously at a dose of 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered subcutaneously at a dose of at least 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of about 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of at least 150 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of about 300 mg once every 1 month. In some embodiments, the fusion

proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of 300 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of about 600 mg once every 1 month. In some embodiments, the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them are administered as a fixed dose subcutaneously of 600 mg once every 1 month.

10 Kits

[0258] Any of the compositions described herein may be comprised in a kit. In a non-limiting example, the kit comprises one or more of the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them.

[0259] The kit may further include reagents or instructions for using the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them in a subject. It may also include one or more buffers.

[0260] The components of the kits may be packaged either in aqueous media or in lyophilized form. The container means of the kits will generally include at least one vial, test tube, flask, bottle, syringe, or other container means, into which a component may be placed, and preferably, suitably aliquoted. Where there is more than one component in the kit (labeling reagent and label may be packaged together), the kit also will generally contain a second, third, or other additional container into which the additional components may be separately placed. The kits may also comprise a second container means for containing a sterile, pharmaceutically acceptable buffer and/or other diluent. However, various combinations of components may be comprised in a vial. The kits of the present disclosure also typically include a means for containing the fusion proteins or component peptides described herein or the nucleic acid molecules, or the expression vectors that encode them, and any other reagent containers in close confinement for commercial sale.

[0261] When the components of the kit are provided in one and/or more liquid solutions, the liquid solution is an aqueous solution, with a sterile aqueous solution being particularly preferred. However, the components of the kit may be provided as dried powder(s). When reagents and/or components are provided as a dry powder, the powder can be reconstituted by

the addition of a suitable solvent. It is envisioned that the solvent may also be provided in another container means.

EXAMPLES

[0262] The examples of the present disclosure are offered by way of illustration and explanation, and are not intended to limit the scope of the present disclosure. The results described in each Example are reflective of the particular conditions outlined in the experiments described therein.

Example 1. Heparin Chromatography for Relaxin-2 Fusion Protein Analogs

[0263] Heparin chromatography is a method that can be used at early candidate screening to better understand a molecule’s propensity to interact with elements of the vasculature when dosed in patients. Heparin and heparin sulfate proteoglycans are negatively charged polysaccharides present in vasculature and in tissues, of which positively charged molecules may bind at physiological pH (*i.e.*, pI > 7.4). Here, heparin chromatography was employed to screen for candidates/variants with reduced heparin binding, which is predictive of good PK properties. Materials used for the heparin chromatography are provided in Table 11.

Table 11. Materials

Item	Vendor	Cat No.
POROS™ Heparin 2.1x30mm Column	Thermo Fisher	4333411

Methods

- [0264] Mobile Phase A (Binding): 20mM Tris pH 7.4; Mobile Phase B (Elution): 20mM Tris pH 7.4 + 1M NaCl; Injection: 10µg; Detection: 220nm.
- Equilibrated heparin column using mobile phase A for 10 minutes at 0.5mL/min prior to analysis.
 - Diluted samples for analysis to 1 mg/mL with 20 mM Tris pH 7.4 to minimize ionic strength.
 - Ran the Heparin Chromatography method on the Agilent HPLC, using gradient shown in Table 12, below:

Table 12. HPLC Gradient

Time (min)	Flow (mL/min)	%A	%B
0	0.5	100	0
1	0.5	100	0
6	0.5	50	50
6.5	0.5	50	50
7	0.5	0	100
8	0.5	0	100
8.5	0.5	100	0
10	0.5	100	0

4. Included a positive control (no Heparin binding, Human IgG pool) and negative control (SE301 or AT1R).
5. Analyzed samples for retention time and reported relative retention time compared to the positive control (*i.e.*, RT sample/RT positive control).
6. Calculated the approximate concentration of NaCl needed to elute using the following calculation:

$[NaCl] = (RT\ sample - 1) * 100$

[0265] The results of the calculation are shown in Table 13.

Table 13. Retention Time, Relative Retention Time, and NaCl Concentration for Samples

Sample	RT	RRT	[NaCl]
Positive Control	1.5	N/A	50
Negative Control	3.5	2.3	250
Sample	2.0	1.3	100

Results

[0266] Table 14 shows the results of the heparin chromatography for a variety of relaxin-2 analog fusion proteins.

Table 14. Heparin Chromatography

		Heparin Chromatography	
Sample	Theoretical pI	RT	~[NaCl] (mM) at elution
IgG	N/A	2.0	20
Prior fusion protein	8.5 (9.4*)	4.6	278
SEQ ID NO: 300	8.2	3.9	208
SEQ ID NO: 302	7.9	3.3	152
SEQ ID NO: 303	7.9	3.4	163
SEQ ID NO: 305	7.6	2.7	91
SEQ ID NO: 306	7.6	2.8	99
SEQ ID NO: 308	7.2	2.4	62
SEQ ID NO: 309	7.2	2.5	70
SEQ ID NO: 310	6.8	2.2	39
SEQ ID NO: 311	6.8	2.2	43
SEQ ID NO: 359	8.4	3.6	183
SEQ ID NO: 360	8.3	3.2	140

*Experimentally determined using imaged capillary isoelectric focusing.

[0267] IgG is from Jackson ImmunoResearch (Catalog # 009-000-003). The “Prior fusion protein” is a LALA IgG-RelB-Linker-RelA fusion with a theoretical pI of 8.5, but an experimentally determined pI of 9.4. Its linker protein comprises only one acidic amino acid. SEQ ID NOs: 300, 302, 303, 305, 306, and 308-311 have linker proteins comprising at least two acidic amino acids as well as LALA IgG (SEQ ID NO: 77 or 81). The final two fusion proteins have linker proteins comprising only one acidic amino acid and have higher theoretical pI’s. As shown in Table 14, above, there is a correlation between lower pI and lower non-specific binding found through heparin chromatography.

Example 2. Low pI Relaxin-2 Fusion Protein Analogs Tend to Have Decreased Self Association as Measured by Affinity-Capture Self-Interaction Nanoparticle Spectroscopy (AC-SINS)

[0268] Understanding a molecule’s propensity to self-associate is critical when evaluating biophysical properties of a development candidate. There are numerous ways to evaluate a molecule’s propensity to self-associate, concentrating the molecule to high concentrations and evaluating by SEC (%Monomer) or measuring changes in turbidity (OD 340nm), using DLS to calculate the second virial coefficient (B_{22}) or self-interaction coefficient (k_d), or using AC-SINS ($\Delta\lambda_{\text{max}}$). All three of these methods provide useful information but use different amounts of material to perform the evaluation. AC-SINS has emerged as a high throughput method for evaluating self-association using minimal material but still giving locally high concentrations by using affinity capture on gold nanoparticles. In short, gold nanoparticles are pre-coated

- with anti-human antibodies (Fc, Fab and H+L), which when incubated with target antibodies in dilute solutions, capture and concentrate in solution the antibody of interest. When the immobilized molecules of interest interact, the inter-particle distances decrease between gold nanoparticles, leading to increased plasmon wavelengths (*i.e.*, red shift) that can be quantified using UV-VIS spectroscopy. Materials used for the spectroscopy are provided in Table 15.

Table 15. Materials

Item	Vendor	Cat No.
1M sodium acetate pH 4.3	Molecular Dimensions	MD2-019-PH
1x DPBS	Gibco	14190-136
Panitumumab (Low Assoc Ctrl)	MyBioSource	MBS156169
Ipilimumab (Med Assoc Ctrl)	MyBioSource	MBS156153
Ganitumab (High Assoc Ctrl)	MyBioSource	MBS156142
20 nm gold nanoparticles	Ted Pella	15705
PEG methyl ether thiol (2kDa)	Sigma	729140
Goat anti-Human IgG, Fc γ	Jackson ImmunoResearch	109-005-098
Goat non-specific mAb	Jackson ImmunoResearch	005-000-003
Zeba Desalting Columns 40K 5 mL	Thermo Fisher	87770
Zeba Desalting Columns 40K 2 mL	Thermo Fisher	87768
Zeba Desalting Columns 40K 0.5 mL	Thermo Fisher	87766
Costar 384-well Polystyrene plates	Fisher Scientific	12-565-506
96-well Polypropylene plates	Grenier Bio-One	652230P

Methods

- 10 **[0269] Preparing Buffer Solutions:** To prepare 20mM sodium acetate pH 4.3, 2mL 1M sodium acetate pH 4.3 stock was diluted to 100mL with MilliQ water. pH was measured 4.3 ± 0.1 and the solution was sterile filtered. The solution remained stable at room temperature for 1 month. To 1g PEG methyl ether thiol, was added 10mL MilliQ water. This was vortexed briefly to suspend solids, making a 50 mM solution. To prepare a 10 μ M solution for final dilution, the
- 15 dilution scheme below was followed:
- Dilute 50mM stock to 1mM (20 μ L 50mM stock + 980 μ L MilliQ water)
 - Dilute 1mM step to 100 μ M (10 μ L 1mM stock + 90 μ L MilliQ water)
 - Dilute 100 μ M step to 10 μ M (100 μ L 100 μ M stock + 900 μ L MilliQ water)
 - Volumes can be scaled according to number of samples to assay
- 20 e. Remaining 50mM stock should be aliquoted and kept at -20°C until needed
- [0270] Preparing Gold NanoParticle Solution:** Goat anti-human Fc IgG antibody (capture) and goat IgG antibody (non-capture) were buffer exchanged into 20 mM sodium acetate, pH 4.3.

After buffer exchange, concentrations were normalized to 0.4 mg/mL for both antibodies. A 4:1 volume ratio mixture of capture (anti-Fc):non-capture (Goat IgG) solution was prepared for 80% capture capacity coating solution to be used to incubate gold nanoparticles (AuNPs). [0271] A 9:1 volume ratio of AuNPs:coating solution was made. The solution was incubated at room temperature, overnight in the dark. After incubation, thiolated PEG was added to 0.1 μM final concentration from the diluted 10 μM stock to block empty sites on the AuNPs (*i.e.*, 5mL solution of AuNPs, add 50μL 10μM stock) and incubated at RT for one hour in the dark. [0272] Preparing AuNP Solution: 2mL of coated AuNP solution was centrifuged at 20,000 x g for 15 minutes to sediment the AuNPs and 1800μL supernatant was carefully removed using a 1mL pipette. The pelleted AuNPs were gently resuspended using a 200μL pipette to generate a 10x concentrated stock of coated AuNPs. [0273] Preparing Target Antibody Solution (either method follows this): For each sample analyzed, 10μL of AuNP concentrate was incubated with 100μL antibody test solution (normalize to 0.05 mg/mL) at room temperature in the dark for 2 hours in a 96-well polypropylene plate. Two blank solutions were prepared with 10μL 10x AuNP concentrated to 100μL PBS for purposes of blanking the assay and determining wavelength shift upon addition of test antibody. Ganitumab was included as a positive control (high association, red shift) and Panitumumab as a negative control (no association, no UV shift). Each sample was prepared in duplicate for analysis. After the 2-hour incubation, 100μL of resulting solution was transferred to a UV transparent polystyrene plate (384-well format). Two blank solutions were transferred to properly assess wavelength shift, then add duplicate standards and samples for analysis. The plate was then centrifuged for 1 minute at 1000 x g to level the solutions in the wells. Absorbance data were collected from 510 to 570 nm in 2 nm steps to determine wavelength shifts for each sample relative to AuNPs alone.

Results

[0274] The results from ASCINS are shown below in Table 16.

Table 16. pI Variants Have Decreased Self- Association Propensity

Sample	Isoelectric Point (Calculated)	$\Delta\lambda_{\text{max}}$
Prior fusion protein (Control)	8.5	15.2
Prior fusion protein (LALA)	8.5	15.9
SEQ ID NO: 300	8.2	7.5
SEQ ID NO: 301	7.9	1.2
SEQ ID NO: 302	7.9	7.0

Sample	Isoelectric Point (Calculated)	$\Delta\lambda_{\max}$
SEQ ID NO: 303	7.9	6.7
SEQ ID NO: 305	7.6	1.8
SEQ ID NO: 306	7.6	1.9
SEQ ID NO: 308	7.2	-0.6
SEQ ID NO: 309	7.2	-0.4
SEQ ID NO: 310	6.8	0.4
SEQ ID NO: 311	6.8	0.4
SEQ ID NO: 359	8.4	10.1
SEQ ID NO: 360	8.3	6.1

[0275] As shown in Table 16, above, fusion proteins with low pI also have a tendency to show low self-aggregation.

Example 3. Relaxin-2 Fusion Protein Analogs Induce cAMP Response in RXFP1

5 Transfected Cells

[0276] This Example provides data relating to the potency of various relaxin-2 fusion protein analogs described herein. Potency of the fusion protein analogs were assayed by testing their ability to activate RXFP1 by measuring cAMP signaling.

Methods

- 10 [0277] HEK293 cells were seeded into a 96-well tissue culture plate followed by transient co-transfection with a human RXFP1 and a pGloSensor-22F plasmid. Transfected cells were stimulated by relaxin-2 or fusion protein analogs thereof, inducing Gs-mediated cAMP signaling. cAMP is assayed using the activity of the GloSensor biosensor, which is a mutant luciferase fused to a cAMP binding domain, leading to a production of light in the presence of
- 15 its substrate luciferin. This readout of relative luminescent units (RLU) is used a proxy for cAMP response.

Reagents

- 96-well tissue-culture treated plates. White with clear bottom. (Corning #3610)
- HEK293 cells (ATCC CRL-1573)
- 20 ▪ Poly-D-lysine (Gibco A3890401)
- DPBS (No calcium, no magnesium; Gibco 14190250)
- DMEM (High glucose with L-glutamine and Sodium Pyruvate; Gibco 11995065)
- TrypLE Express (Gibco 12605010)
- FBS (HyClone™, Australian origin; Cytiva SH30084)
- 25 ▪ Penicillin-Streptomycin (Gibco 15140122)
- CO₂-independent media (Gibco 18045088)

- Opti-MEM™ I Reduced Serum media (Gibco 31985062)
- pGloSensor™-22F cAMP plasmid (Promega Cat. #E2301)
- D-luciferin, Potassium Salt (GoldBio LUCK-1G)
- FuGENE HD transfection reagent (Promega #E2311)
- 5 ▪ Reservoirs (Corning/Axygen RES-V-25-SI)
- Relaxin-2 (R&D Biosystems 6586-RN-025)
- RXFP1-containing plasmid (pcDNA5/FRT/TO-human RXFP1, full-length)
- Forskolin (Sigma F6886)
- Plate reader capable of reading luminescence (CLARIOstar Plus)

10 *Reagent preparation*

[0278] D-luciferin, Potassium Salt: D-luciferin was reconstituted in 10 mM HEPES, pH 7.5 at 25 mg/mL (78.5 mM; MW = 318.4). This was aliquoted into single-use aliquots of ~200-500 µL in sterile microfuge tubes and stored at -80°C.

[0279] Relaxin-2 peptide: Relaxin-2 peptides or relaxin-2 fusion protein analogs were
15 reconstituted at 0.1 mg/mL in sterile DPBS (MW = 5,986 Da, $\epsilon = 12,865 \text{ M}^{-1}\text{cm}^{-1}$) and measured at A_{280} to determine final concentration. Aliquots were stored at -20°C.

[0280] Forskolin: Forskolin was reconstituted in 100% DMSO at 5 mM (2.05 mg/mL, MW = 410.5). Aliquots were stored at -20°C.

[0281] cAMP assay media: CO₂-independent media was pre-warmed to 37°C using the bead
20 bath. A single aliquot of D-luciferin was thawed and added at 5% final concentration (e.g., 4.75 mL cAMP assay media + 250 µL of D-luciferin stock; gives 1.25 mg/mL or 3.93 mM final D-luciferin). This was used within the same day or discarded.

Cell Culture and Maintenance

[0282] HEK293 cells (ATCC CRL-1573) were cultured in DMEM + 10% FBS, 1% (1X or 10
25 U/mL) Pen-Strep in a humidified CO₂ incubator at 37°C, 5% CO₂ until 80-100% confluency. Cells were typically split 1:6 for 3 days and maintained in a sterile T-75 tissue culture flask.

cAMP Signaling Assay Protocol

[0283] This protocol was adapted from the GloSensor cAMP assay by Promega.

[0284] Raw data was exported to Excel using the MARS data analysis software that is opened
30 following a run on the CLARIOstar plate reader. These values are measured in RLU, or relative luminescence units.

[0285] As shown in Table 17, all of the low pI relaxin-2 fusion protein analogs were able to induce a cAMP response in RXFP1 transfected cells.

Table 17. cAMP Response in RXFP1 Transfected HEK293 Cells

Agonist	pEC ₅₀	EC ₅₀ in nM
Relaxin	10.38	0.042
Prior fusion protein (Control)	9.51	0.31
Prior fusion protein (LALA)	9.49	0.33
SEQ ID NO: 300	8.66	2.17
SEQ ID NO: 301	8.10	7.87
SEQ ID NO: 302	8.62	2.41
SEQ ID NO: 303	8.72	1.90
SEQ ID NO: 305	7.83	14.7
SEQ ID NO: 306	7.75	17.7
SEQ ID NO: 308	7.25	56.7
SEQ ID NO: 309	7.18	65.8
SEQ ID NO: 310	6.76	173.3
SEQ ID NO: 311	7.02	96.2
SEQ ID NO: 359	9.37	0.42
SEQ ID NO: 360	8.84	1.46

Example 4. *In vitro* Characteristics of Relaxin-2 Fusion Protein Analogs

- 5 [0286] This Example provides *in vitro* characteristics of various relaxin-2 fusion protein analogs described herein.

Methods

- [0287] Heparin chromatography: heparin chromatography was performed to understand the propensity of a relaxin-2 fusion protein analog to interact with elements of the vasculature and/or rapidly distribute into tissues when dosed in patients. Analogs that were found to bind heparin weakly may be predictive of good pharmacokinetic properties. Briefly, a heparin column was equilibrated using mobile phase A (20 mM Tris pH 7.4) for 10 minutes at 0.5 mL/min prior to analysis. 10 µg per sample was run using the Heparin Chromatography method on an Agilent HPLC using 280 nm detection, using gradient shown in Table 18, below
- 15 (mobile phase B: 20 mM Tris pH 7.4, 1 M NaCl).

Table 18. HPLC Gradient

Time (min)	Flow (mL/min)	%A	%B
0	0.5	100	0
6	0.5	50	50
7	0.5	0	100
8	0.5	0	100
8.5	0.5	100	0
10	0.5	100	0

[0288] A positive control (no Heparin binding, pembrolizumab) and negative control (mild Heparin binding, adalimumab) was included, and samples were analyzed for retention time and relative retention time compared to the positive control (*i.e.*, RT sample/RT positive control). The approximate concentration of NaCl needed to elute was calculated using the following calculation:

5 $[NaCl] = (RT\ sample) * 100$

The results of the calculation are shown in Table 19.

Table 19. Retention Time and NaCl Concentration for Samples

Sample	RT	[NaCl]
Positive Control	1.5	150
Negative Control	3.5	350
Sample	2.0	200

10 [0289] Hydrophobic Interaction Chromatography (HIC): HIC is a chromatography method that separates molecules based on their hydrophobicity. To a butyl HIC column pre-equilibrated with high ammonium sulfate buffer, 10µg of protein was injected. The protein was eluted with a gradient from high salt concentration to low salt concentration over ten

15 minutes. Samples were compared for hydrophobicity based on retention time, with high retention time indicative of high hydrophobicity and low retention time indicative of low hydrophobicity. Retention times were converted to approximate salt concentration at elution and compared against high and low hydrophobicity standards.

[0290] Size exclusion chromatography (SEC): SEC is a liquid chromatography method used

20 to determine levels of monomeric and multimeric species in solution for a given analyte. SEC was used to assess the presence of fusion protein aggregates. Samples were prepared and added to a 1.7µm particle SEC column with an aqueous mobile phase comprised of 25mM potassium phosphate and 0.5M potassium chloride pH 8.0. Once elution of sample was verified, the method was capable of quantifying levels of soluble aggregate species in the sample, with high

25 resolution between peaks of monomer and high molecular weight (HMW) species. Percentage of monomer (*i.e.*, %monomer) and other species (*e.g.*, HMW species, low molecular weight species) was calculated by integrating the corresponding elution curve to determine the percent area.

[0291] Capillary isoelectric focusing (cIEF): Imaged cIEF was used to separate differentially

30 charged molecules (*i.e.*, relaxin-2 fusion protein analogs) using electrophoretic mobility in an

ampholyte solution to determine their isoelectric points (pI). Molecules were loaded to a capillary and separated based on their pI by allowing molecules to migrate along an electrical field until the molecules reached the pH corresponding to their pI. UV absorption of the whole capillary was measured throughout the separation, which allowed for real-time observation as well as final quantification.

5 [0292] Baculovirus Particle (BVP) ELISA: BVP ELISA was employed to understand the propensity of a relaxin-2 fusion protein analog for non-specific or non-target interactions. BVPs are empty viral capsids with no viral genome, but in the process of production, budding off from the cell membrane allows them to take components of the cell membrane along with them. Thus, the BVPs possess a highly diverse cell surface with many moieties present, which
10 mimic what the molecule of interest (*i.e.*, relaxin-2 fusion protein analog) may encounter *in vivo*. Briefly, BVPs are coated on a plate by adding 25 μ L of BVP solution to each well. BVP solution was made by diluting BVP stock (Medna Scientific; Cat. No. E3001) to 1×10^6 PFU/mL with 0.1 M carbonate buffer, pH 9.6. Following overnight incubation at 5°C, BVP
15 solution was blotted from wells and wells were washed three times with PBST. Plates were blocked with 100 μ L/well of 1x BSA in PBS blocking buffer (Cepham Life Sciences; Cat. No. 10615). Plates were incubated at 25°C on a plate shaker for 1 hour. Blocking solution was blotted from wells and wells were washed three times with PBST. Samples (*i.e.*, relaxin-2 fusion protein analogs) were prepared in duplicate to cover dilution range from 3 μ M to 0.1
20 nM and added to plates. Plates were incubated at 25°C for 1 hour, after which the wells were blotted and washed three times with PBST. 25 μ L/well of 1:10,000 diluted detection monoclonal antibody (Peroxidase AffiniPure Goat Anti-Human IgG, Fc γ fragment specific; Jackson ImmunoResearch; Cat. No. 50-194-1564) was added, and plates were incubated at 25°C for 1 hour, after which the wells were blotted and washed three times with PBST. 1-
25 Step™ Ultra TMB-ELISA Substrate Solution (Life Technologies; Cat. No. 34029) was then added. After about 2 minutes, 25 μ L 2N HCl was added to quench the reaction, and a plate reader was used to analyze the plate at 450 nm with correction at 570 nm.

[0293] Potency assay: HEK293 cells were seeded into a 96-well tissue culture plate followed by transient co-transfection with a human RXFP1 and a pGloSensor-22F plasmid. Transfected
30 cells were stimulated by relaxin-2 or fusion protein analogs thereof, inducing Gs-mediated cAMP signaling. cAMP is assayed using the activity of the GloSensor biosensor, which is a mutant luciferase fused to a cAMP binding domain, leading to a production of light in the

presence of its substrate luciferin. This readout of relative luminescent units (RLU) is used as a proxy for cAMP response.

[0294] cAMP Signaling Assay Protocol: this protocol is adapted from the GloSensor cAMP assay by Promega. Raw data was exported to Excel using the MARS data analysis software that is opened following a run on the CLARIOstar plate reader. These values are measured in RLU, or relative luminescence units.

[0295] Affinity-Capture Self-Interaction Nanoparticle Spectroscopy (AC-SINS): AC-SINS was performed to understand the propensity of a molecule (*i.e.*, relaxin-2 fusion protein analog) to self-associate. Briefly, gold nanoparticles were pre-coated with anti-human antibodies (Fc, Fab and H+L), which when incubated with target antibodies in dilute solutions, capture and concentrate in solution the antibody of interest. When the immobilized molecules of interest interact, the inter-particle distances decrease between gold nanoparticles, leading to increased plasmon wavelengths (*i.e.*, red shift) that can be quantified using UV-VIS spectroscopy. Materials used for the spectroscopy are provided in Table 20.

Table 20. Materials for AC-SINS

Item	Vendor	Cat No.
1M sodium acetate pH 4.3	Molecular Dimensions	MD2-019-PH
1x DPBS	Gibco	14190-136
Panitumumab (Low Assoc Ctrl)	MyBioSource	MBS156169
Ipilimumab (Med Assoc Ctrl)	MyBioSource	MBS156153
Ganitumab (High Assoc Ctrl)	MyBioSource	MBS156142
20 nm gold nanoparticles	Ted Pella	15705
PEG methyl ether thiol (2kDa)	Sigma	729140
Goat anti-Human IgG, Fcγ	Jackson ImmunoResearch	109-005-098
Goat non-specific mAb	Jackson ImmunoResearch	005-000-003
Zeba Desalting Columns 40K 5 mL	Thermo Fisher	87770
Zeba Desalting Columns 40K 2 mL	Thermo Fisher	87768
Zeba Desalting Columns 40K 0.5 mL	Thermo Fisher	87766
Costar 384-well Polystyrene plates	Fisher Scientific	12-565-506
96-well Polypropylene plates	Grenier Bio-One	652230P

[0296] Goat anti-human Fc IgG antibody (capture) and goat IgG antibody (non-capture) were buffer exchanged into 20 mM sodium acetate, pH 4.3. After buffer exchange, concentrations were normalized to 0.4 mg/mL for both antibodies. A 4:1 volume ratio mixture of capture (anti-Fc):non-capture (Goat IgG) solution was prepared for 80% capture capacity coating solution to be used to incubate gold nanoparticles (AuNPs). A 9:1 volume ratio of AuNPs:coating solution was made. The solution was incubated at room temperature, overnight

in the dark. After incubation, thiolated PEG was added to 0.1 μ M final concentration from the diluted 10 μ M stock to block empty sites on the AuNPs (*i.e.*, 5mL solution of AuNPs, add 50 μ L 10 μ M stock) and incubated at RT for one hour in the dark.

[0297] 2mL of coated AuNP solution was centrifuged at 20,000 x g for 15 minutes to sediment the AuNPs and 1800 μ L supernatant was carefully removed using a 1mL pipette. The pelleted AuNPs were gently resuspended using a 200 μ L pipette to generate a 10x concentrated stock of coated AuNPs. For each sample analyzed, 5 μ L of AuNP concentrate was incubated with 45 μ L antibody test solution (normalized to 0.05 mg/mL) at room temperature in the dark for 2 hours in a 384-well polypropylene plate. After the 2-hour incubation, absorbance data was collected from 450 nm to 650 nm in 1 nm steps to determine wavelength shifts for each sample relative to AuNPs alone.

[0298] Nanoscale Differential Scanning Fluorimetry (NanoDSF): NanoDSF was performed using the NanoTemper Prometheus Panta to investigate the conformational stability of a relaxin-2 protein fusion analog. Conformational stability was measured by applying a thermal ramp to a solution containing the molecule of interest, measuring the intrinsic fluorescence, backscattering, and using dynamic light scattering (DLS) to provide various thermal stability parameters, including the temperature at which fusion protein unfolding begins (T_{onset}), the temperature at which half of the fusion protein in a given sample is unfolded (T_{m1}), and the temperature at which fusion protein aggregation begins (T_{agg}).

[0299] Sequences: Sequences of relaxin-2 fusion protein analogs are described throughout the present disclosure. SEQ ID NOs: 496, 497, and 501 are set forth below:

DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW
YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEK
TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGKG
GSDSWKEEVIKLCGRELVRQAIAICGKSTASDAAGANANAGARQLYSALANKCCHVG
CTKRSLARFC (SEQ ID NO: 496);

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW
YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK
TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKG
GGGSGGGSGGGGSQLYSALANKCCHVGCTKRSLARFCGGGGSGGGSGGGSSWME
EVIKLCGRELVRQAIAICGMSTWS (SEQ ID NO: 497); and

MPRLFFFHLLGVCLLLNQFSRAVADSWMEEVIKLCGRELVRAQIAICGMSTWSKRSL
SQEDAPQTPRPVAEIVPSFINKDTETINMMSEFVANLPQELKLTLSMQPALPQLQQ
HVPVLKDSSLLFEEFKKLIRNRQSEAADSSPSELKYLGLDTHSRKKRQLYSALANKC
CHVGCTKRSLARFC (SEQ ID NO: 501).

5

Results

[0300] The results are shown below in Tables 21, 22, and 23.

Table 21. *In vitro* Characteristics of Relaxin-2 Fusion Protein Analogs.

Sample	Heparin Binding		cIEF	BVP ELISA	Potency ³	AC-SINS	NanoDSF	
	RT ¹	[NaCl] (mM) ²	Isoelectric Point (pI)	Normalized Score	(nM)	Δλ _{max}	T _{onset} (°C)	T _{m1} (°C)
Wild-type human relaxin-2	ND	ND	9.4	N/A	0.1	N/A	N/A	N/A
SEQ ID NO: 497	ND	ND	9.0	28	0.3	7	61.4	68.9
SEQ ID NO: 496	4.75	400	9.1	34	0.2	14	59.7	68.4
SEQ ID NO: 361	3.88	330	8.9	2	2.5	8	60.5	70.4
SEQ ID NO: 362	NT	NT	ND	ND	12.3	1	63.3	70.7
SEQ ID NO: 363	3.32	280	8.5	1	2.9	7	62.8	70.6
SEQ ID NO: 304	3.43	290	8.5	1	2.5	7	61.6	70.6
SEQ ID NO: 364	2.71	230	7.9	1	16.0	2	62.9	70.9
SEQ ID NO: 307	2.79	240	7.9	1	15.8	2	63.0	71.0
SEQ ID NO: 365	2.42	210	7.5	1	60.3	0	63.9	71.1
SEQ ID NO: 366	2.5	210	7.1	1	62.8	0	63.6	71.2
SEQ ID NO: 367	2.19	190	7.1	1	140.0	0	62.4	71.0
SEQ ID NO: 368	2.23	190	ND	1	101.2	0	62.8	70.8
SEQ ID NO: 369	3.63	310	ND	1	0.5	10	62.9	70.8

Sample	Heparin Binding		cIEF	BVP ELISA	Potency ³	AC-SINS	NanoDSF	
	RT ¹	[NaCl] (mM) ²	Isoelectric Point (pI)	Normalized Score	(nM)	$\Delta\lambda_{\max}$	T _{onset} (°C)	T _{m1} (°C)
SEQ ID NO: 370	3.2	270	ND	1	1.8	6	63.0	71.2
SEQ ID NO: 313	2.7	230	8.0	1	4.2	5	63.0	69.9
SEQ ID NO: 315	3	250	8.0	1	3.3	11	61.9	69.3
SEQ ID NO: 317	2.5	210	7.5	1	8.0	7	61.9	69.7
SEQ ID NO: 319	3.1	260	8.0	1	5.8	4	62.6	69.6
SEQ ID NO: 321	2.6	220	7.4	1	10.2	3	62.3	69.9
SEQ ID NO: 323	3	250	7.4	ND	ND	ND	ND	ND
SEQ ID NO: 325	2.3	200	7.1	1	23.4	4	60.9	69.9
SEQ ID NO: 326	2.6	220	7.5	1	18.9	4	62.3	70.1
SEQ ID NO: 327	2.8	240	7.5	ND	9.3	7	60.9	69.2
SEQ ID NO: 328	2.3	200	7.1	1	41.9	5	61.4	69.9
SEQ ID NO: 84	3.1	260	8.5	2	1.9	8	61.1	69.3
SEQ ID NO: 85	3.1	260	8.5	2	2.0	9	60.8	69.4
SEQ ID NO: 86	2.8	240	7.9	3	4.0	5	60.4	69.6
SEQ ID NO: 87	2.8	240	7.9	2	5.2	6	62.0	69.7
SEQ ID NO: 88	3.1	260	8.5	10	1.4	9	60.6	69.5
SEQ ID NO: 89	3.1	260	8.4	3	2.5	9	60.1	69.4
SEQ ID NO: 90	3.5	300	8.8	4	0.6	15	60.8	69.4
SEQ ID NO: 91	2.7	230	7.4	1	3.9	8	61.1	69.6
SEQ ID NO: 92	2.7	230	7.4	1	4.3	9	61.1	69.6
SEQ ID NO: 93	2.4	200	7.0	1	11.1	5	60.7	69.5
SEQ ID NO: 94	2.5	210	7.0	2	12.2	5	59.8	69.5

Sample	Heparin Binding		cIEF	BVP ELISA	Potency ³	AC-SINS	NanoDSF	
	RT ¹	[NaCl] (mM) ²	Isoelectric Point (pI)	Normalized Score	(nM)	$\Delta\lambda_{\max}$	T _{onset} (°C)	T _{m1} (°C)
SEQ ID NO: 95	2.7	230	7.4	3	6.8	6	59.7	69.4
SEQ ID NO: 96	2.8	240	7.4	3	9.9	7	60.3	69.3
SEQ ID NO: 97	3.1	260	8.0	5	1.3	13	60.4	69.2
SEQ ID NO: 98	2.6	220	7.0	2	8.8	6	61.6	69.5
SEQ ID NO: 99	2.6	220	7.0	1	9.4	8	60.6	69.3
SEQ ID NO: 100	2.3	200	6.8	1	28.7	4	60.7	69.5
SEQ ID NO: 101	2.3	200	6.8	1	29.4	3	62.1	69.7
SEQ ID NO: 102	2.6	220	7.0	1	7.5	8	61.7	69.6
SEQ ID NO: 103	2.6	220	7.0	2	12.2	6	61.3	69.6
SEQ ID NO: 104	2.9	250	7.4	3	2.8	11	61.5	69.5
SEQ ID NO: 106	2.5	210	7.1	2	14.0	4	60.4	69.4
SEQ ID NO: 108	2.3	200	6.8	1	35.2	2	61.0	69.5
SEQ ID NO: 110	2.5	210	7.0	2	17.2	4	60.5	69.5
SEQ ID NO: 111	2.8	240	7.4	2	3.5	6	60.4	69.6
SEQ ID NO: 112	2.4	200	6.8	1	24.8	3	60.9	69.5
SEQ ID NO: 113	2.3	200	6.8	2	26.0	2	60.2	69.4
SEQ ID NO: 116	2.3	200	6.8	1	25.9	3	60.6	69.5
SEQ ID NO: 117	2.4	200	6.8	1	31.2	2	60.9	69.7

Sample	Heparin Binding		cIEF	BVP ELISA	Potency ³	AC-SINS	NanoDSF	
	RT ¹	[NaCl] (mM) ²	Isoelectric Point (pI)	Normalized Score	(nM)	$\Delta\lambda_{\max}$	T _{onset} (°C)	T _{m1} (°C)
SEQ ID NO: 118	2.7	230	7.1	2	10.1	5	60.5	69.5

¹ Retention time.

² Concentration of NaCl in mM at peak elution from column.

³ Potency based on transient hRXFP1 assay described above.

ND – not determined.

5 N/A – not applicable.

Table 22. *In vitro* Characteristics of Relaxin-2 Fusion Protein Analogs.

Sample	Heparin binding	HIC	SEC	NanoDSF			Potency ¹	Calculated isoelectric point (pI)	cIEF
	[NaCl] (mM) ²	[Salt] (mM)	Monomer (%)	T _{onset} (°C)	T _{m1} (°C)	T _{agg} (°C)	(nM)		pI
SEQ ID NO: 87	217	620	ND	59	69	71	8.5	8	7.6
SEQ ID NO: 119	225	630	95.6	60	70	81	4.9	8	7.6
SEQ ID NO: 120	225	630	95.5	60	70	84	4.8	8	7.6
SEQ ID NO: 121	225	640	95.8	60	70	80	5.5	8	7.6
SEQ ID NO: 122	225	650	95.2	60	69	80	6.5	8	7.6
SEQ ID NO: 123	200	480	93.4	60	69	91	11.7	8	7.6
SEQ ID NO: 124	192	560	95.1	60	69	77	20.8	8	7.6
SEQ ID NO: 125	192	650	95.7	60	69	84	11.1	8	7.6
SEQ ID NO: 126	267	710	95.8	61	69	84	8.3	8.5	8
SEQ ID NO: 127	158	460	94.6	60	69	92	32	7.1	6.7
SEQ ID NO: 128	233	670	96.2	59	69		23.2	7.5	7.1
SEQ ID NO: 129	167	500	89.4	59	69	76	42.4	7.1	6.7
SEQ ID NO: 130	250	710	83.4	58	68	76	24.6	7.5	7.1
SEQ ID NO: 131	200	500	91.9	59	69	76	16.4	7.5	7.1

Sample	Heparin binding	HIC	SEC	NanoDSF			Potency ¹	Calculated isoelectric point (pI)	cIEF
	[NaCl] (mM) ²	[Salt] (mM)	Monomer (%)	T _{onset} (°C)	T _{m1} (°C)	T _{agg} (°C)	(nM)		pI
SEQ ID NO: 132	283	710	86	59	69	76	11.2	8.1	7.6
SEQ ID NO: 133	183	480	86.7	60	69	74	30.6	7.5	7.1
SEQ ID NO: 134	250	690	91.4	60	69	74	21.6	8	7.6
SEQ ID NO: 135	192	520	86	60	69	73	29.5	7.5	7.1
SEQ ID NO: 136	258	730	90.2	59	69	32	17.6	8	7.6
SEQ ID NO: 137	217	520	89.2	59	69	76	11.4	8	7.6
SEQ ID NO: 138	292	730	94.8	60	69		7.5	8.6	8

¹ Potency based on transient hRXFP1 assay described above.

² Concentration of NaCl in mM at peak elution from column.

ND – not determined.

5 **Table 23. *In vitro* Characteristics of Relaxin-2 Fusion Protein Analogs.**

Sample	Heparin binding	SEC	NanoDSF			Potency ¹	Calculated isoelectric point (pI)
	[NaCl] (mM) ²	Monomer (%)	T _{onset} (°C)	T _m (°C)	T _{agg} (°C)	(nM)	
SEQ ID NO: 516	275	86.8	52	65	51	5.6 ± 5.2 (n=2)	7.62
SEQ ID NO: 517	217	93.5	59	69	73	15.5 ± 17 (n=2)	7.61
SEQ ID NO: 518	208	92.9	59	69	73	15.8 ± 14 (n=2)	7.16
SEQ ID NO: 519	183	93.9	59	69	73	38.1 ± 37 (n=2)	7.14
SEQ ID NO: 520	258	90.4	60	68	62	4.9 ± 4.7 (n=2)	7.97
SEQ ID NO: 521	242	94.6	59	69	73	3.3 ± 3.6 (n=2)	7.97
SEQ ID NO: 522	242	91.9	60	70	73	6.5 ± 6.8 (n=2)	7.62
SEQ ID NO: 523	217	94.9	60	69	73	9.3 ± 8.9 (n=2)	7.61

¹ Potency based on transient hRXFP1 assay described above.

² Concentration of NaCl in mM at peak elution from column.

ND – not determined.

- 10 **[0301]** All samples in Tables 21, 22, and 23 are LALA PA LS IgG-RelB-Linker-RelA fusions containing the LALA PA LS IgG (SEQ ID NO: 79 or 83) except for wild-type human relaxin-2

and SEQ ID NO: 497. As shown in Tables 21, 22 and 23, above, there is a correlation between lower pI and lower non-specific binding found through heparin chromatography.

[0302] Confirmatory AC-SINS and BVP ELISA assays, and additional cAMP potency assays were performed on a subset of relaxin-2 fusion protein analogs, with results shown in Table

5 24.

Table 24. Additional Potency Assays for Relaxin-2 Fusion Protein Analogs.

Sample	pI	ACSINS (nm)	BVP ELISA	THP1 (endogenous RXFP1) cAMP EC50 (nM) (n)	Transient HEK293 hRXFP1cAMP EC50 (nM) (n)	Transient HEK293 rRXFP1cAMP EC50 (nM) (n)
Wild-type human relaxin-2	ND	ND	ND	0.2 ± 0.2 (7)	0.039 ± 0.015 (3)	0.122 ± 0.07 (3)
SEQ ID NO: 497	ND	28	7	ND	0.3**	0.95 ± 0.10 (2)
SEQ ID NO: 496	9.1	14	34	2.0 ± 1.3 (4)	0.19 ± 0.15 (2)	1.15 ± 0.23 (2)
SEQ ID NO: 367	7	0	1	ND	~150	ND
SEQ ID NO: 313	7.9	3	2	49 ± 9 (4)	10.0 ± 4.27 (3)	15.1 ± 2.17 (3)
SEQ ID NO: 317	7.5	7	1	63 ± 3 (3)	38.2 (1)	31.2 ± 11.1 (3)
SEQ ID NO: 86	7.9	5	3	30 ± 20 (3)	7.46 ± 3.32 (3)	24.5 ± 18.8 (3)
SEQ ID NO: 87	7.9	6	2	25 ± 12 (4)	8.70 ± 4.40 (3)	10.3 ± 3.45 (3)
SEQ ID NO: 90	8.8	15	4	4.4 ± 0.9 (2)	0.6 ± 0.5 (3)+I:BC	ND
SEQ ID NO: 91	7.4	8	1	30 ± 20 (3)	10.2 ± 5.86 (3)	12.4 ± 3.07 (3)
SEQ ID NO: 93	7	5	2	90 ± 10 (2)	19.1 ± 4.80 (3)	21.3 ± 9.59 (2)
SEQ ID NO: 95	7.4	6	3	26 ± 4 (4)	10.9 ± 5.26 (3)	13.5 ± 0.98 (2)
SEQ ID NO: 98	7	6	1	100 ± 40 (2)	21.5 ± 13.5 (3)	29.1 ± 5.71 (2)
SEQ ID NO: 104	7.4	11	3	11 ± 2 (3)	6.17 ± 2.21 (3)	6.74 ± 0.73 (2)
SEQ ID NO: 111	7.4	6	3	80 ± 50 (2)	5.94 ± 1.32 (3)	6.74 ± 4.57 (2)
SEQ ID NO: 118	7.1	5	2	200 ± 100 (2)	25.0 ± 6.20 (3)	20.3 ± 1.12 (2)

ND – not determined.

- [0303] A subset of relaxin-2 fusion protein analog (SEQ ID NO: 496, SEQ ID NO: 313, SEQ ID NO: 87, SEQ ID NO: 90, SEQ ID NO: 95, and SEQ ID NO: 104) samples was tested under various developability assessments. Under high concentration stress (target concentration of about 100 mg/mL), none of the samples showed loss of protein concentration based on UV.
- 5 Thermal stress induced increased turbidity/opalescence for all samples tested. Agitation stress had no effect on SEQ ID NO: 313 and SEQ ID NO: 104 samples. Under chemical stress (target concentration of about 5 mg/mL), SEQ ID NO: 496 and SEQ ID NO: 90 samples showed reduction in concentration for all chemical stresses tested, while SEQ ID NO: 313, SEQ ID NO: 87, SEQ ID NO: 95, and SEQ ID NO: 104 samples appeared stable. All samples showed
- 10 oxidation induced reduction in concentration, with SEQ ID NO: 496 and SEQ ID NO: 90 oxidized samples showing elevated high molecule weight species detected by size exclusion chromatography. In addition, based on non-reducing capillary electrophoresis samples (CE-SDS NR), no significant fragmentation was observed for any stresses in any of the tested samples.
- 15 [0304] The formation of stress induced post translational modifications (PTMs) was also tested. Stresses included incubation at 40°C for 4 weeks, room temperature and high pH (Tris buffer pH 8) for 2 weeks, room temperature and low pH (glycine buffer pH 3) for 2 weeks and room temperature oxidative stress (0.02% hydrogen peroxide) for 24 hours. SEQ ID NO: 313 and SEQ ID NO: 87 did not show any stress induced modifications; SEQ ID NO: 90 and SEQ
- 20 ID NO: 95 showed aspartic acid isomerization in the linker region; SEQ ID NO: 496 showed asparagine deamidation in the linker region; and SEQ ID NO: 95 and SEQ ID NO: 104 showed aspartic acid isomerization in the relaxin sequences.
- [0305] During manufacturability assessments, color change and aggregation were observed with multiple molecules under certain stress conditions, which is common in oxidized proteins.
- 25 The color change is typically driven by tryptophan oxidation, which drives a change in absorbance at 320 nm and 365 nm (Ambrogelly (2021) Antibodies 10(2):21). In order to probe light sensitivity of relaxin-2 fusion protein analogs SEQ ID NO: 522 and SEQ ID NO: 523, a light box was created using a tabletop 25 °C incubator with a transparent glass door. A photometer was attached to the inside of the incubator, a rectangular LED with an adjustable
- 30 light intensity switch was placed on the outside of the incubator, and the light intensity was adjusted to 1000 lux, which is similar to the light intensity in standard manufacturing suite rooms. Samples were placed in transparent glass vials with 200 µL glass inserts to allow for maximum surface area for light exposure, while maintaining minimal sample volume

requirements. Relaxin-2 fusion protein analogs SEQ ID NO: 522 and SEQ ID NO: 523 were incubated at 25 °C, 1000 lux for 7 or 14 days. Samples were also subjected to thermal stress via incubation at 40 °C for 7 or 14 days. After light or heat exposure, samples were evaluated using size exclusion high-performance liquid chromatography (SEC) to assess aggregate formation and CE-SDS to assess purity. As shown in Table 25, under these conditions, SEQ ID NO: 522 and SEQ ID NO: 523 are both resistant to thermal and light stress as assessed by aggregate formation and purity.

Table 25. Light and Heat Stress Stability of Relaxin-2 Fusion Protein Analogs.

Sample	Condition	SEC		CE-SDS	
		Monomer (%)	HMW (%)	Reduced purity (%)	Non-reduced purity (%)
SEQ ID NO: 522	Control (unstressed)	96.2	3.8	99.5	90.4
	Light (7 days)	95.5	4.5	99.5	90.4
	Light (14 days)	95.7	4.3	99.5	90.6
	40 °C (7 days)	95.6	4.4	99.5	90.1
	40 °C (14 days)	95.2	4.8	99.5	89.9
SEQ ID NO: 523	Control (unstressed)	90.6	9.4	99.5	94.7
	Light (7 days)	90.1	9.9	99.5	94.4
	Light (14 days)	90.5	9.5	99.5	94.6
	40 °C (7 days)	90.4	9.6	99.5	94.7
	40 °C (14 days)	90.3	9.7	99.5	94.9

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[0306] A separate study was performed to investigate the *in vitro* potency of SEQ ID NO: 87 as compared to wild-type (WT) human relaxin-2, using mammalian cell systems that either transiently, stably, or endogenously expressed human RXFP1 or orthologs from cynomolgus monkey and rat. Table 26 shows a summary of cAMP response induced by SEQ ID NO: 87 and wild-type human relaxin-2 on HEK293 cells transiently expressing human, monkey, and rat RXFP1. As shown in Table 26 and FIGs. 1A-1C, the average EC50 for SEQ ID NO: 87 for human (FIG. 1A), rat (FIG. 1B), and monkey (FIG. 1C) RXFP1 was 10±4 nM, 10±9 nM, and 30±20 nM, respectively.

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Table 26. Summary of cAMP Response in Cells Transiently Expressing RXFP1.

	Wild-type human relaxin-2 EC ₅₀		SEQ ID NO: 87 EC ₅₀	
	nM	ng/mL	nM	ng/mL
	Mean±SD (n)	Mean±SD (n)	Mean±SD (n)	Mean±SD (n)
Human RXFP1 in HEK293	0.05±0.02 (6)	0.3±0.1 (6)	10±4 (6)	800±300 (6)
Rat RXFP1 in HEK293	0.1±0.02 (3)	0.6±0.1 (3)	30±20 (3)	2000±1000 (3)
Cynomolgus monkey RXFP1 in HEK293	0.04±0.01 (3)	0.2±0.1 (3)	10±9 (3)	800±600 (3)

[0307] To test the selectivity of SEQ ID NO: 87, CHO-K1 cells stably expressing human RXFP1 or human RXFP2 were used. As shown in Table 27, the EC₅₀ for SEQ ID NO: 87 for human RXFP1 was 40±20 nM, and for human RXFP2, was ~100-fold less potent (EC₅₀ of ≥2000 nM), demonstrating that SEQ ID NO: 87 is selective for RXFP1.

Table 27. Summary of cAMP Response in Cells Stably or Endogenously Expressing RXFP1.

	Wild-type human relaxin-2 EC ₅₀		SEQ ID NO: 87 EC ₅₀	
	nM	ng/mL	nM	ng/mL
	Mean±SD (n)	Mean±SD (n)	Mean±SD (n)	Mean±SD (n)
Human RXFP1 (stable) in CHO-K1	0.2±0.1 (4)	1±0.6 (4)	40±20 (4)	2000±1000 (4)
Human RXFP2 (stable) in CHO-K1	10±10 (4)	90±60 (4)	>2000 (4)	>10 ⁶ (4)
THP-1 (endogenous RXFP1)	0.07±0.03 (5)	0.4±0.2 (5)	10±6 (5)	900±400 (5)

10

[0308] In some cases, transient or stable ectopic expression of proteins in cells can result in over-expression of targets, which may impact the potency and efficacy of test articles. To address this, the potency of SEQ ID NO: 87 was tested in the human leukemia monocytic cell line, THP-1, which endogenously expressed RXFP1. As shown in Table 27, the EC₅₀ for SEQ ID NO:87 was found to be 10±6 nM, consistent with what was found in the *in vitro* RXFP1 potency assays described above.

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Example 5. Pharmacokinetic (PK) and Pharmacodynamic (PD) Properties of Relaxin-2 Fusion Protein Analogs

[0309] Pharmacokinetic (PK) values were determined by measuring the concentration of a relaxin-2 fusion protein analog in the plasma of rats following a 5 mg/kg intravenous (IV) injection of the respective protein analog over time. PK values were determined for a subset of relaxin-2 fusion protein analog (SEQ ID NO: 496, SEQ ID NO: 497, SEQ ID NO: 367, SEQ ID NO: 313, SEQ ID NO: 87, SEQ ID NO: 95, SEQ ID NO: 90, and SEQ ID NO: 104) samples described herein (FIG. 2A). Rat PK parameters are shown in Table 28, below.

10 **Table 28. Summary of PK Parameters.**

Parameter	SEQ ID NO: 496	SEQ ID NO: 313	SEQ ID NO: 87	SEQ ID NO: 90	SEQ ID NO: 95	SEQ ID NO: 104	SEQ ID NO: 367	SEQ ID NO: 497
	rat (mL/h or mL)							
Clearance CL	2.76	0.69	0.52	0.29	0.32	0.52	0.356	ND
Central Volume 1	6.73	11.5	11.28	13.46	9.45	16.63	15.798	ND
Peripheral Clearance	28.24	16.8	8.42	32.18	1.12	2.28	12.014	ND
Peripheral Volume	413.8	56.3	47.82	249.95	17.41	50.22	21.655	ND
Peripheral Clearance 2	ND	ND	0.13	ND	3.95	ND	ND	ND
Peripheral Volume 2	ND	ND	0.11	ND	6.07	ND	ND	ND

ND – not determined.

[0310] FIG. 2B shows a separate experiment with PK values determined using the same methods described for FIG. 2A, for a subset of relaxin-2 fusion protein analog (SEQ ID NO: 87, SEQ ID NO: 496, and SEQ ID NO: 497) samples described herein.

[0311] FIG. 2C shows a separate experiment with PK values determined using the same methods described for FIG. 2A, for a subset of relaxin-2 fusion protein analog (SEQ ID NO: 522 and SEQ ID NO: 523) samples described herein.

Example 6. Hemodynamics and Renal Blood Flow Effects of Relaxin-2 Fusion Protein Analogs

[0312] The high isoelectric point (pI) of relaxin and related molecules presents significant pharmacokinetic (PK) and biophysical challenges, reflected in the rapid decline observed in

serum concentration for these molecules in the earliest timepoints of the PK curve. Without being bound by any theory, this high clearance phenomenon has been attributed to non-specific binding of high pI molecules to negatively charged heparin proteoglycans in the vasculature and in tissues. These issues were resolved through structure-guided engineering of the relaxin-2 fusion protein analogs to reduce their pI, as shown in Examples 1-5.

[0313] To assess the impact of the changes to lower pI, the PK and pharmacodynamic (PD) effects of the relaxin-2 fusion protein analogs were measured in rats. One of the most readily quantifiable activities of relaxin is to produce an observable increase in renal arterial blood flow (RABF) shortly following administration. This is a PD effect that has been shown to be observable in both rats and human patients with administration of serelexin and can be modeled to establish a PK/PD relationship for test compounds.

[0314] Naïve male Sprague-Dawley rats (weight range: 0.308–0.399 kg) were anesthetized via 5% isoflurane driven by 100% oxygen in an induction chamber. Once consciousness was lost, animals were removed from the chamber and an endotracheal tube was inserted for mechanical positive-pressure ventilation. The ventilator was connected to a vaporizer that delivered approximately 1–2% isoflurane driven by 100% oxygen for the duration of the experiment. Anesthetic depth was assessed prior to surgery and approximately every 15 minutes during the experimental procedure. Animals were maintained at approximately $37 \pm 0.5^{\circ}\text{C}$ on a heating pad, and body temperature was monitored throughout the protocol with a rectal temperature probe.

[0315] A Millar pressure catheter was placed in the right carotid artery to measure systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and heart rate (HR). Mean arterial pressure (MAP) was calculated. A small incision was made along the linea alba to access the abdominal cavity. The left renal artery was dissected and a doppler flow probe was placed around the artery. Renal artery blood flow (RABF) was continuously monitored throughout the experimental period, and renal vascular resistance ($\text{RVR} = \text{MAP}/\text{RABF}$) was calculated.

[0316] Following an approximately 10–15-minute equilibration period, baseline (BL) measurements were collected for 15 minutes. Individual animals were deemed acceptable for use in the study based on health status, body weight, hemodynamic parameters and renal blood flow. Following BL measurements, rats received a bolus intravenous (IV) administration (Dose 1) of either vehicle (10 mM histidine, 50 mM NaCl, 6.5% trehalose in deionized water pH 6.0) or a relaxin-2 fusion protein analog (test compound). Immediately following the bolus

IV dose, rats in each group received a maintenance dose via IV infusion (Dose 2) of the respective test compound over a 180-minute dosing period.

[0317] Blood samples were collected prior to Dose 1 (before the end of BL) and at 5 minutes, 1 hour, 2 hours and 3 hours after the start of Dose 2. Samples were obtained from a jugular vein cannula into a K2EDTA tube. Tubes were stored on wet ice until centrifugation in a refrigerated centrifuge. The resultant plasma was frozen on dry ice and stored at -80°C. At the conclusion of the study, rats were euthanized by exsanguination.

[0318] Mean values taken from 15-minute blocks during BL and from the 180-minute dose period were used for analysis. Values from each individual animal were pooled to determine an average for each variable for each group (if applicable). Average percent change from baseline values were determined for each variable. The term “dosing period” will describe the period during bolus and maintenance dose infusion (180 minutes) and will be used for the remainder of this report.

[0319] In one experiment, the effect on renal blood flow in rats of relaxin-2 fusion protein analogs SEQ ID NO: 313 and SEQ ID NO: 87 were compared to prior fusion protein SEQ ID NO: 496. Table 29 below shows the potency of relaxin-2 fusion protein analogs in recombinant human and rat RXFP1 assays (as described in Example 4).

Table 29. Fusion Protein Analogs in Human and Rat RXFP1 Potency Assays

	HEK293 cells expressed RXFP1 cAMP assay (EC50 (nM) ± SD (n))	
	Human RXFP1	Rat RXFP1
Wild-type human relaxin-2	0.04 ± 0.01 (4)	0.11 ± 0.06 (4)
SEQ ID NO: 496	0.2 ± 0.2 (3)	1.2 ± 0.2 (3)
SEQ ID NO: 313	10 ± 4 (4)	17 ± 5 (4)
SEQ ID NO: 87	7 ± 4 (4)	10 ± 3 (4)
SEQ ID NO: 90	0.9 ± 0.5 (2)	3 (1)

[0320] As shown in FIG. 3, administration of SEQ ID NO: 313 and SEQ ID NO: 87 at a bolus intravenous dose of 0.3 mg/kg and intravenous infusion of 0.2 mg/kg/hr caused a greater increase in rat RABF than administration of prior fusion protein SEQ ID NO: 496 at a bolus intravenous dose of 0.3 mg/kg and intravenous infusion of 0.5 mg/kg/hr. As such, despite the reduced *in vitro* potency observed for SEQ ID NO: 313 and SEQ ID NO: 87, these fusion proteins demonstrate greater increase in rat RABF.

[0321] Additional experiments were performed to further evaluate the effect of fusion protein analog SEQ ID NO: 87 and SEQ ID NO: 497 on renal blood flow. In these experiments, the

average potency of relaxin-2 fusion protein analogs in recombinant human and rat RXFP1 assays are shown in Table 30, below.

Table 30. Fusion Protein Analogs in Human and Rat RXFP1 Potency Assays

	EC50 for cAMP generation in recombinant RXFP1 assay (nM)	
	Human RXFP1	Rat RXFP1
Wild-type human relaxin-2	0.04	0.1
SEQ ID NO: 496	0.2	1
SEQ ID NO: 87	10	35
SEQ ID NO: 497	0.3	1

5

[0322] SEQ ID NO: 87 was infused by cannulated femoral vein using a syringe pump. The dose was infused intravenously (1 ml/kg) as a bolus followed by continuous infusion of PBS at the rate of 0.5 mL/kg/hr to maintain the circulating fluid volume.

[0323] As shown in FIG. 4B, the measured serum concentration (using human Fc levels as proxy) for 0.3 mg/kg SEQ ID NO: 497 was ~10 fold lower than that of 0.3 mg/kg SEQ ID NO: 87. Given the fact that the *in vitro* potency of SEQ ID NO: 497 in the rat RXFP1 signaling assay was found to be more than 30-fold higher than the *in vitro* potency of SEQ ID NO: 87 (see, Table 30), one would expect that the two molecules would give at least comparable increases in RABF when administered at the same dose. Instead, the efficacy of SEQ ID NO: 497 was comparable to a dose of SEQ ID NO: 87 that was 10-fold lower (0.03 mg/kg) (FIG. 4A), implying that the efficacy of SEQ ID NO: 87 was more than 10-fold higher than expected based on PK and *in vitro* potency data. The plasma concentration for 0.03 mg/kg SEQ ID NO: 87 was nearly identical to that for 0.3 mg/kg SEQ ID NO: 497.

[0324] The PBS data in FIG. 4A show that there is a small effect on renal blood flow from the volume expansion from the intravenous bolus that returned to baseline by 90 minutes. Using the 90-minute timepoint to fit the dose response for SEQ ID NO: 87 from 0.03 mg/kg to 10 mg/kg, the EC50 for SEQ ID NO: 87 in the rat *in vivo* was estimated to be ~2200 ng/mL (FIG. 4C) which corresponds to about 34 nM, consistent with the average EC50 for SEQ ID NO: 87 signaling as shown in Table 30.

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[0325] Additionally, as shown in FIGs. 5A and 5B, a low dose of SEQ ID NO: 87 increased and maintained RABF more than SEQ ID NO: 497. At 0.3 mg/kg, infusion of SEQ ID NO: 87 resulted in increased RABF by approximately 25% over baseline, which was maintained over the 90-minute experimental time course. At 0.3 mg/kg, infusion of SEQ ID NO: 497 resulted

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in increased RABF by approximately 15% over baseline, and RABF levels dropped close to baseline within 90 minutes post-infusion (FIG. 5A). Quantification of the area under the curve (AUC) showed that infusion of SEQ ID NO: 87 significantly increased RABF about 2-fold more than infusion of SEQ ID NO: 497 (FIG. 5B).

- 5 [0326] Without being bound by any theory, it is hypothesized that the enhanced effect of SEQ ID NO: 87 is due to an increase in distribution of SEQ ID NO: 87 to target tissues well above levels expected from plasma levels because of reduced heparin binding, as well as decreased non-specific cellular uptake, blood clearance and potentially higher bioavailability of SEQ ID NO: 87 compared to the more highly charged SEQ ID NO: 497 molecule.

10 **Example 7. Therapeutic Effect of a Relaxin-2 Fusion Protein Analog in a Rat Pulmonary Arterial Hypertension Model**

[0327] Pulmonary arterial hypertension (PAH) is characterized by a progressive pulmonary vascular remodeling of the distal precapillary arteries that causes a significant increase of the right ventricle (RV) load, ultimately leading to right heart failure and premature death. Using
15 monocrotaline (MCT) rat model as an *in vivo* PAH model, rats reproducibly develop pulmonary hypertension with a mean pulmonary pressure of ~40 mmHg approximately 4 weeks after single MCT administration. MCT is an 11-membered macrocyclic pyrrolizidine alkaloid derived from the seeds of the *Crotalaria spectabilis* plant. The MCT alkaloid is activated to the reactive pyrrole metabolite dehydromonocrotaline (MCTP) in the liver, a
20 reaction that is highly dependent on cytochrome P-450 (CYP3A4). When administered, MCT induces a syndrome characterized, among other manifestations, by pulmonary hypertension (PH), pulmonary mononuclear vasculitis, and right-ventricular hypertrophy through injury to pulmonary endothelial cells. The therapeutic potential of the SEQ ID NO: 87 relaxin-2 fusion protein analog was evaluated in a rat model of MCT-induced PAH.

- 25 [0328] On Study Day 1, naïve young (200–240 g) male Sprague Dawley rats in groups 1-5 received a 60 mg/kg dose (1 mL/kg s.c. in 100% DMSO) of MCT. Rats in Group 1 and 4 received anti-mouse CD20 antibody (20 mg/kg, i.p.) on days 8, 9, 10, and 17. Rats in Group 1 and 2 received SEQ ID NO: 87 (10 mg/kg, i.v.) on days 7, 10, 14, 17, 21 and 24. Beginning on study day 8, rats in Group 5 were dosed orally twice daily with sildenafil (positive control,
30 30 mg/kg, p.o., BID) with the last dose administered on study day 28. Rats in Group 6 were administered DMSO as control. 12 rats were tested in each of Groups 1 to 4, and 10 rats were tested in each of Group 5 and 6.

[0329] Cage side observations were done once daily for general health and appearance, mortality and signs of pain or distress. Body weights were recorded pre-dose on study day 0, and weekly throughout the study and on the day of the terminal procedure. On Study Day 28, animals were anesthetized with urethane (1.25 g/kg, i.p.). Blood samples were collected from the Retro-Orbital plexus for PK and biomarker analysis (e.g., N-terminal (NT)-pro hormone BNP (NT-proBNP)). Serum NT pro-BNP was analyzed using Rat NT-proBNP Assay Kit - Meso Scale Discovery, MD, USA (catalog no. K153JKD). Rats were ventilated using RoVent® Jr. Small Animal Ventilator from Kent Scientific Corporation. The mean right ventricular pressure and mean pulmonary artery pressure were measured via a 1.6 French solid-state catheter purchased from Transonic Inc. using an open chest approach. Data were recorded and analyzed using SP200 Pressure System and LabChart software (ADI instruments). The animals were then humanely euthanized via exsanguination while under deep anesthesia. At necropsy, the heart and lungs were collected from each animal for weighing. After weighing, both the right ventricle and lung samples, were fixed in formalin and then stored at room temperature. The brain was also collected and weighed to normalize with the rat body weight. Immunohistochemistry analysis was performed on the formalin fixed lungs and ventricles.

[0330] An assay was developed to quantify the presence of SEQ ID NO: 87 in mouse serum samples, coming from both serum and plasma. The assay utilizes a quantitative sandwich enzyme immunoassay, with an affinity-purified polyclonal antibody specific for Human Fc coated to a 96-well plate. Samples containing molecules with Human Fc were added to wells, incubated, and washed before the addition of an enzyme-linked polyclonal antibody specific for Human Fc. After incubation with the enzyme-linked antibody, wells were washed, and the enzyme-substrate was added and allowed to develop before quenching with acid. After quenching with an acid plate, read the plate at 450 and 570nm within 30 minutes of color change. Values from each animal were pooled to determine an average of each variable for each group (if applicable). The mean right ventricular pressure (mRVP) and mean pulmonary artery pressure (mPAP) were recorded, and Right Ventricular Systolic Pressure (RVSP) was analyzed.

[0331] SEQ ID NO: 87 was administered in the MCT-induced PAH model at 10 mg/kg, i.v. twice weekly for 3 weeks with therapeutic dosing initiated one week after MCT injection. To mitigate efficacy reducing anti-drug antibody (ADA) generation to the test article, the study was performed with and without B-cell depletion by injecting anti-mouse CD20 antibody to rats. Cardiac hemodynamics including right ventricular systolic pressure (RVSP) and mean pulmonary arterial pressure (mPAP) were measured using an open chest approach. The Fulton

Index, the ratio of right ventricular weight to the weight of the left ventricle and septum, was measured at week 4. Blood samples for serum NT pro-BNP, PK and ADA analysis were collected.

[0332] MCT treatment of rats significantly increased RVSP (FIGs. 6A and 6B), mPAP (FIGs. 7A and 7B), Fulton Index value (FIGs. 8A and 8B), and NT-pro-BNP (FIGs. 9A and 9B) while decreasing survival compared to the naïve group (no MCT) over a 4-week period. As shown, rats treated with SEQ ID NO: 87 demonstrated significant improvements in RVSP (FIG. 6B), mPAP (FIG. 7B), and Fulton Index value (FIG. 8B) in rats where B cells were depleted. In addition, there was a clear survival benefit following treatment with SEQ ID NO: 87, with treated rats being the only group showing 100% survival.

[0333] In addition, histopathology analysis revealed that SEQ ID NO: 87 significantly improved lung inflammation and reduced pulmonary arterial muscularization (FIGs. 10A and 10B, respectively). To assess lung inflammation, histopathology analysis was performed on tissues stained using hematoxylin and eosin. The lung histopathology sum score was calculated as the sum scores of parameters analyzed, including pulmonary arterial hypertrophy, vasculitis/necrosis, alveolar histiocytosis, perivascular and interstitial inflammation, hemorrhage, and fibrin deposition. Significant improvement was observed in the overall lung histopathology sum score as well as in the degree of vasculitis/necrosis, hemorrhage, and fibrin deposition in the lung tissues of rats, compared to rats that received vehicle control. To assess pulmonary arterial muscularization, histopathology analysis was performed using tissues stained with an anti-alpha smooth muscle actin (SMA) antibody to quantify muscularization, and Verhoeff stain to stain internal elastic laminae of arterioles. Thickening of the arterial wall, primarily by smooth muscle hypertrophy, was seen at all levels of the pulmonary arterial tree in animals exposed to MCT. This was associated with an increased arterial medial hypertrophy ratio across five vessel sizes quantified. Medial thickening relative to external diameter was best developed in the smallest caliber arteries and arterioles with less dramatic medial hypertrophy seen in the intermediate and larger caliber arteries. Lungs from rats treated with SEQ ID NO: 87 had lower arteriolar, small, and intermediate artery medial hypertrophy ratios than untreated animals. For small caliber arteries, rats treated with SEQ ID NO: 87 had significantly lower ratios than untreated animals.

[0334] No mortality was observed in B cell depleted rats treated with SEQ ID NO: 87 compared to the vehicle and sildenafil treated groups (FIG. 11).

Example 8. Anti-Fibrotic Effect of Relaxin-2 Fusion Protein Analogs in a Mouse Model of Kidney Fibrosis

[0335] This Example describes evaluation of the anti-fibrotic effect of relaxin-2 fusion protein analogs SEQ ID NO: 496, SEQ ID NO: 313, and SEQ ID NO: 87 in a mouse unilateral ureteral obstruction (UUO) model of kidney fibrosis. The UUO model induces renal fibrosis, where the primary feature of UUO is tubular injury because of obstructed urine flow. Furthermore, experimental UUO in rodents is believed to mimic human chronic obstructive nephropathy in an accelerated manner. Renal fibrosis is the common pathway for most forms of progressive renal disease. Because removal of the obstruction is generally not sufficient to reverse fibrosis, model animals may benefit from an accompanying treatment. UUO is a model widely used to study obstructive nephropathy.

[0336] An initial study evaluated the effect of SEQ ID NO: 496 and SEQ ID NO: 313. Sixty-five male C57BL/6 mice were used for the study (8-10 weeks of age at initiation). UUO was induced on Day 0 by ligation of a ureter of the left kidney, while the contra-lateral kidney served as a control. The UUO surgery was performed according to a standard procedure under deep anesthesia. Briefly, the kidney and ureter were exposed through midline abdominal incision after removal of hair from abdominal area. The left ureter was completely obstructed with two ligations. The first suture was placed 1mm below the kidney and the other suture was placed 1mm below the renal pelvis with silk or prolene suture. The wound was closed with 2 to 3 staples. The animal was returned to its cage and monitored until it started to move. On the day of surgical procedure and for 72 hours post-surgery, animals were provided with pain medication Buprenorphine. A control group (n=5) underwent sham surgery). UUO mouse groups were treated with 10 mg/kg SEQ ID NO: 496 (n=10), 20 mg/kg SEQ ID NO: 496 (n=10), 10 mg/kg SEQ ID NO: 313 (n=10), or 20 mg/kg SEQ ID NO: 313 (n=10). The treatment groups received intravenous injections 2 days before surgery (Day -2) and on Day 2 and Day 5 post-surgery. A positive control group (n=10) received enalapril, an ACE inhibitor medication used to treat high blood pressure, diabetic kidney disease, and heart failure, which was provided through drinking water at 200 mg/L beginning on Day -2 and continued through study termination. A negative control group (n=10) was treated with vehicle (PBS). The study was terminated on Day 7 post-surgery, and fibrosis symptoms as well as in-life parameters were assessed.

[0337] No adverse clinical symptoms were developed in any of the animals post-UUO surgery. The animals tolerated treatment with SEQ ID NO: 496, SEQ ID NO: 313, and enalapril well,

and 100% survival was recorded. On Day 7 post-surgery, left kidneys were harvested, weighed, and fixed for histology.

[0338] All groups with surgically induced UUO showed reduced body weight relative to the sham surgery group. At Day 4 post-surgery, body weights began to trend toward recovery for all UUO groups. Additionally, all UUO groups showed a significant increase in kidney weight relative to the sham surgery group, and there was no statistically significant change in kidney weight across the treatment or control UUO groups.

[0339] Histological analysis of kidney sections fixed on Day 7 post-surgery showed a significant increase in collagen deposition in renal parenchyma in all UUO groups relative to the sham surgery group (FIG. 12). Animals treated with SEQ ID NO: 496 and SEQ ID NO: 313 at 20 mg/kg showed significantly reduced collagen deposition relative to the vehicle-treated control group.

[0340] The anti-fibrotic effect of SEQ ID NO: 87 was observed following a similar procedure. Mice treated with SEQ ID NO: 87 showed a significant decrease in collagen deposition following UUO induction relative to vehicle-treated mice (FIG. 13). Tissue TNF α levels were evaluated via electrochemiluminescence, and mice treated with SEQ ID NO: 87 also showed a significant decrease in TNF α levels relative to vehicle-treated mice (FIG. 14). Reduction of IL-1 β and IL-6 in fibrotic kidney was also observed in the SEQ ID NO: 87-treated mice relative to vehicle treated mice.

20 **Example 9. Effect of Relaxin-2 Fusion Protein Analogs on Isoproterenol-Induced Cardiac Hypertrophy and Fibrosis**

[0341] This Example describes evaluation of the effect of relaxin-2 fusion protein analog SEQ ID NO: 87 on cardiac hypertrophy and fibrosis following isoproterenol challenge. Isoproterenol is a drug that increases heart rate and heart muscle contractions and can lead to cardiac hypertrophy and increased fibrosis.

[0342] All animals were treated and cared for in accordance with the Guide for the Care and Use of Laboratory Animals (National Institutes of Health, revised 2011), and protocols were approved by an Institutional Animal Care and Use Committee. Male C57BL/6J mice were obtained at 10-11 weeks of age with body weight ranging between 25 grams and 30 grams. The animals were housed in the vivarium on a conventional 12 hr light/dark cycle. After equilibration housing for 1 week, micro-osmotic minipump implantation was performed on mice. Briefly, mice were anesthetized using 1% to 3% isoflurane given by inhalation through a vaporizer. Osmotic minipumps with a flow rate of 0.25 μ l/h were surgically implanted

subcutaneously into the subscapular space of mice. Each pump delivered a constant dose (0.25 µl/h) of infused drug (isoproterenol in PBS containing 0.002% ascorbic acid at 15 mg/kg per day) or vehicle (PBS with 0.002% ascorbic acid) for 2 weeks. Postoperative analgesia was achieved with a single dose of meloxicam SR (2.5 mg/kg) during minipump implantation and another single dose of meloxicam SR (2.5 mg/kg) one day after the surgery. Mice were treated with either vehicle or 10 mg/kg of SEQ ID NO: 87 one day before minipump implantation. Mice were then dosed with relaxin-2 fusion protein analog SEQ ID NO: 87 bi-weekly for the duration of the study (total of 14 days). To reduce anti-drug activity, mice were injected intraperitoneally with 20 mg/kg of anti-mouse CD20 to deplete all B cells one day post minipump implantation.

[0343] After 14 days of incubation, animals were euthanized via CO₂ inhalation followed by cervical dislocation. The body weights were measured. Whole hearts were explanted, washed in PBS, dried with paper towel, and weighed. The fresh heart tissues were immediately snap frozen in liquid nitrogen and stored for further collagen content analysis. Tibia was obtained by blunt limb dissection and tibia length was measurement using a digital caliper. Heart weights (HW) were normalized by body weight (BW) and by tibial length (TL). Data (HW/TL, and HW/BW) were analyzed using standard software. As shown in FIG. 15, isoproterenol administration caused a significant increase in cardiac hypertrophy, as measured via normalized heart weight (HW/BW), relative to vehicle treated mice. Coadministration of SEQ ID NO: 87 with isoproterenol significantly attenuated the isoproterenol-induced cardiac hypertrophy.

[0344] Collagen content in each heart ventricle was measured via a hydroxyproline assay kit. The snap frozen whole heart ventricle tissues were weighed, chopped, and transferred into screw-capped tubes. Tissue was hydrolysed at 100 mg/ml in 6M HCl and incubated for 20 hrs at 95 °C in a calibrated oven or thermoblock. The hydrolyzed samples were then diluted with 4M HCl before assay analysis. To perform the assay analysis, 35 µl hydrolysate or hydroxyproline standard were mixed with 75 µl assay buffer in each well of a 96-well plate. The plate was incubated 20 minutes at room temperature while shaking. After, 75 µl of detection reagent was added to each well, the plate was mixed well and incubated 60 minutes at 60 °C in an oven or incubator. The plate was cooled down to room temperature, read at 570 nm, and hydroxyproline concentrations of each sample were determined by the standard curve. Data were analyzed using standard software. As shown in FIG. 16, isoproterenol administration caused a significant increase in fibrosis, as measured via collagen content,

relative to vehicle treated mice. Coadministration of SEQ ID NO: 87 with isoproterenol significantly attenuated the isoproterenol-induced fibrosis.

Example 10. Evaluating Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of a Relaxin-2 Fusion Protein Analog.

- 5 [0345] This Example describes a double-blind, randomized, placebo-controlled, single ascending dose study being performed to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and immunogenicity of SEQ ID NO: 87 in healthy subjects.

Study design

- 10 [0346] Approximately 48 participants are enrolled in the study. A single ascending dose of SEQ ID NO: 87 or matching placebo (*i.e.*, identical buffer without addition of SEQ ID NO: 87) was administered to study participants via intravenous infusion (IV) or subcutaneous (SC) injection in the doses described below. In each cohort, 6 participants receive SEQ ID NO: 87 and 2 participants receive placebo. Infusions were between 30 and 60 minutes in duration. Cohort A receives 0.3 mg/kg IV of SEQ ID NO: 87 or matching placebo. Cohort B receives 1
- 15 mg/kg IV of SEQ ID NO: 87 or matching placebo. Cohort C receives 300 mg SC of SEQ ID NO: 87 or matching placebo. In some cases, Cohort C is dosed concurrently with Cohort B. Cohort D receives 3 mg/kg IV of SEQ ID NO: 87 or matching placebo. Cohort E receives 600 mg SC of SEQ ID NO: 87 or matching placebo. In some cases, Cohort E is dosed concurrently with Cohort D. Cohort F receives 10 mg/kg IV of SEQ ID NO: 87 or matching placebo.

- 20 [0347] A master randomization schedule and code break envelopes was created, and delivered to the site's unblinded pharmacy before dosing. The active and placebo products are infused through a line that is covered to conceal active from placebo. A printed randomization schedule is generated using a permuted blocked fixed method. The people receiving the treatment(s), the people administering the treatment(s), and the people analyzing the results and data are
- 25 blinded.

Primary outcome

- [0348] The primary outcome of the study is to evaluate the safety and tolerability of SEQ ID NO: 87 after single ascending doses. The primary outcome is assessed by monitoring: 1) the incidence of adverse events (AEs) and serious adverse events (SAEs); 2) changes in clinical
- 30 laboratory safety parameters including blood test results for hematology, serum chemistry, and coagulation studies; 3) changes in vital signs measurements; and 4) changes in electrocardiogram (ECG) findings. Adverse events are assessed by clinical examination,

review of patient data and self-reporting. Adverse events are collected via verbal interview by clinic staff during the study period either in person during confinement or clinic visits or via telephone during remote contacts. Vital signs measurements includes resting heart rate and systolic and diastolic blood pressure (BP) using standard manual or electronic clinical procedures. These procedures are completed using standard nursing practices or, in the case of ECG, the instructions provided by the manufacturer. These individual data are utilized to determine safety by physician assessment. Additionally, the totality of the data presented are also factored into the determination of safety.

[0349] Adverse events and serious adverse events are assessed at Screening, Day -1, Day 1, Day 2, Day 3, Day 6, Day 8, Day 15, Day 29, Day 43, and Day 57 post dose administration. Laboratory safety parameters are assessed at Screening, Day -1, Day 1, Day 2, Day 8, Day 15, Day 29, Day 43, and Day 57 post dose administration. Vital signs are assessed at Screening, Day -1, Day 1, Day 2, Day 3, Day 6, Day 8, Day 15, Day 29, Day 43, and Day 57 post dose administration. ECG is performed at Screening, Day -1, Day 1, and Day 2 post dose administration.

Secondary outcomes

[0350] A secondary outcome of the study is to characterize the pharmacokinetic (PK) profile of SEQ ID NO: 87 in healthy participants after single ascending doses of SEQ ID NO: 87. Standard PK parameters are assessed: C_{max} , T_{max} , AUC-last (AUC from 0 to the last measurable concentration), AUC-inf (AUC from 0 to infinity), $t_{1/2}$, CL (clearance), and V_z (terminal phase volume of distribution). Blood sampling for PK parameter assessment occurs at Predose, End of infusion, 6 hrs, and 12 hrs post dose on Day 1, 24 hrs post dose on Day 2, 48 hours post dose on Day 3, 120 hours post dose on Day 6, 168 hours post dose on Day 8, Day 15, Day 29, Day 43 and Day 57 post dose.

[0351] Another secondary outcome of the study is to evaluate the pharmacodynamic (PD) effect of single ascending doses of SEQ ID NO: 87 in healthy participants. The change from baseline to day 2 is assessed in the following PD parameters: renal plasma flow (RPF), as measured by change in plasma para-aminohippurate (PAH) over time; renal blood flow (RBF); and filtration fraction (FF), as calculated by glomerular filtration rate (GFR) divided by RPF. Blood sampling for RPF/GFR assessment occurs on Days 2, 8, and 15 for IV Cohorts A, B and D and on Days 15 and 29 for IV Cohort F. Blood sampling for RPF/GFR assessment occurs on Days 2, 15, and 29 for SC Cohorts C and E.

Subject eligibility

[0352] Participants meet the following criteria to be enrolled in this study:

- is a male or a female of non–childbearing potential between the ages of 18 and 55 years;
- is judged to be in good health based upon medical history, physical examination, vital signs, ECGs, and routine laboratory tests;
- has a body mass index (BMI) between 18 and 32 kg per meter square at screening;
- understands the study procedures and agrees to participate in the study by giving written informed consent; and
- is at least 18 years of age and no more than 55 years of age.

10 [0353] Participants were excluded from the study if any of the following criteria apply:

- is mentally or legally incapacitated, has significant emotional problems at the time of the study, or has a history of significant psychiatric disorders at the discretion of the investigator;
- has any clinically significant physical examination abnormalities observed during the screening visit or would not be a good candidate for participation in the study in the opinion of the investigator;
- has clinically significant abnormal complete blood count, clinical chemistry, or urine analysis at screening or Day -1 (in asymptomatic participants, any abnormal laboratory results, including creatine phosphokinase within 3 times the upper limit of normal with suspected cause due to rigorous physical activities, may be repeated once during the screening period);
- was hospitalized for any reason within 30 days of the screening visit;
- has any history of clinically significant renal, neurologic, gastrointestinal, hepatic, or respiratory disease (note that subjects with fully resolved childhood asthma with no recurrence in adulthood may be enrolled);
- has a history of anaphylaxis or other significant allergy in the opinion of the investigator;
- has a history of clinically significant cardiovascular disease including arrhythmias, conduction abnormalities, or clinically significant abnormal vital signs;
- was previously administered relaxin or relaxin fusion proteins; or
- was dosed in any clinical research study evaluating another investigational drug (including biologics) or therapy (including specific immunotherapy) within 90 days or less than or equal to 5 half-lives (whichever is longer) of an investigational biologic

drug, or less than or equal to 4 weeks for other investigational products, before the screening visit.

Partial Results

[0354] Preliminary PK and PD results were obtained from healthy human patients administered a single 0.3 mg/kg IV dose of SEQ ID NO: 87 (FIGs. 17A and 17B, respectively). As shown in FIG. 17A, SEQ ID NO: 87 demonstrated a desirable PK profile in four individual healthy patients after IV administration and a terminal half-life of 17 days, which is more than double the predicted terminal half-life of 6 days as obtained from simulations in non-human primate models (dashed line). The PD effect of SEQ ID NO: 87 in healthy human patients was investigated by assessing the change from baseline of renal plasma flow (RPF) at days 2, 8, and 15 (FIG. 17B). Briefly, patients were administered a bolus of para-aminohippurate (PAH) and plasma PAH was measured at days 2, 8, and 15. Effective RPF at each time point was calculated by using the formulas:

$$RPF \text{ (ml/min)} = \frac{Cl_{PAH \text{ ml/min}}}{\text{extraction ratio}},$$

$$Cl_{PAH \text{ ml/min}} = \frac{\text{rate of PAH infusion}}{\text{concentration}_{PAH \text{ mg/ml}}},$$

As shown in FIG. 17B, a single 0.3 mg/kg IV dose of SEQ ID NO: 87 resulted in a substantial increase of at least about 30% in RPF on day 2 post dose compared to patients that received the placebo (PBO), and demonstrated persistence of effect for at least 8 days post dose.

[0355] SEQ ID NO: 87 also demonstrated a desirable PK profile in healthy human patients administered a single 150 mg SC dose (FIG. 18), with terminal half-life not yet determined. Based on the data, SC bioavailability was in the range of 50-60%.

[0356] The preliminary data from healthy patients administered SEQ ID NO: 87 by IV and SC, supports a Q4W dosing schedule. The PK data showed low intersubject variability ($\leq 20\%$) in serum concentrations, and no evidence of immune-mediated drug clearance. SEQ ID NO: 87 was found to be safe and well tolerated with minimal adverse events, and no drug-related SAEs. Expected on target effects were observed (*e.g.*, mild orthostatic tachycardia without BP effect in some subjects), and no infusion or injection site reactions were reported.

Example 11. Single-Dose, Open-Label Study to Evaluate the Safety, Tolerability, and Hemodynamic Effects of a Relaxin-2 Fusion Protein Analog.

[0357] This prophetic Example describes a single-dose, open-label study to evaluate the safety, tolerability, and hemodynamics of SEQ ID NO: 87 in subjects with combined postcapillary

and precapillary pulmonary hypertension (CpcPH) or isolated postcapillary pulmonary hypertension (IpcPH) and heart failure with preserved ejection fraction (HFpEF).

Background and rationale

[0358] SEQ ID NO: 87 is a relaxin peptide Fc-fusion biologic that is being developed for the treatment of combined precapillary and postcapillary pulmonary hypertension (CpcPH) and isolated postcapillary pulmonary hypertension (IpcPH). Relaxin is an insulin-like peptide, originally identified as a pregnancy-associated hormone, that has antifibrotic, anti-inflammatory, and vasodilatory properties in both men and women. It produces these effects by binding and activating its G-protein coupled receptor, relaxin family peptide receptor 1 (RXFP1), which then triggers a variety of signaling pathways including cAMP (cyclical adenosine monophosphate), cGMP (cyclical guanosine monophosphate), and MAPKs (mitogen activating protein kinases) as well as altering gene expression of transforming growth factor-beta (TGF- β), MMPs (matrix metalloproteinases), angiogenic growth factors, and endothelin-1 receptors.

[0359] Pulmonary hypertension (PH) is a condition that leads to dyspnea, reduced exercise capacity, and hypoxemia and has a high mortality risk. It is defined as a mean pulmonary arterial pressure (mPAP) ≥ 20 mm Hg. Because this condition occurs in many different clinical settings, the World Health Organization (WHO) has divided PH into 5 different groups. CpcPH is a subgroup of WHO Group 2 pulmonary hypertension (PH), pH due to left-sided heart disease (PH-LHD). LHD includes the following: heart failure with preserved ejection fraction (EF), defined as heart failure with EF $>50\%$ (HFpEF); heart failure with reduced EF, defined as heart failure with EF $<40\%$ (HFrEF); and heart failure due to left heart valvular disease (either mitral or aortic valvular disease).

[0360] The unique hemodynamics seen in Group 2 PH-LHD that differentiates it from other forms of PH is an elevated pulmonary arterial wedge pressure (PAWP) ≥ 15 mm Hg. The elevated wedge pressure reflects elevated left atrial pressure and is an indicator of abnormal left ventricular filling consistent with left heart disease. In group 2 PH, the elevation in mPAP may be due to primarily elevated post-capillary pressures due to elevations in PAWP. An additional subgroup of Group 2 PH has elevations in pre-capillary pressures, which are thought to be due to chronic elevations in mPAP leading to remodeling of the pulmonary arterial vasculature, similar to what is seen in pulmonary arterial hypertension (PAH; Group 1 PH). These 2 forms of PH-LHD are known as isolated post-capillary PH (IpcPH), and combined pre- and post-capillary PH (CpcPH).

[0361] CpcPH is defined hemodynamically by a pulmonary vascular resistance (PVR) ≥ 3 Wood units, mean pulmonary artery pressure (mPAP) ≥ 20 mm Hg, and pulmonary capillary wedge pressure (PCWP) ≥ 15 mm Hg. In previous clinical trials, native human relaxin (serelaxin) was shown to modulate the hemodynamics of patients with acute heart failure associated with PH (Ponikowski *et al.* (2014) *Eur. Heart J.* 35 (7):431-441). In one study, infusion of serelaxin for 20 hours resulted in a rapid and significant decline in mPAP, PVR, and PCWP. In a second trial, infusion of serelaxin for 24 hours in patients with stable heart failure and PH resulted in a sustained and significant increase in cardiac index (CI), and a sustained decrease in PCWP and systemic vascular resistance (SVR) [Group C in Dschietzig, *et al.* (2009) *Ann. N Y Acad. Sci.* 1160:387-392]. Clinical risk factors for CpcPH include obesity, hypertension, diabetes, and metabolic syndrome. Right ventricular (RV) dysfunction occurs more frequently in CpcPH than in IpcPH (Lteif, *et al.* (2021) *J. Am. Heart Assoc.* 10(11):e020633).

[0362] IpcPH is a subtype of Group 2 PH (PH-LHD) where the elevated pulmonary artery pressure is due to passive backflow of elevated pressure from the left atrium and is not associated with major changes in the morphology of the pulmonary arteries and arterioles. It is defined hemodynamically by a PVR < 3 Wood units, mPAP ≥ 20 mm Hg, and PCWP ≥ 15 mm Hg. Both IpcPH and CpcPH lead to an increase in right ventricular afterload, and this can lead to right heart dysfunction and death (Thenappan (2019) *Advances in Pulmonary Hypertension.* 18:87-91).

[0363] Patients with CpcPH have a worse prognosis than those with IpcPH. The 5-year survival rate for patients with CpcPH is 23% (Ibe *et al.* (2021) *PLoS One.* 16(3):e0247987).

[0364] In this study, patients with CpcPH or IpcPH with HFpEF will be subjected to right heart catheterization (RHC) and will receive an intravenous (IV) dose of SEQ ID NO: 87. Hemodynamic measurements will be obtained for 8 hours after the dose of SEQ ID NO: 87 to determine the change in PVR and PCWP as well as other hemodynamic assessments over time.

Study design

[0365] Up to 25 participants may be enrolled in the study, across up to 3 cohorts, including a low-dose cohort (cohort A) with at least 2 participants with CpcPH, a cohort at the expected therapeutic dose (cohort B) with at least 6 participants with CpcPH and at least 3 participants with IpcPH, and a high dose cohort (cohort C) with at least 9 participants, including at least 6 participants with CpcPH and at least 3 participants with IpcPH.

[0366] During the screening period, participants will undergo assessments to ensure that they are appropriate for participation in the study.

[0367] Participants will require a 3-day admission to the clinical unit and then continue to be followed through Day 43. On Day -1, participants will be admitted to the clinical unit and have baseline assessments performed, including an echocardiogram. On Day 1, participants will have a right heart catheter (RHC) placed and baseline hemodynamic measurements will be obtained before dosing with SEQ ID NO: 87. Participants will be administered a dose of SEQ ID NO: 87 via at least a 30-minute intravenous (IV) infusion, and hemodynamic measures, heart rate (HR), and blood pressure (BP) will be obtained over an 8-hour period beginning after the end of the infusion. After the last hemodynamic measure is obtained, the RHC will be removed, and the participant will remain overnight for observation. Participants may be discharged from the clinical unit on Day 2 once all assessments are completed. The participant will return to the clinical unit on Days 8, 15, and 29 postdose for additional follow-up. Participants will return to the clinical unit for an end of study visit on Day 43.

15 Treatment plan

[0368] Each participant will receive a single open-label intravenous dose of SEQ ID NO: 87, based on a mg/kg body weight calculation (from Day -1), administered via at least a 30-minute infusion. SEQ ID NO: 87 will be administered with the participant in a semirecumbent position.

20 [0369] Up to 25 participants may be enrolled across up to 3 cohorts. Cohort A will enroll at least 2 participants with CpcPH at a proposed dose of 0.3 mg/kg SEQ ID NO: 87. Cohort B will enroll at least 6 participants with CpcPH and at least 3 participants with IpcPH at a dose of 1 mg/kg, and cohort C will enroll at least 6 participants with CpcPH and at least 3 participants with IpcPH at a dose of 3 mg/kg.

25 [0370] Because this is the initial clinical assessment of SEQ ID NO: 87 in patients with CpcPH or IpcPH, and the safety, PK, PD/efficacy, and immunogenicity profile of the compound are still being elucidated in healthy volunteers, this study is designed to have the flexibility to accommodate the inherent dynamic nature of Phase 1 clinical studies and the proposed doses may be adjusted. Participants will not receive a dose higher than 6 mg/kg.

30 [0371] Dosing of the first 2 participants in each cohort will be separated by at least 7 days. After the first 2 participants within a cohort are dosed, no stagger between dosing of participants within a cohort is required.

Study entry criteria

[0372] Patients who meet the following inclusion criteria will be enrolled in the study:

1. Is a male or a female of non-childbearing potential between the ages of 18 and 80 years.
A female of non-childbearing potential is a woman who meets either of the following criteria:
- 5 a. Is in a postmenopausal state defined as no menses for 12 months without an alternative medical cause and follicle-stimulating hormone (FSH) level consistent with postmenopause (≥ 40 mIU/mL);
- b. Has a documented hysterectomy, bilateral oophorectomy, or salpingectomy.
2. Has one of the following:
- 10 a. Diagnosis of HFmrEF (heart failure with mid-range ejection fraction): defined as signs and symptoms of New York Heart Association (NYHA) class II-III heart failure and left ventricular ejection fraction (LVEF) 40% to 49%;
- b. Diagnosis of HFpEF, defined as signs and symptoms of NYHA class II-III heart failure and LVEF $\geq 50\%$ and at least ONE of the following: i. Heart Failure Association-Pre-test
- 15 assessment, Echocardiography and natriuretic peptide score, Functional testing in cases of uncertainty, Final etiology (HFA-PEFF) score ≥ 5 points; ii. HFA-PEFF score 2-4 points AND abnormal diastolic stress testing or invasive hemodynamic measurements.
3. Has demonstrated CpcPH or IpcPH, based on RHC performed within 6 months of or during screening documenting the following:
- 20 a. For patients with CpcPH: PVR ≥ 3 Wood units, or For patients with IpcPH: PVR < 3 Wood units;
- b. mPAP of > 20 mm Hg;
- c. PCWP > 15 mm Hg or PCWP > 12 mm Hg and ≤ 14 mm Hg with evidence on left atrial volume index (LAVI) on echocardiography of ≥ 34 mL/m².
- 25 4. Is receiving chronic medication for heart failure or for any underlying condition, administered at a stable (per investigator) dose for ≥ 30 days before screening. Diuretics and/or anticoagulants are excepted from this rule but should not be newly started or stopped within 30 days of screening, and a prescribed dose change should not occur within 7 days of screening.
5. Is able to adhere to the study visit schedule and understand and comply with all protocol
- 30 requirements.
6. Agrees not to participate in any other trials of investigational drugs/devices while enrolled in this study.

7. Understands the study procedures and agrees to participate in the study by giving written informed consent
- [0373]** Patients are excluded from the study if any of the following exclusion criteria apply:
8. Has a confirmed diagnosis of PH in WHO Group 1, WHO Group 3, WHO Group 4, or
- 5 WHO Group 5.
9. Has documented significant lung disease, defined as any of the following:
 - a. Chronic obstructive pulmonary disease (COPD) with post-bronchodilator forced expiratory volume in the first second (FEV1) <50% predicted;
 - b. Restrictive lung disease with total lung capacity <60% predicted;
 - 10 c. More than mild interstitial lung disease (ILD), with forced vital capacity <70% or FEV1 <60% predicted (still appropriate if absence of more than mild ILD, fibrosis, or COPD on computed tomography imaging).
 10. Has cardiovascular comorbidities, which include any of the following:
 - a. Moderate to severe rheumatic heart disease with mitral stenosis;
 - 15 b. Any history of greater than moderate mitral or aortic regurgitation valvular disease or greater than mild aortic or mitral stenosis. Severe tricuspid regurgitation may be included unless it is due to primary valvular disease, *e.g.*, from endocarditis, carcinoid, or mechanical destruction or pacemaker lead;
 - c. Acute coronary syndrome, coronary artery bypass graft, or percutaneous coronary
 - 20 intervention within 3 months of screening;
 - d. Uncontrolled heart rate (HR) (>110 beats per minute [bpm] at screening) from atrial fibrillation or atrial flutter;
 - e. History of or anticipated heart transplant or ventricular assist device implantation;
 - f. Anticipated implantation of pacemaker, pacemaker implantation within 14 days of
 - 25 screening, or history of implantable cardioverter defibrillator placement;
 - g. Occurrence of myocardial infarction within 3 months of screening;
 - h. History of known pericardial constriction, hypertrophic cardiomyopathy, cardiac sarcoidosis, or amyloid cardiomyopathy and/or infectious or infiltrative myopathy;
 - i. Uncontrolled systemic hypertension as evidenced by sitting sBP >160 mm Hg or sitting
 - 30 diastolic blood pressure (dbP) >110 mm Hg during screening after a period of rest;
 - j. Sitting sBP <120 mm Hg or sitting dbP <50 mm Hg during screening;
 - k. Resting HR of <50 bpm or >115 bpm at screening;
 - l. Stroke within 90 days of screening;

- m. Acutely decompensated heart failure that required hospitalization within 14 days of screening;
- n. ECG during screening with heart rate–corrected QT interval (QTc) by Fridericia’s method (QTcF) >470 milliseconds (ms) for males or >480 ms for females, or >500 ms if a
5 ventricular conduction defect (right bundle branch block, left bundle branch block, or interventricular conduction delay) is present;
- o. Personal or family history of Brugada syndrome;
- p. Personal or family history of long QT syndrome unless the participant’s ECG shows a normal QTc;
- 10 q. Arrhythmogenic right ventricular cardiomyopathy unless the participant has recent cardiac magnetic resonance imaging that shows no evidence of this diagnosis;
- r. Any history of mitral or aortic valve replacement or repair (mechanical or biomechanical);
- s. Complex congenital heart disease.
- 15 11. Was hospitalized for any indication with discharge within 14 days of screening.
- 12. Received any of the following classes of pulmonary arterial hypertension–specific therapies: endothelin receptor antagonists, prostacyclin analogs, soluble guanylate cyclase stimulators, and PDE5 (phosphodiesterase type 5) inhibitors within 30 days of screening.
- 13. Received IV inotropes (*e.g.*, dobutamine, dopamine, norepinephrine, vasopressin)
20 within 30 days of screening.
- 14. Has a known history of chronic liver disease, active hepatitis B infection (positive hepatitis B surface antigen and positive hepatitis B core antibodies), or hepatitis C infection (positive hepatitis C antibodies) at the screening visit. In patients with isolated positive hepatitis B core antibodies, a hepatitis B DNA test will be done to confirm the active hepatitis
- 25 B. In patients with positive hepatitis C antibodies, hepatitis C RNA will be done to confirm the active hepatitis C.
- 15. Has HIV infection or HIV seropositivity at the screening visit.
- 16. Has active tuberculosis, as determined by Quantiferon Gold test and confirmed by chest x-ray.
- 30 17. Has any of the following clinical laboratory values before screening as specified:
 - a. Serum alanine aminotransferase or aspartate aminotransferase levels >3× the upper limit of normal (ULN) or total bilirubin >3× ULN within 30 days of screening;

- b. Estimated glomerular filtration rate $<15 \text{ mL/min/1.73m}^2$ (CKD EPI [Chronic Kidney Disease Epidemiology Collaboration] equation) within 30 days of screening or required renal replacement therapy within 90 days of screening;
- c. Glycosylated hemoglobin (HbA1c) $>9\%$ within 30 days of screening;
- 5 d. Platelet count $<50,000/\text{mm}^3$ within 30 days of screening.
- 18. Has a history of severe allergic or anaphylactic reaction or hypersensitivity to recombinant proteins or excipients in the investigational product.
- 19. Had major surgery within 60 days of screening. Participants must have completely recovered from any previous surgery before screening.
- 10 20. Had a prior heart-lung transplant or has a life expectancy of <12 months.
- 21. Is pregnant or breastfeeding.
- 22. Has a history of active malignancy except for fully excised or treated basal cell carcinoma, cervical carcinoma in situ, or ≤ 2 squamous cell carcinomas of the skin.
- 23. Has a history of clinically significant (as determined by the investigator) endocrine,
- 15 hematologic, hepatic, (auto)immune, infectious (requiring chronic antibiotics), metabolic, urologic, pulmonary, neurologic, neuromuscular, dermatologic, psychiatric, renal, and/or another disease that may limit participation in the study.
- 24. Has body mass index (BMI) $<18 \text{ kg/m}^2$ or $\geq 40 \text{ kg/m}^2$.
- 25. Has a history of drug or alcohol abuse or has a positive urine drug screen for prohibited
- 20 drugs.
- 26. Received any vaccination, including COVID-19 vaccination, within 2 weeks before dosing or plans to receive a vaccine during the study.
- 27. Was previously administered relaxin or relaxin fusion proteins.
- 28. Was dosed in any clinical research study evaluating another investigational drug
- 25 (including biologics) or therapy (including specific immunotherapy) within 90 days or ≤ 5 half-lives (whichever is longer) of an investigational biologic drug, or ≤ 4 weeks for other investigational products, before the screening visit.
- 29. Is mentally or legally incapacitated, has significant emotional problems at the time of the study, or has a history of significant psychiatric disorders at the discretion of the
- 30 investigator.
- 30. Has a history of any illness that, in the opinion of the investigator, might confound the results of the study or pose additional risk to the participant.

* * *

[0374] The invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

- 5 [0375] All references (*e.g.*, publications or patents or patent applications) cited herein are incorporated herein by reference in their entireties and for all purposes to the same extent as if each individual reference (*e.g.*, publication or patent or patent application) was specifically and individually indicated to be incorporated by reference in its entirety for all purposes.

[0376] Other embodiments are within the following claims.

10

CLAIMS

1. A fusion protein comprising, from N-terminus to C-terminus,
a first peptide;
a linker peptide; and
a second peptide,
wherein:
(a) the first peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 502 and the second peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 503 or 504; or
the first peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 503 or 504 and the second peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 502; and
(b) the fusion protein has a pI from 6.0 to 8.2.
2. The fusion protein of claim 1, wherein the first peptide comprises the amino acid sequence X₁₁LCGRELVRAQIAIC (SEQ ID NO: 505), wherein X₁₁ is K, Q, D, E, L, I or Y.
3. The fusion protein of claim 1 or 2, wherein the first peptide consists of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, or 29 amino acids.
4. The fusion protein of claim 1, wherein the first peptide comprises the amino acid sequence X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein:
X₁₂ is K, Q, D, E, L, I, or Y;
X₁₃ is any amino acid except M, W, or C;
X₁₄ is K, Q, D, E, L, I, or Y;
X₁₅ is Q, D, E, L, I, Y or R; and
X₁₆ is R or Q.
5. The fusion protein of claim 4, wherein the first peptide comprises the amino acid sequence X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein:
X₁₂ is K, Q, D, E, L, I, or Y;

X₁₃ is H, K, Q, Y, L, N, I, S, T, or F;

X₁₄ is K, Q, D, E, L, I, or Y;

X₁₅ is Q, D, E, L, I, Y or R; and

X₁₆ is R or Q.

6. The fusion protein of claim 4 or 5, wherein X₁₃ is Q.
7. The fusion protein of any one of claims 4-6, wherein the first peptide consists of 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids.
8. The fusion protein of claim 1, wherein the second peptide comprises the amino acid sequence X₁₁LCGRELVRAQIAIC (SEQ ID NO: 505), wherein X₁₁ is K, Q, D, E, L, I or Y.
9. The fusion protein of claim 8, wherein the second peptide consists of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, or 29 amino acids.
10. The fusion protein of any one of claims 1, 8, and 9, wherein the second peptide comprises the amino acid sequence X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein:
 - X₁₂ is K, Q, D, E, L, I, or Y;
 - X₁₃ is any amino acid except M, W, or C;
 - X₁₄ is K, Q, D, E, L, I, or Y;
 - X₁₅ is Q, D, E, L, I, Y or R; and
 - X₁₆ is R or Q.
11. The fusion protein of claim 1, wherein the second peptide comprises the amino acid sequence X₁₂CCX₁₃VGCTX₁₄X₁₅SLAX₁₆FC (SEQ ID NO: 506), wherein:
 - X₁₂ is K, Q, D, E, L, I, or Y;
 - X₁₃ is H, K, Q, Y, L, N, I, S, T, or F;
 - X₁₄ is K, Q, D, E, L, I, or Y;
 - X₁₅ is Q, D, E, L, I, Y or R; and
 - X₁₆ is R or Q.

12. The fusion protein of claim 10 or 11, wherein X_{13} is Q.
13. The fusion protein of any one of claims 10-12, wherein the second peptide consists of 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids.
14. The fusion protein of any one of the preceding claims, wherein the linker peptide comprises an amino acid sequence with 12-15 amino acids.
15. The fusion protein of any one of the preceding claims, wherein:
the linker peptide comprises the amino acid sequence ASDAAGAX₈AX₉AGA (SEQ ID NO: 17), wherein:
X₈ is D, E, N, or Q; and
X₉ is D, E, N, or Q; or
the linker peptide comprises the amino acid sequence GGEGSGGEGX₁₀GGG (SEQ ID NO: 25), wherein:
X₁₀ is E or S.
16. The fusion protein of claim 15, wherein X₈ is D, E, N, or Q, and X₉ is D, E, or Q; or X₈ is D, E, or Q, and X₉ is D, E, N, or Q.
17. The fusion protein of any one of the preceding claims, wherein the linker peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 18, 19, 20, 21, 22, 23, 24, 26, and 27.
18. A fusion protein comprising, from N-terminus to C-terminus,
a first peptide;
a linker peptide; and
a second peptide,
wherein:
(a) the first peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 1, wherein the amino acid at at least one of positions 4 or 25 of the first peptide is not M; and the second peptide comprises an amino acid sequence that has 0,

1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 8, wherein the amino acid at position 22 of the second peptide is not R; or

the first peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 8, wherein the amino acid at position 22 of the second peptide is not R; and the second peptide comprises an amino acid sequence that has 0, 1, 2, 3, 4, or 5 amino acid modifications relative to the amino acid sequence of SEQ ID NO: 1, wherein the amino acid at at least one of positions 4 or 25 of the first peptide is not M; and

(b) the fusion protein has a pI from 6.0 to 8.2.

19. The fusion protein of claim 18, wherein the linker peptide comprises an amino acid sequence with 12-15 amino acids.

20. The fusion protein of claim 18 or 19, wherein:

the linker peptide comprises the amino acid sequence ASDAAGAX₈AX₉AGA (SEQ ID NO: 17), wherein:

X₈ is D, E, N, or Q; and

X₉ is D, E, N, or Q; or

the linker peptide comprises the amino acid sequence GGEGSGGEGX₁₀GGG (SEQ ID NO: 25), wherein:

X₁₀ is E or S.

21. The fusion protein of claim 20, wherein X₈ is D, E, N, or Q, and X₉ is D, E, or Q; or X₈ is D, E, or Q, and X₉ is D, E, N, or Q.

22. A fusion protein comprising, from N-terminus to C-terminus:

a first peptide;

a linker peptide; and

a second peptide,

wherein:

the linker peptide comprises the amino acid sequence ASDAAGAX₈AX₉AGA (SEQ ID NO: 17), wherein:

X₈ is D, E, N, or Q; and

X₉ is D, E, N, or Q; or

the linker peptide comprises the amino acid sequence GGEGSGGEGX₁₀GGG (SEQ ID NO: 25), wherein:

X₁₀ is E or S.

23. The fusion protein of claim 22, wherein X₈ is D, E, N, or Q, and X₉ is D, E, or Q; or X₈ is D, E, or Q, and X₉ is D, E, N, or Q.

24. The fusion protein of any one of claims 18-23, wherein the linker peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 18, 19, 20, 21, 22, 23, 24, 26, and 27.

25. The fusion protein of any one of claims 1-3, and 10-24, wherein the first peptide comprises the amino acid sequence DSX₁QEEVIX₂LCGRELVRAQIAICGX₃ST (SEQ ID NO: 7), wherein:

X₁ is not M, H, or C;

X₂ is K, Q, D, E, L, I or Y; and

X₃ is K or Q.

26. The fusion protein of any one of claims 1-3, and 10-25, wherein the first peptide comprises the amino acid sequence DSX₁QEEVIX₂LCGRELVRAQIAICGX₃ST (SEQ ID NO: 7), wherein:

X₁ is W, Y, F, L, I, V or A;

X₂ is K, Q, D, E, L, I or Y; and

X₃ is K or Q.

27. The fusion protein of claim 25 or 26, wherein X₁ is Y.

28. The fusion protein of any one of claims 25-27, wherein the first peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, 5, and 6.

29. The fusion protein of any one of claims 1-3, and 10-28, wherein the first peptide consists of 27, 28, or 29 amino acids.
30. The fusion protein of any one of claims 1, 4-9, and 14-24, wherein the first peptide comprises the amino acid sequence QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein:
- X₄ is K, Q, D, E, L, I, or Y;
 - X₅ is any amino acid except M, W, or C;
 - X₆ is K, Q, D, E, L, I, or Y; and
 - X₇ is Q, D, E, L, I, Y or R.
31. The fusion protein of any one of claims 1, 4-9, 14-24, and 30, wherein the first peptide comprises the amino acid sequence QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein:
- X₄ is K, Q, D, E, L, I, or Y;
 - X₅ is H, K, Q, Y, L, N, I, S, T, or F;
 - X₆ is K, Q, D, E, L, I, or Y; and
 - X₇ is Q, D, E, L, I, Y or R.
32. The fusion protein of claim 30 or 31, wherein X₅ is Q.
33. The fusion protein of any one of claims 30-32, wherein the first peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, and 507.
34. The fusion protein of any one of claims 1, 4-9, 14-24, and 30-33, wherein the first peptide consists of 24 or 25 amino acids.
35. The fusion protein of any one of claims 1, 4-9, and 14-24, wherein the second peptide comprises the amino acid sequence DSX₁QEEVIX₂LCGRELVRAQIAICGX₃ST (SEQ ID NO: 7), wherein:
- X₁ is not M, H, or C;

X₂ is K, Q, D, E, L, I or Y; and

X₃ is K or Q.

36. The fusion protein of any one of claims 1, 4-9, 14-24, and 35, wherein the second peptide comprises the amino acid sequence DSX₁QEEVIX₂LCGRELVRAQIAICGX₃ST (SEQ ID NO: 7), wherein:

X₁ is W, Y, F, L, I, V or A;

X₂ is K, Q, D, E, L, I, or Y; and

X₃ is K or Q.

37. The fusion protein of claim 35 or 36, wherein X₁ is Y.

38. The fusion protein of any one of claims 35-37, wherein the second peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, 5, and 6.

39. The fusion protein of any one of claims 1, 4-9, 14-24, and 35-38, wherein the second peptide consists of 27, 28, or 29 amino acids.

40. The fusion protein of any one of claims 1-3, and 10-24, wherein the second peptide comprises the amino acid sequence QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein:

X₄ is K, Q, D, E, L, I, or Y;

X₅ is any amino acid except M, W, or C;

X₆ is K, Q, D, E, L, I, or Y; and

X₇ is Q, D, E, L, I, Y or R.

41. The fusion protein of any one of claims 1-3, 10-24, and 40, wherein the second peptide comprises the amino acid sequence QLYSALANX₄CCX₅VGCTX₆X₇SLAQFC (SEQ ID NO: 16), wherein:

X₄ is K, Q, D, E, L, I, or Y;

X₅ is H, K, Q, Y, L, N, I, S, T, or F;

X₆ is K, Q, D, E, L, I, or Y; and

X₇ is Q, D, E, L, I, Y or R.

42. The fusion protein of claim 40 or 41, wherein X₅ is Q.
43. The fusion protein of any one of claims 40-42, wherein the second peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 9, 10, 11, 12, 13, 14, 15, and 507.
44. The fusion protein of any one of claims 1-3, 10-24, and 40-43, wherein the second peptide consists of 24 or 25 amino acids.
45. The fusion protein of any one of claims 1-3 and 10-24, wherein:
- the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 8;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 9;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 10;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 11;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 12;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 13;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 14;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 15;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 1 and the second peptide comprises the amino acid sequence of SEQ ID NO: 507;
 - the first peptide comprises the amino acid sequence of SEQ ID NO: 2 and the second peptide comprises the amino acid sequence of SEQ ID NO: 8;

the first peptide comprises the amino acid sequence of SEQ ID NO: 5 and the second peptide comprises the amino acid sequence of SEQ ID NO: 14;

the first peptide comprises the amino acid sequence of SEQ ID NO: 5 and the second peptide comprises the amino acid sequence of SEQ ID NO: 15;

the first peptide comprises the amino acid sequence of SEQ ID NO: 5 and the second peptide comprises the amino acid sequence of SEQ ID NO: 507;

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 8;

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 9;

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 10;

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 11;

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 12;

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 13;

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 14;

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 15; or

the first peptide comprises the amino acid sequence of SEQ ID NO: 6 and the second peptide comprises the amino acid sequence of SEQ ID NO: 507;.

46. The fusion protein of any one of claims 1, 4-9, and 14-24, wherein:

the first peptide comprises the amino acid sequence of SEQ ID NO: 8 and the second peptide comprises the amino acid sequence of SEQ ID NO: 1;

the first peptide comprises the amino acid sequence of SEQ ID NO: 8 and the second peptide comprises the amino acid sequence of SEQ ID NO: 2;

the first peptide comprises the amino acid sequence of SEQ ID NO: 8 and the second peptide comprises the amino acid sequence of SEQ ID NO: 3;

the first peptide comprises the amino acid sequence of SEQ ID NO: 8 and the second peptide comprises the amino acid sequence of SEQ ID NO: 4;

the first peptide comprises the amino acid sequence of SEQ ID NO: 8 and the second peptide comprises the amino acid sequence of SEQ ID NO: 5;

the first peptide comprises the amino acid sequence of SEQ ID NO: 8 and the second peptide comprises the amino acid sequence of SEQ ID NO: 6;

the first peptide comprises the amino acid sequence of SEQ ID NO: 9 and the second peptide comprises the amino acid sequence of SEQ ID NO: 1;

the first peptide comprises the amino acid sequence of SEQ ID NO: 9 and the second peptide comprises the amino acid sequence of SEQ ID NO: 2;

the first peptide comprises the amino acid sequence of SEQ ID NO: 9 and the second peptide comprises the amino acid sequence of SEQ ID NO: 3;

the first peptide comprises the amino acid sequence of SEQ ID NO: 9 and the second peptide comprises the amino acid sequence of SEQ ID NO: 4;

the first peptide comprises the amino acid sequence of SEQ ID NO: 9 and the second peptide comprises the amino acid sequence of SEQ ID NO: 5;

the first peptide comprises the amino acid sequence of SEQ ID NO: 9 and the second peptide comprises the amino acid sequence of SEQ ID NO: 6;

the first peptide comprises the amino acid sequence of SEQ ID NO: 10 and the second peptide comprises the amino acid sequence of SEQ ID NO: 1;

the first peptide comprises the amino acid sequence of SEQ ID NO: 10 and the second peptide comprises the amino acid sequence of SEQ ID NO: 2;

the first peptide comprises the amino acid sequence of SEQ ID NO: 10 and the second peptide comprises the amino acid sequence of SEQ ID NO: 3;

the first peptide comprises the amino acid sequence of SEQ ID NO: 10 and the second peptide comprises the amino acid sequence of SEQ ID NO: 4;

the first peptide comprises the amino acid sequence of SEQ ID NO: 10 and the second peptide comprises the amino acid sequence of SEQ ID NO: 5;

the first peptide comprises the amino acid sequence of SEQ ID NO: 10 and the second peptide comprises the amino acid sequence of SEQ ID NO: 6;

the first peptide comprises the amino acid sequence of SEQ ID NO: 11 and the second peptide comprises the amino acid sequence of SEQ ID NO: 1;

the first peptide comprises the amino acid sequence of SEQ ID NO: 13 and the second peptide comprises the amino acid sequence of SEQ ID NO: 6;

the first peptide comprises the amino acid sequence of SEQ ID NO: 14 and the second peptide comprises the amino acid sequence of SEQ ID NO: 1;

the first peptide comprises the amino acid sequence of SEQ ID NO: 14 and the second peptide comprises the amino acid sequence of SEQ ID NO: 2;

the first peptide comprises the amino acid sequence of SEQ ID NO: 14 and the second peptide comprises the amino acid sequence of SEQ ID NO: 3;

the first peptide comprises the amino acid sequence of SEQ ID NO: 14 and the second peptide comprises the amino acid sequence of SEQ ID NO: 4;

the first peptide comprises the amino acid sequence of SEQ ID NO: 14 and the second peptide comprises the amino acid sequence of SEQ ID NO: 5;

the first peptide comprises the amino acid sequence of SEQ ID NO: 14 and the second peptide comprises the amino acid sequence of SEQ ID NO: 6;

the first peptide comprises the amino acid sequence of SEQ ID NO: 15 and the second peptide comprises the amino acid sequence of SEQ ID NO: 1;

the first peptide comprises the amino acid sequence of SEQ ID NO: 15 and the second peptide comprises the amino acid sequence of SEQ ID NO: 2;

the first peptide comprises the amino acid sequence of SEQ ID NO: 15 and the second peptide comprises the amino acid sequence of SEQ ID NO: 3;

the first peptide comprises the amino acid sequence of SEQ ID NO: 15 and the second peptide comprises the amino acid sequence of SEQ ID NO: 4;

the first peptide comprises the amino acid sequence of SEQ ID NO: 15 and the second peptide comprises the amino acid sequence of SEQ ID NO: 5;

the first peptide comprises the amino acid sequence of SEQ ID NO: 15 and the second peptide comprises the amino acid sequence of SEQ ID NO: 6;

the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 1;

the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 2;

the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 3;

the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 4;

the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 5; or

the first peptide comprises the amino acid sequence of SEQ ID NO: 507 and the second peptide comprises the amino acid sequence of SEQ ID NO: 6.

47. The fusion protein of any one of claims 1-3, 10-29, and 40-45, wherein the fusion protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 28-75 and 508-515.

48. The fusion protein of any one of claims 1-47, further comprising an IgG Fc.

49. The fusion protein of claim 48, wherein the IgG Fc comprises the amino acid alanine at each of EU positions 234 and 235.

50. The fusion protein of claim 48 or 49, wherein the IgG Fc comprises the amino acid alanine at EU position 329.

51. The fusion protein of any one of claims 48-50, wherein the IgG Fc comprises the amino acid alanine at each of EU positions 234, 235, and 329.

52. The fusion protein of any one of claims 48-51, wherein the IgG Fc comprises the amino acids alanine, alanine, alanine, leucine, and serine at EU positions 234, 235, 329, 428, and 434, respectively.

53. The fusion protein of any one of claims 48-51, wherein the IgG Fc comprises the amino acids lysine, phenylalanine, and tyrosine at EU positions 433, 434, and 436, respectively.

54. The fusion protein of any one of claims 48-53, wherein the IgG Fc comprises the amino acids tyrosine, threonine, and glutamate at EU positions 252, 254, and 256, respectively.

55. The fusion protein of any one of claims 48-54, wherein the IgG Fc comprises the amino acids leucine and serine at EU positions 428 and 434, respectively.
56. The fusion protein of claim 48, wherein the IgG Fc comprises an amino acid sequence at least 85% identical to the amino acid sequence of a human IgG1 Fc.
57. The fusion protein of claim 56, wherein the IgG Fc comprises the amino acid sequence of a human IgG1 Fc.
58. The fusion protein of claim 56 or 57, wherein the IgG Fc comprises an amino acid sequence at least 95% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 76-83.
59. The fusion protein of claim 56 or 57, wherein the IgG Fc comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 76-83.
60. The fusion protein of any one of claims 48-59, wherein the IgG Fc is linked to the N-terminus of the first peptide, optionally via an IgG Fc linker.
61. The fusion protein of any one of claims 48-59, wherein the IgG Fc is linked to the C-terminus of the second peptide, optionally via an IgG Fc linker.
62. The fusion protein of claim 60 or 61, wherein the IgG Fc linker comprises or consists of the amino acid sequence GGS or EGGS (SEQ ID NO: 299).
63. The fusion protein of any one of claims 1-3, 10-24, and 40-45, wherein the fusion protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 84-138 and 516-523.
64. The fusion protein of any one of claims 1-3, 10-24, and 40-45, wherein the fusion protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 139-193, 524-531, and 549.

65. A polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-6, 8-15, 18-24, 26-75, 84-193, 507-531, and 549-558.
66. A polynucleotide comprising a nucleotide sequence encoding the fusion protein of any one of claims 1-64 or the polypeptide of claim 65.
67. The polynucleotide of claim 66, wherein the polynucleotide is a DNA molecule.
68. The polynucleotide of claim 67, comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 194-248, 410-464, and 532-547.
69. The polynucleotide of claim 66, wherein the polynucleotide is an RNA molecule.
70. An expression vector comprising the polynucleotide of any one of claims 66-69.
71. The expression vector of claim 70, wherein the expression vector is a plasmid.
72. The expression vector of claim 70, wherein the expression vector is a viral vector.
73. A host cell comprising the polynucleotide of any one of claims 66-69 or the expression vector of any one of claims 70-72.
74. The host cell of claim 73, wherein the host cell is a prokaryotic cell.
75. The host cell of claim 74, wherein the prokaryotic cell is an *E. coli* cell or a *Bacillus* cell.
76. The host cell of claim 73, wherein the host cell is a eukaryotic cell.
77. The host cell of claim 76, wherein the eukaryotic cell is selected from the group consisting of a yeast cell, an insect cell, and a mammalian cell.

78. The host cell of claim 77, wherein the mammalian cell is selected from the group consisting of a CHO cell, a HeLa cell, and a 293 cell.
79. A population of cells comprising two or more of the host cells of any one of claims 73-78.
80. A method of producing the fusion protein of any one of claims 1-64 or polypeptide of claim 65, comprising culturing the host cell of any one of claims 73-78 under conditions such that the fusion protein is produced.
81. A pharmaceutical composition comprising an effective amount of the fusion protein of any one of claims 1-64, the polypeptide of claim 65, the polynucleotide of any one of claims 66-69, or the expression vector of any one of claims 70-72.
82. The pharmaceutical composition of claim 81, wherein the fusion protein has a circulating half-life of at least 14 days when administered to a human.
83. The pharmaceutical composition of claim 81 or 82, wherein the fusion protein has bioavailability of at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, or at least 70% when administered to a human.
84. The pharmaceutical composition of claim 82 or 83, wherein the administration is via intravenous administration or subcutaneous administration.
85. A method of enhancing a relaxin-2-related activity in a primary cell, comprising contacting the primary cell with the fusion protein of any of claims 1-64, thereby enhancing relaxin-2-related activity in the cell.
86. The method of claim 85, wherein the fusion protein activates relaxin-2 receptor (RXFP1) on a cell surface.

87. The method of claim 85 or 86, wherein the method elevates cAMP levels in the primary cell, inducing vasodilation, inducing the expression of angiogenic factors, inducing the expression of MMPs, and/or inducing collagen degradation.
88. The method of any one of claims 85-87, wherein the primary cell is selected from the group consisting of endothelial cells, vascular smooth muscle cells, other vascular cells, cardiomyocytes, other cardiac cells, and fibroblasts.
89. The method of any one of claims 85-88, wherein the primary cell is within a subject.
90. The method of claim 89, wherein the subject has a relaxin-2-associated disorder.
91. The method of claim 90, wherein the relaxin-2-associated disorder is selected from the group consisting of kidney diseases, fibrotic diseases, and cardiovascular diseases.
92. The method of claim 90 or 91, wherein the disorder is selected from the group consisting of pulmonary hypertension, pulmonary arterial hypertension (PAH), pulmonary hypertension due to left heart disease (PH-LHD), combined precapillary and postcapillary pulmonary hypertension (CpcPH), isolated postcapillary pulmonary hypertension (IpcPH), heart failure, heart failure with preserved ejection fraction (HFpEF), heart failure with mid-range ejection fraction (HFmrEF), heart failure with reduced ejection fraction (HFrEF), valvular heart disease, joint disease, frozen shoulder (also known as adhesive capsulitis), kidney disease, chronic kidney disease, and hypertensive kidney disease.
93. The method of claim 90 or 91, wherein the disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH) with heart failure with preserved ejection fraction (HFpEF).
94. The method of claim 90 or 91, wherein the disorder is isolated postcapillary pulmonary hypertension (IpcPH) with heart failure with preserved ejection fraction (HFpEF).

95. The method of claim 90 or 91, wherein the disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH) with heart failure with mid-range ejection fraction (HFmrEF).

96. The method of claim 90 or 91, wherein the disorder is isolated postcapillary pulmonary hypertension (IpcPH) with heart failure with mid-range ejection fraction (HFmrEF).

97. A method of treating a relaxin-associated disorder in a subject in need thereof, comprising administering to the subject an effective amount of the fusion protein of any one of claims 1-64, the polynucleotide of any one of claims 66-69, the expression vector of any one of claims 70-72, or the pharmaceutical composition of any one of claims 81-84, thereby treating the relaxin-associated disorder.

98. The method of claim 97, wherein the relaxin-associated disorder is a relaxin-2-associated disorder.

99. The method of claim 98, wherein the relaxin-2-associated disorder is selected from the group consisting of kidney diseases, fibrotic diseases, and cardiovascular diseases.

100. The method of claim 98 or 99, wherein the disorder is selected from the group consisting of pulmonary hypertension, pulmonary arterial hypertension (PAH), pulmonary hypertension due to left heart disease (PH-LHD), combined precapillary and postcapillary pulmonary hypertension (CpcPH), isolated postcapillary pulmonary hypertension (IpcPH), heart failure, heart failure with preserved ejection fraction (HFpEF), heart failure with mid-range ejection fraction (HFmrEF), heart failure with reduced ejection fraction (HFrEF), kidney disease, chronic kidney disease, and hypertensive kidney disease.

101. The method of claim 98 or 99, wherein the disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH) with heart failure with preserved ejection fraction (HFpEF).

102. The method of claim 98 or 99, wherein the disorder is isolated postcapillary pulmonary hypertension (IpcPH) with heart failure with preserved ejection fraction (HFpEF).

103. The method of claim 98 or 99, wherein the disorder is combined precapillary and postcapillary pulmonary hypertension (CpcPH) with heart failure with mid-range ejection fraction (HFmrEF).

104. The method of claim 98 or 99, wherein the disorder is isolated postcapillary pulmonary hypertension (IpcPH) with heart failure with mid-range ejection fraction (HFmrEF).

105. The method of any one of claims 97-104, wherein the method decreases arterial pressure, increases renal artery blood flow, increases cardiac filling at diastole, resolves established fibrosis, and/or suppresses new fibrosis development in the subject.

106. The method of any one of claims 97-104, wherein the method increases renal plasma flow in the subject.

107. The method of claim 106, wherein the increase in the renal plasma flow in the subject persists after 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 1 month after a single administration of the fusion protein.

108. The method of any one of claims 97-107, wherein the subject is administered the fusion protein by intravenous administration.

109. The method of claim 108, wherein the subject is administered from about 0.1 mg/kg to about 20 mg/kg of the fusion protein.

110. The method of claim 108 or 109, wherein the subject is administered about 0.3 mg/kg of the fusion protein.

111. The method of claim 108 or 109, wherein the subject is administered about 1 mg/kg of the fusion protein.

112. The method of claim 108 or 109, wherein the subject is administered about 3 mg/kg of the fusion protein.

113. The method of claim 108 or 109, wherein the subject is administered about 10 mg/kg of the fusion protein.
114. The method of any one of claims 97-107, wherein the subject is administered the fusion protein by subcutaneous administration.
115. The method of claim 114, wherein the subject is administered about 100 mg to about 1500 mg of the fusion protein.
116. The method of claim 114 or 115, wherein the subject is administered about 150 mg of the fusion protein.
117. The method of claim 114 or 115, wherein the subject is administered about 300 mg of the fusion protein.
118. The method of claim 114 or 115, wherein the subject is administered about 600 mg of the fusion protein.
119. The method of any one of claims 97-118, wherein the subject is administered the fusion protein once every 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 1 month.
120. The method of any one of claims 97-119, wherein the fusion protein is present in subject serum at a level of at least about 1 µg/mL, about 2 µg/mL, about 3 µg/mL, about 4 µg/mL, or about 5 µg/mL 1 day after administration.
121. The method of any one of claims 97-120, wherein the fusion protein is present in subject serum at a level of at least about 1 µg/mL, about 2 µg/mL, about 3 µg/mL, about 4 µg/mL, or about 5 µg/mL 2 days after administration.
122. The method of any one of claims 97-121, wherein the fusion protein is present in subject serum at a level of at least about 1 µg/mL, about 2 µg/mL, about 3 µg/mL, about 4 µg/mL, or about 5 µg/mL 3 days after administration.

123. The method of any one of claims 97-122, wherein the fusion protein is present in subject serum at a level of at least about 1 µg/mL, about 2 µg/mL, about 3 µg/mL, about 4 µg/mL, or about 5 µg/mL 4 days after administration.

124. The method of any one of claims 97-123, wherein the fusion protein is present in subject serum at a level of at least about 1 µg/mL, about 2 µg/mL, about 3 µg/mL, about 4 µg/mL, or about 5 µg/mL 5 days after administration.

125. The method of any one of claims 97-124, wherein the fusion protein is present in subject serum at a level of at least about 1 µg/mL, about 2 µg/mL, about 3 µg/mL, about 4 µg/mL, or about 5 µg/mL 6 days after administration.

126. The method of any one of claims 97-125, wherein the fusion protein is present in subject serum at a level of at least about 1 µg/mL, about 2 µg/mL, about 3 µg/mL, about 4 µg/mL, or about 5 µg/mL 7 days after administration.

127. The method of any one of claims 97-126, wherein the fusion protein is present in subject serum at a level of at least about 1 µg/mL, about 2 µg/mL, about 3 µg/mL, about 4 µg/mL, or about 5 µg/mL 14 days after administration.