CLAIMS

1. A modified relaxin polypeptide comprising a non-naturally encoded amino acid, wherein:

(a) the relaxin polypeptide comprises the relaxin A chain polypeptide of SEQ ID NO: 4 and the relaxin B chain polypeptide of SEQ ID NO: 5 or SEQ ID NO: 6 substituted with a non-naturally encoded amino acid at a position selected from the group consisting of: A chain residue 1, A chain residue 5, A chain residue 13, A chain residue 18, and B chain residue 7; and

(b) the non-naturally encoded amino acid is para-acetyl-phenylalanine that is optionally linked to a linker, polymer, water soluble polymer, or biologically active molecule.

2. The modified relaxin polypeptide of claim 1, wherein the relaxin B chain polypeptide is a polypeptide of SEQ ID NO: 6.

3. The modified relaxin polypeptide of claim 1 or claim 2, wherein said non-naturally encoded amino acid is at the position of A chain residue 1.

4. The modified relaxin polypeptide of any one of claims 1-3, wherein said non-naturally encoded amino acid is linked to said linker, polymer, water soluble polymer or biologically active molecule.

5. The modified relaxin polypeptide of any one of claims 1-4, wherein said non-naturally encoded amino acid is linked to said linker, polymer, water soluble polymer or biologically active molecule by an oxime linkage.

6. The modified relaxin polypeptide of any one of claims 1-4, wherein the non-naturally encoded amino acid is linked to a water soluble polymer.

7. The modified relaxin polypeptide of any one of claims 1-4, wherein the non-naturally encoded amino acid is linked to polymer comprising poly(ethylene glycol).

8. The modified relaxin polypeptide of claim 7, wherein said poly(ethylene glycol) has an average molecular weight of between about 0.1 kDa and about 100 kDa, between about 0.1 kDa and about 50 kDa, between about 1 kDa and about 40 kDa, between about 5 kDa and about 40 kDa, or about 20 kDa.

9. The modified relaxin polypeptide of any one of claims 1-8, wherein said modified relaxin polypeptide is recombinant, is produced in a eukaryotic host cell, is produced in a non-eukaryotic host cell, or is produced by *in vitro* translation.

10. The modified relaxin polypeptide of any one of claims 1-9, wherein the modified relaxin polypeptide exhibits an increased serum half-life compared to the wild-type relaxin polypeptide consisting of SEQ ID NO: 4 and SEQ ID NO: 5, wherein the serum half-life is optionally increased by an amount selected from at least about two- fold, at least about three-fold, at least about five-fold, or at least about ten-fold.

11. The modified relaxin polypeptide of any one of claims 1-10, wherein the modified relaxin polypeptide is biologically active.

12. The modified relaxin polypeptide of any one of claims 1-11 for use as a medicament.

13. The modified relaxin polypeptide of any one of claims 1-11 for use in treatment of a subject that suffers from atherosclerosis; Type 1 diabetes; Type 2 diabetes; coronary artery disease; scleroderma; stroke; diastolic dysfunction; familial hypercholesterolemia; isolated systolic hypertension; primary hypertension; secondary hypertension; left ventricular hypertrophy; arterial stiffness associated with long-term tobacco smoking; arterial stiffness associated with obesity; arterial stiffness associated with age; systemic lupus erythematosus; preeclampsia; hypercholesterolemia; or for use in increasing arterial compliance in perimenopausal, menopausal, and post-menopausal women at risk of the afore-mentioned disorders; or to modulate vasoconstriction, NO production, or platelet aggregation; or for use in treatment of angiotensin-II (AngII)-mediated vasoconstriction or endothelin-1 (ET-1)-mediated vasoconstriction; or for use in treatment of heart failure, congestive heart failure, loss or damage of myocardial

tissue, increase in ventricular filling pressure, ventricular wall stress, or an impaired integration of arterial and venous vasodilation.

14. The use of the modified relaxin polypeptide of any one of claims 1-11 in the manufacture of a medicament for the treatment of a subject that suffers from atherosclerosis; Type 1 diabetes; Type 2 diabetes; coronary artery disease; scleroderma; stroke; diastolic dysfunction; familial hypercholesterolemia; isolated systolic hypertension; primary hypertension; secondary hypertension; left ventricular hypertrophy; arterial stiffness associated with long-term tobacco smoking; arterial stiffness associated with obesity; arterial stiffness associated with age; systemic lupus erythematosus; preeclampsia; hypercholesterolemia; or for use in increasing arterial compliance in perimenopausal, menopausal, and post-menopausal women at risk of the afore-mentioned disorders; or to modulate vasoconstriction, NO production, or platelet aggregation; or for use in treatment of angiotensin-II (AngII)- mediated vasoconstriction or endothelin-1 (ET-1)-mediated vasoconstriction; or for use in treatment of heart failure, congestive heart failure, loss or damage of myocardial tissue, increase in ventricular filling pressure, ventricular wall stress, or an impaired integration of arterial and venous vasodilation.

15. A host cell comprising a nucleic acid encoding the relaxin A chain polypeptide of SEQ ID NO: 4 or the relaxin B chain polypeptide of SEQ ID NO: 5 or SEQ ID NO: 6 substituted with a non-naturally encoded amino acid at a position selected from the group consisting of: A chain residue 1, A chain residue 5, A chain residue 13, A chain residue 18, and B chain residue 7, wherein the non-naturally encoded amino acid is para-acetyl-phenylalanine, the host cell comprises an orthogonal tRNA synthetase and/or an orthogonal tRNA that, when said nucleic acid is translated, results in incorporation of said non-naturally encoded amino acid in said relaxin A chain polypeptide or relaxin B chain polypeptide, and the polynucleotide comprises at least one selector codon optionally selected from the group consisting of an amber codon, ochre codon, opal codon, a unique codon, a rare codon, and a four-base codon, wherein said selector codon encodes said non-naturally encoded amino acid.

16. A method of manufacturing the modified relaxin polypeptide of any one of claims 1 to 11, comprising: culturing cells comprising (1) a polynucleotide or polynucleotides encoding said relaxin A chain polypeptide and said relaxin B chain polypeptide comprising a selector codon that encodes said non-naturally encoded amino acid, (2) an orthogonal RNA synthetase and (3) an orthogonal tRNA under conditions to permit expression of the relaxin polypeptide comprising said non-naturally encoded amino acid; and purifying the relaxin polypeptide comprising said non-naturally encoded amino acid.