CLAIMS

What is claimed is:

1. A composition of variant Factor VII polypeptides, the variant Factor VII polypeptides comprising an amino acid sequence having at least two sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the at least two sequence alterations are (1) a glutamine residue substituted for the proline residue in position 10, and (2) a glutamic acid residue substituted for the lysine residue in position 32; wherein the ratio of moles of conjugated sialic acid per mole of N-linked glycan is within a range selected from the group consisting of (1) from 0 to 5;(2) from 0 to 4; (3) from 0 to 3; (4) from 0 to 2; (5) from 0 to 1 and (6) from 0 to 0.5.

2. The composition of claim 1, wherein the variant Factor VII polypeptide comprises at least four sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the at least four sequence alterations are (1) a glutamine residue substituted for the proline residue in position 10, (2) a glutamic acid residue substituted for the lysine residue in position 32, (3) a glutamic acid residue substituted for the arginine residue in position 36, and (4) a glutamic acid residue substituted for the alanine residue in position 34.

3. An isolated variant Factor VII polypeptide comprising an amino acid sequence having at least two sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the at least two sequence alterations are (1) a glutamine residue substituted for the proline residue in position 10, and (2) a glutamic acid residue substituted for the lysine residue in position 32, wherein the polypeptide has a ratio of moles of conjugated sialic acid to moles of N-linked glycan between 0 and 5.0.

4. The isolated variant Factor VII polypeptide of claim 3, wherein the polypeptide further comprises one or more sequence alterations selected from the group consisting of: a) a glutamic acid residue substituted for the arginine residue in position 36 relative to SEQ ID NO: 16, b) a glutamic acid residue substituted for the alanine residue in position 34 relative to SEQ ID No: 16, c) an asparagine residue substituted for the threonine residue in position 106 relative

to SEQ ID NO: 16, and d) an asparagine residue substituted for the valine residue in position 253 relative to SEQ ID NO:16.

5. The isolated variant Factor VII polypeptide of claim 3, wherein the polypeptide further comprises two or more sequence alterations selected from the group consisting of: a) a glutamic acid residue substituted for the arginine residue in position 36 relative to SEQ ID NO: 16, b) a glutamic acid residue substituted for the alanine residue in position 34 relative to SEQ ID No: 16, c) an asparagine residue substituted for the threonine residue in position 106 relative to SEQ ID NO: 16, and d) an asparagine residue substituted for the valine residue in position 253 relative to SEQ ID NO:16.

6. The isolated variant Factor VII polypeptide of claim 3, wherein the polypeptide further comprises three or more sequence alterations selected from the group consisting of: a) a glutamic acid residue substituted for the arginine residue in position 36 relative to SEQ ID NO: 16, b) a glutamic acid residue substituted for the alanine residue in position 34 relative to SEQ ID No: 16, c) an asparagine residue substituted for the threonine residue in position 106 relative to SEQ ID NO: 16, and d) an asparagine residue substituted for the valine residue in position 253 relative to SEQ ID NO:16.

7. The isolated variant Factor VII polypeptide of claim 3, wherein the polypeptide further comprises four or more sequence alterations selected from the group consisting of: a) a glutamic acid residue substituted for the arginine residue in position 36 relative to SEQ ID NO: 16, b) a glutamic acid residue substituted for the alanine residue in position 34 relative to SEQ ID No: 16, c) an asparagine residue substituted for the threonine residue in position 106 relative to SEQ ID NO: 16, and d) an asparagine residue substituted for the valine residue in position 253 relative to SEQ ID NO:16.

8. A composition of Factor VII polypeptides, wherein the Factor VII polypeptides comprise the amino acid sequence of SEQ ID NO: 16 and the ratio of moles of conjugated sialic acid to moles of N-linked glycan in the composition is within a range selected from the group

consisting of (a) from 1 to 5; (b) from 1 to 4; (c) from 1 to 3; (d) from 1 to 2; and (e) from 0.5 to 1.

9. A method of preparing an isolated desialylated Factor VII polypeptide, said method comprising

(1) obtaining a sialylated Factor VII polypeptide ;

(2) contacting the sialylated Factor VII polypeptide with sialidase under conditions such that sufficient amounts of covalently attached sialic acid residues are removed from the sialylated Factor VII polypeptide to produce a desialylated Factor VII polypeptide having a ratio of moles of conjugated sialic acid to moles of N-linked glycan selected from the group consisting of a) less than 0.05, b) less than 0.1, c) less than 1.0, d) less than 2.0, e) less than 3.0, f) less than 4.0, g) less than 5.0; and h) less than 6.0; and

(3) isolating the desialylated Factor VII polypeptide thereby produced.

10. The method of claim 9, wherein the Factor VII polypeptide comprises the wild-type Factor VII sequence of SEQ ID NO: 16.

11. The method of claim 9, wherein the Factor VII polypeptide comprises a variant sequence comprising two or more sequence alterations relative to SEQ ID NO: 16.

12. The method of claim 9, wherein the Factor VII polypeptide comprises a variant sequence comprising four or more sequence alterations relative to SEQ ID NO: 16.

13. The method of claim 9, wherein the Factor VII polypeptide comprises a variant sequence comprising six or more sequence alterations relative to SEQ ID NO: 16.

14. A method of preparing an isolated desialylated Factor VII polypeptide, said method comprising

(1) producing a Factor VII polypeptide in a recombinant cell line that is deficient in its ability to sialylate peptides such that it produces a desialylated Factor VII polypeptide having a

ratio of moles of conjugated sialic acid to moles of N-linked glycan selected from the group consisting of a) less than 0.05, b) less than 0.1, c) less than 1.0, d) less than 2.0, e) less than 3.0, f) less than 4.0, g) less than 5.0; and h) less than 6.0; and

(2) isolating the desialylated Factor VII polypeptide thereby produced.

15. The method of claim 14, wherein the Factor VII polypeptide comprises the wild-type Factor VII sequence of SEQ ID NO: 16.

16. The method of claim 14, wherein the Factor VII polypeptide comprises a variant sequence comprising two or more sequence alterations relative to SEQ ID NO: 16.

17. The method of claim 14, wherein the Factor VII polypeptide comprises a variant sequence comprising four or more sequence alterations relative to SEQ ID NO: 16.

18. The method of claim 14, wherein the Factor VII polypeptide comprises a variant sequence comprising six or more sequence alterations relative to SEQ ID NO: 16.

19. A method of preparing an isolated desialylated Factor VII polypeptide, said method comprising

(1) generating a recombinant cell line that coexpresses a recombinant Factor VII polypeptide and a recombinant sialidase enzyme;

(2) culturing said recombinant cell line to allow expression of both the recombinant Factor VII polypeptide and the recombinant sialidase enzyme, wherein said recombinant sialidase enzyme removes sufficient amounts of covalently attached sialic acid residues to produce a desialylated Factor VII polypeptide having a ratio of moles of conjugated sialic acid to moles of N-linked glycan selected from the group consisting of a) less than 0.05, b) less than 0.1, c) less than 1.0, d) less than 2.0, e) less than 3.0, f) less than 4.0, g) less than 5.0; and h) less than 6.0; and

(3) isolating the desialylated Factor VII polypeptide thereby produced.

20. The method of claim 19, wherein the Factor VII polypeptide comprises the wild-type Factor VII sequence of SEQ ID NO: 16.

21. The method of claim 19, wherein the Factor VII polypeptide comprises a variant sequence comprising two or more sequence alterations relative to SEQ ID NO: 16.

22. The method of claim 19, wherein the Factor VII polypeptide comprises a variant sequence comprising four or more sequence alterations relative to SEQ ID NO: 16.

23. The method of claim 19, wherein the Factor VII polypeptide comprises a variant sequence comprising six or more sequence alterations relative to SEQ ID NO: 16.

24. An isolated variant Factor VII polypeptide selected from the group consisting of:

(1) a polypeptide comprising a Factor VII amino acid sequence having sequence alterations relative to the sequence of SEQ ID NO: 16, wherein the sequence alterations consist of (1) a glutamine residue substituted for the proline residue in position 10, (2) a glutamic acid residue substituted for the lysine residue in position 32, and (3) a sequence alteration such that N-linked glycosylation at position 145 is disrupted;

(2) a polypeptide comprising a Factor VII amino acid sequence having sequence alterations relative to the sequence of SEQ ID NO: 16, wherein the sequence alterations consist of (1) a glutamine residue substituted for the proline residue in position 10, (2) a glutamic acid residue substituted for the lysine residue in position 32, and (3) a sequence alteration such that N-linked glycosylation at position 322 is disrupted;

(3) a polypeptide comprising a Factor VII amino acid sequence having sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the sequence alterations consist of (1) a glutamine residue substituted for the proline residue in position 10, and (2) a glutamic acid residue substituted for

the lysine residue in position 32, and (3) sequence alterations such that N-linked glycosylation at positions 145 and 322 is disrupted;

(4) a polypeptide comprising a Factor VII amino acid sequence having sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the sequence alterations consist of (1) a glutamine residue substituted for the proline residue in position 10, and (2) a glutamic acid residue substituted for the lysine residue in position 32, wherein positions 145 and 322 are asparagine and have attached N-linked glycosylation;

(5) a polypeptide comprising a Factor VII amino acid sequence having sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the sequence alterations consist of (1) a glutamine residue substituted for the proline residue in position 10, (2) a glutamic acid residue substituted for the lysine residue in position 32, (3) a glutamic acid residue substituted for the alanine residue in position 34, (4) a glutamic acid residue substituted for the arginine residue in position 36, and (5) a sequence alteration such that N-linked glycosylation at position 145 is disrupted;

(6) a polypeptide comprising a Factor VII amino acid sequence having sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the sequence alterations consist of (1) a glutamine residue substituted for the proline residue in position 10, (2) a glutamic acid residue substituted for the lysine residue in position 32, (3) a glutamic acid residue substituted for the alanine residue in position 34, (4) a glutamic acid residue substituted for the arginine residue in position 36, and (5) a sequence alteration such that N-linked glycosylation at position 322 is disrupted;

(7) a polypeptide comprising a Factor VII amino acid sequence having sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the sequence alterations consist of (1) a glutamine residue substituted for the proline residue in position 10, (2) a glutamic acid residue substituted for the lysine residue in position 32, (3) a glutamic acid residue substituted for the alanine residue in position 34, (4) a glutamic acid residue substituted for the

arginine residue in position 36, and (5) a sequence alterations such that N-linked glycosylation at positions 145 and 322 is disrupted; and

(8) a polypeptide comprising a Factor VII amino acid sequence having sequence alterations relative to the amino acid sequence of SEQ ID NO: 16, wherein the sequence alterations consist of (1) a glutamine residue substituted for the proline residue in position 10, (2) a glutamic acid residue substituted for the lysine residue in position 32, (3) a glutamic acid residue substituted for the alanine residue in position 34, and (4) a glutamic acid residue substituted for the arginine residue in position 36, wherein positions 145 and 322 are asparagine and have attached N-linked glycosylation.

25. A method for treating a mammal having a disease or a disorder wherein blood clot formation is desirable, said method comprising administering to a mammal in need thereof an effective amount of the composition of variant Factor VII polypeptides of claim 1, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

26. A method for treating a mammal having a disease or a disorder wherein blood clot formation is desirable, said method comprising administering to a mammal in need thereof an effective amount of the isolated variant Factor VII polypeptides of claim 3, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

27. A method for treating a mammal having a disease or a disorder wherein blood clot formation is desirable, said method comprising administering to a mammal in need thereof an effective amount of the composition of Factor VII polypeptides of claim 8, wherein the disease

or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

28. A method for treating a mammal having a disease or a disorder wherein blood clot formation is desirable, said method comprising administering to a mammal in need thereof an effective amount of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 9, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

29. A method for treating a mammal having a disease or a disorder wherein blood clot formation is desirable, said method comprising administering to a mammal in need thereof an effective amount of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 14, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

30. A method for treating a mammal having a disease or a disorder wherein blood clot formation is desirable, said method comprising administering to a mammal in need thereof an effective amount of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 19, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding,

thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

31. Use of the composition of variant Factor VII polypeptides of claim 1 in the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

32. Use of the isolated variant Factor VII polypeptides of claim 3 in the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

33. Use of the composition of Factor VII polypeptides of claim 8 in the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

34. Use of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 9 in the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

35. Use of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 14 in the treatment of a disease or disorder is selected from the

group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

36. Use of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 19 in the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

37. Use of the composition of variant Factor VII polypeptides of claim 1 in the preparation of a medicament for the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

38. Use of the isolated variant Factor VII polypeptides of claim 3 in the preparation of a medicament for the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

39. Use of the composition of Factor VII polypeptides of claim 8 in the preparation of a medicament for the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

40. Use of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 9 in the preparation of a medicament for the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

41. Use of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 14 in the preparation of a medicament for the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

42. Use of a composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 19 in the preparation of a medicament for the treatment of a disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

43. A pharmaceutical composition comprising the composition of variant Factor VII polypeptides of claim 1 and a pharmaceutically acceptable excipient.

44. A pharmaceutical composition comprising the isolated variant Factor VII polypeptides of claim 3 and a pharmaceutically acceptable excipient.

45. A pharmaceutical composition comprising the composition of Factor VII polypeptides of claim 8 and a pharmaceutically acceptable excipient.

46. A pharmaceutical composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 9 and a pharmaceutically acceptable excipient.

47. A pharmaceutical composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 14 and a pharmaceutically acceptable excipient.

48. A pharmaceutical composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 19 and a pharmaceutically acceptable excipient.

49. A method for treating a mammal having a disease or a disorder wherein blood clot formation is desirable, comprising administering to a mammal in need thereof an effective amount of a Factor VII polypeptide comprising the amino acid sequence of SEQ ID NO: 16 in which the ratio of moles of conjugated sialic acid to moles of N-linked glycan is less than 0.05, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

50. The method of claim 29, wherein the Factor VII polypeptide contains no detectable amount of conjugated sialic acid.

CLAIMS

1. A method of preparing an isolated desialylated Factor VII polypeptide, the method comprising

(1) generating a recombinant cell line that coexpresses a recombinant Factor VII polypeptide and a recombinant sialidase enzyme;

(2) culturing said recombinant cell line to allow expression of both the recombinant Factor VII polypeptide and the recombinant sialidase enzyme, wherein the recombinant sialidase enzyme removes sufficient amounts of covalently attached sialic acid residues to produce a desialylated Factor VII polypeptide having a ratio of moles of conjugated sialic acid to moles of N-linked glycan selected from the group consisting of a) less than 0.05, b) less than 0.1, c) less than 1.0, d) less than 2.0, e) less than 3.0, f) less than 4.0, g) less than 5.0; and h) less than 6.0; and

(3) isolating the desialylated Factor VII polypeptide thereby produced.

2. The method of claim 1, wherein the isolated desialylated Factor VII polypeptide comprises the wild-type Factor VII amino acid sequence of SEQ ID NO: 16.

3. The method of claim 1, wherein the isolated desialylated Factor VII polypeptide comprises a variant amino acid sequence comprising two or more sequence alterations relative to SEQ ID NO: 16.

4. The method of claim 1, wherein the isolated desialylated Factor VII polypeptide comprises the wild-type Factor VII amino acid sequence of SEQ ID NO: 16 and is glycosylated at amino acid positions 145 and 322.

5. The isolated desialylated Factor VII polypeptides prepared by the method of claim 1 for use in the treatment of a mammal having a disease or a disorder wherein blood clot formation is desirable.

6. The isolated desialylated Factor VII polypeptides of claim 5, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or

resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

7. A pharmaceutical composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 1 and a pharmaceutically acceptable excipient.

8. A method of preparing an isolated desialylated Factor VII polypeptide, the method comprising

(1) producing a Factor VII polypeptide in a recombinant cell line that is deficient in its ability to sialylate peptides such that it produces a desialylated Factor VII polypeptide having a ratio of moles of conjugated sialic acid to moles of N-linked glycan selected from the group consisting of a) less than 0.05, b) less than 0.1, c) less than 1.0, d) less than 2.0, e) less than 3.0, f) less than 4.0, g) less than 5.0; and h) less than 6.0; and

(2) isolating the desialylated Factor VII polypeptide thereby produced.

9. The method of claim 8, wherein the isolated desialylated Factor VII polypeptide comprises the wild-type Factor VII amino acid sequence of SEQ ID NO: 16.

10. The method of claim 8, wherein the isolated desialylated Factor VII polypeptide comprises a variant amino acid sequence comprising two or more sequence alterations relative to SEQ ID NO: 16.

11. The method of claim 8, wherein the isolated desialylated Factor VII polypeptide comprises the wild-type Factor VII amino acid sequence of SEQ ID NO: 16 and is glycosylated at amino acid positions 145 and 322.

12. The isolated desialylated Factor VII polypeptides prepared by the method of claim 8 for use in treatment of a mammal having a disease or a disorder wherein blood clot formation is desirable.

13. The isolated desialylated Factor VII polypeptides of claim 12, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or

resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

14. A pharmaceutical composition comprising isolated desialylated Factor VII polypeptides prepared by the method of claim 8 and a pharmaceutically acceptable excipient.

15. A composition of isolated desialylated Factor VII polypeptides, wherein the Factor VII polypeptides comprise the amino acid sequence of SEQ ID NO: 16 and the ratio of moles of conjugated sialic acid to moles of N-linked glycan in the composition is within a range selected from the group consisting of (a) from 1 to 5; (b) from 1 to 4; (c) from 1 to 3; (d) from 1 to 2; and (e) from 0.5 to 1.

16. The composition of claim 15, wherein the isolated desialylated Factor VII polypeptides are glycosylated at amino acid positions 145 and 322.

17. The composition of claim 15 for use in the treatment of a mammal having a disease or a disorder wherein blood clot formation is desirable.

18. The composition of claim 17, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding in a mammal undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

19. Human Factor VIIa polypeptide in which the ratio of moles of conjugated sialic acid to moles of N-linked glycan is less than 1.0; wherein the human Factor VIIa polypeptide comprises the amino acid sequence of SEQ ID NO: 16 and has glycans covalently attached at amino acid residues 145 and 322, for use in treating a patient having a disease or a disorder wherein blood clot formation is desirable.

20. The human Factor VIIa polypeptide of claim 19, wherein the ratio of moles of conjugated sialic acid to moles of N-linked glycan is less than 0.1.

21. The human Factor VIIa polypeptide of claim 19, wherein the human Factor VIIa polypeptide contains no detectable amount of conjugated sialic acid.

22. The human Factor VIIa polypeptide of claim 19, wherein the half-life of the human Factor VIIa polypeptide is less than one hour.

23. The human Factor VIIa polypeptide of claim 19, wherein the half-life of the human Factor VIIa polypeptide is less than 0.5 hour.

24. The human Factor VIIa polypeptide of claim 19, wherein the disease or disorder is hemorrhage.

25. The human Factor VIIa polypeptide of claim 19, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding while undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.

26. The use of a human Factor VIIa polypeptide in which the ratio of moles of conjugated sialic acid to moles of N-linked glycan is less than 1.0; wherein the human Factor VIIa polypeptide comprises the amino acid sequence of SEQ ID NO: 16 and has glycans covalently attached at amino acid residues 145 and 322, in the manufacture of a medicament for treating a patient having a disease or a disorder wherein blood clot formation is desirable.

27. The use of claim 26, wherein the ratio of moles of conjugated sialic acid to moles of N-linked glycan is less than 0.1.

28. The use of claim 27, wherein the human Factor VIIa polypeptide contains no detectable amount of conjugated sialic acid.

29. The use of claim 26, wherein the half-life of the human Factor VIIa polypeptide is less than one hour.

30. The use of claim 26, wherein the half-life of the human Factor VIIa polypeptide is less than 0.5 hour.

31. The use of claim 26, wherein the disease or disorder is hemorrhage.

32. The use of claim 26, wherein the disease or disorder is selected from the group consisting of a hemorrhage, gastrointestinal bleeding, uncontrolled bleeding, bleeding while undergoing transplantation or resection or surgery, variceal bleeding, thrombocytopenia, hemophilia, intracranial hemorrhage, aortic aneurysm, and over administration of an anticoagulant.