CLAIMS

1. An isolated variant Factor VII polypeptide that possesses Factor VII activity comprising an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 16,

wherein the variant comprises the N-linked glycosylation sites of wild-type human Factor VII at amino acid residues 145 and 322 with reference to SEQ ID NO: 16 and further comprises additional N-linked glycosylation site(s) beyond the two present in wild-type Factor VII of SEQ ID NO: 16, and

further wherein the polypeptide has a ratio of moles of conjugated sialic acid to moles of N-linked glycan between 0 and 1.0.

2. The isolated variant Factor VII polypeptide of claim 1, wherein the variant comprises the amino acid substitution V253N.

3. The isolated variant Factor VII polypeptide of claim 1, wherein the variant comprises the amino acid substitution T106N.

4. The isolated variant Factor VII polypeptide of claim 1, wherein the variant Factor VII polypeptide comprises one or more amino acid substitutions selected from the group consisting of P10Q, K32E, R36E, A34E, T106N, and V253N.

5. The isolated variant Factor VII polypeptide of claim 1, wherein the variant Factor VII polypeptide comprises two or more amino acid substitutions selected from the group consisting of P10Q, K32E, R36E, A34E, T106N, and V253N.

6. The isolated variant Factor VII polypeptide of claim 1, wherein the variant Factor VII polypeptide comprises three or more amino acid substitutions selected from the group consisting of P10Q, K32E, R36E, A34E, T106N, and V253N.

7. The isolated variant Factor VII polypeptide of claim 1, wherein the variant Factor VII polypeptide has an amino acid sequence that consists of the amino acid sequence of SEQ ID NO:17.

8. The isolated variant Factor VII polypeptide of claim 1, characterized by having at least 50% of the activity to promote blood clotting as wild type Factor VII measured under the same conditions.

9. An isolated variant Factor VII polypeptide according to claim 1, wherein the ratio of moles of conjugated sialic acid to moles of N-linked glycan is less than 0.1.

10. A method of preparing the isolated variant Factor VII polypeptide of claim 1, the method comprising

(1) obtaining a sialylated Factor VII polypeptide comprising an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 16 and comprising the N-linked glycosylation sites of wild-type human Factor VIII at amino acid residues 145 and 322 with reference to SEQ ID NO: 16 and further comprising additional N-linked glycosylation site(s) beyond the two present in wild-type Factor VII of SEQ ID NO: 16;

(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 between 0 and 1.0 and

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

11. A method of preparing the isolated variant Factor VII polypeptide according to claim 1, said method comprising

(1) producing a Factor VII polypeptide comprising an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 16 and comprising the N-linked glycosylation sites of wild-type human Factor VII at amino acid residues 145 and 322 with reference to SEQ ID NO: 16 and further comprising additional N-linked glycosylation site(s) beyond the two present in wild-type Factor VII of SEQ ID NO: 16 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 between 0 and 1.0; and

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

12. A method of preparing the isolated variant Factor VII polypeptide according to claim 1, said method comprising

(1) obtaining a recombinant cell line that coexpresses (a) a recombinant Factor VII polypeptide comprising an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 16 and comprising the N-linked glycosylation sites of wild-type human Factor VII at amino acid residues 145 and 322 with reference to SEQ ID NO: 16 and further comprising additional N-linked glycosylation site(s) beyond the two present in wild-type Factor VII of SEQ ID NO: 16; and (b) 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 between 0 and 1.0; and

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

13. The method of claim 10, wherein the variant Factor VII polypeptide comprises a variant sequence comprising four or more sequence alterations one being V253N and the others selected from the group consisting of P10Q, K32E, R36E, A34E, and T106N.

14. A pharmaceutical composition comprising the isolated variant Factor VII polypeptide of claim 1 and a pharmaceutically acceptable excipient.

15. Use of an effective amount of the isolated variant Factor VII polypeptide of claim 1, in the manufacture of a medicament for the treatment of a disease or a disorder wherein blood clot formation is desirable, 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, over administration of an anticoagulant, penetrating traumatic injury; blunt traumatic injury; bleeding in elective surgery; bleeding in cardiac surgery; bleeding in spinal surgery; orthopedic surgery; neurosurgery; oncology surgery; post-partum surgery; menorrhagia; bleeding in stem cell transplantation; bleeding in liver transplantation; gastrointestinal bleeding; active variceal bleeding in cirrhosis; non variceal bleeding in cirrhosis; diffuse alveolar hemorrhage; aortic aneurysm; intracerebral hemorrhage; traumatic brain injury; brain contusion; reversal of warfarin; reversal of heparin; reversal of anticoagulants; reversal of anti-thrombotics; Factor VII deficiency; burns; prophylaxis in hemophilia patients with inhibitors; partial hepatectomy for non-cirrhotic and cirrhotic patients; acquired hemophilia; idiopathic thrombocytopenic purpura; Glanzmann's Thrombasthenia; Glanzmann's Thrombasthenia refractory to platelet transfusion and Bernard-Soulier Syndrome, and wherein the medicament is to be administered to a mammal.

16. The use of claim 15, wherein the disease or disorder is a hemorrhage.

17. An isolated variant Factor VII polypeptide that possesses Factor VII activity comprising an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 16 and comprising the sequence alterations P10Q and K32E, wherein the variant comprises N-linked glycosylation sites of wild-type human Factor VII at amino acid residues 145 and 322 with reference to SEQ ID NO: 16 and further wherein the polypeptide has a ratio of moles of conjugated sialic acid to moles of N-linked glycan between 0 and 1.0.

18. Use of an effective amount of the isolated variant Factor VII polypeptide of claim 17, in the manufacture of a medicament for the treatment of a disease or a disorder wherein blood clot formation is desirable, , 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, over administration of an anticoagulant, penetrating traumatic injury; blunt traumatic injury; bleeding in elective surgery; bleeding in cardiac surgery; bleeding in spinal surgery; orthopedic surgery; neurosurgery; oncology surgery; post-partum surgery; menorrhagia; bleeding in stem cell transplantation; bleeding in liver transplantation; gastrointestinal bleeding; active variceal bleeding in cirrhosis; non variceal bleeding in cirrhosis; diffuse alveolar hemorrhage; aortic aneurysm; intracerebral hemorrhage; traumatic brain injury; brain contusion; reversal of warfarin; reversal of heparin; reversal of anticoagulants; reversal of anti-thrombotics; Factor VII deficiency; burns; prophylaxis in hemophilia patients with inhibitors; partial hepatectomy for non-cirrhotic and cirrhotic patients; acquired hemophilia; idiopathic thrombocytopenic purpura; Glanzmann’s Thrombasthenia; Glanzmann’s Thrombasthenia refractory to platelet transfusion and Bernard-Soulier Syndrome, and wherein the medicament is to be administered to a mammal.

19. An effective amount of the isolated variant Factor VII polypeptide of claim 1, for use in the treatment of a disease or a disorder wherein blood clot formation is desirable, 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, over administration of an anticoagulant, penetrating traumatic injury; blunt traumatic injury; bleeding in elective surgery; bleeding in cardiac surgery; bleeding in spinal surgery; orthopedic surgery; neurosurgery; oncology surgery; post-partum surgery; menorrhagia; bleeding in stem cell transplantation; bleeding in liver transplantation; gastrointestinal bleeding; active variceal bleeding in cirrhosis; non variceal bleeding in cirrhosis; diffuse alveolar hemorrhage; aortic aneurysm; intracerebral hemorrhage; traumatic brain injury; brain contusion; reversal of warfarin; reversal of heparin; reversal of anticoagulants; reversal of anti-thrombotics; Factor VII deficiency; burns; prophylaxis in hemophilia patients with inhibitors; partial hepatectomy for

non-cirrhotic and cirrhotic patients; acquired hemophilia; idiopathic thrombocytopenic purpura; Glanzmann's Thrombasthenia; Glanzmann's Thrombasthenia refractory to platelet transfusion and Bernard-Soulier Syndrome.

20. The use of claim 19, wherein the disease or disorder is a hemorrhage.

21. An effective amount of the isolated variant Factor VII polypeptide of claim 17, for use in the treatment of a disease or a disorder wherein blood clot formation is desirable, 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, over administration of an anticoagulant, penetrating traumatic injury; blunt traumatic injury; bleeding in elective surgery; bleeding in cardiac surgery; bleeding in spinal surgery; orthopedic surgery; neurosurgery; oncology surgery; post-partum surgery; menorrhagia; bleeding in stem cell transplantation; bleeding in liver transplantation; gastrointestinal bleeding; active variceal bleeding in cirrhosis; non variceal bleeding in cirrhosis; diffuse alveolar hemorrhage; aortic aneurysm; intracerebral hemorrhage; traumatic brain injury; brain contusion; reversal of warfarin; reversal of heparin; reversal of anticoagulants; reversal of anti-thrombotics; Factor VII deficiency; burns; prophylaxis in hemophilia patients with inhibitors; partial hepatectomy for non-cirrhotic and cirrhotic patients; acquired hemophilia; idiopathic thrombocytopenic purpura; Glanzmann's Thrombasthenia; Glanzmann's Thrombasthenia refractory to platelet transfusion and Bernard-Soulier Syndrome.