Claims:

1. A modified blood coagulation protein comprising:

(a) a blood coagulation protein selected from the group consisting of

(i) a blood coagulation protein with Factor IX (FIX) biological activity; and

ii) a blood coagulation protein with Factor VIII (FVIII) biological activity; and

(b) at least one polysialic acid (PSA) containing an active aminooxy group bound to said blood coagulation protein of (a) at one or more oxidized carbohydrate moieties;

wherein said modified blood coagulation protein has an oxime linkage between said one or more oxidized carbohydrate moieties and the active aminooxy group on the PSA;

wherein said modified blood coagulation protein has a specific activity of at least 50% relative to an unmodified blood coagulation protein.

2. The modified blood coagulation protein of claim 1 wherein said blood coagulation protein is a blood coagulation protein with FIX biological activity, and wherein said modified blood coagulation protein has a specific activity of at least 60% relative to an unmodified blood coagulation protein.

3. The modified blood coagulation protein of claim 1 wherein said blood coagulation protein is a blood coagulation protein with FVIII biological activity, and wherein said modified blood coagulation protein has a specific activity of at least 70% relative to an unmodified blood coagulation protein.

4. The modified blood coagulation protein of any one of claims 1-3 wherein the polysialic acid (PSA) containing an active aminooxy group comprises 1-50 ethylene glycol units.

5. The modified blood coagulation protein of claim 4 wherein the polysialic acid (PSA) containing an active aminooxy group has 2 or 4 ethylene glycol units.

6. The modified blood coagulation protein of any one of claims 1-5 wherein the PSA is comprised of 5-500 sialic acid units.

7. The modified blood coagulation protein of any one of claims 1-6 wherein the PSA is comprised of 10-300 sialic acid units.

8. The modified blood coagulation protein of any one of claims 1-5 wherein the PSA has a molecular weight from 2,000 Da to 45,000 Da.

9. The modified blood coagulation protein of any one of claims 1-5 and 8 wherein the PSA has a molecular weight from 3,000 Da to 35,000 Da.

10. The modified blood coagulation protein of any one of claims 1-5 and 8-9 wherein the PSA has a molecular weight from 5,000 Da to 25,000 Da.

11. The modified blood coagulation protein of any one of claims 1-10 wherein the oxidized carbohydrate moiety of the blood coagulation protein is located in the activation peptide of the blood coagulation protein.

12. The modified blood coagulation protein of any one of claims 1-11 wherein the blood coagulation protein is a full-length blood coagulation protein.

13. The modified blood coagulation protein of any one of claims 1-11 wherein the blood coagulation protein molecule is a full-length blood coagulation protein with FIX biological activity.

14. The modified blood coagulation protein of any one of claims 1-11 wherein the blood coagulation protein molecule is a full-length blood coagulation protein with FVIII biological activity.

15. The modified blood coagulation protein of any one of claims 1-14 wherein the PSA has a molecular weight from 3,000 Da to 35,000 Da and comprises 1-50 ethylene glycol units, and wherein the carbohydrate moiety is oxidized by the oxidizing agent sodium periodate ($NaIO_4$).

16. The modified blood coagulation protein of any one of claims 1-14 wherein the PSA has a molecular weight from 3,000 Da to 35,000 Da and has

2 or 4 ethylene glycol units, and wherein the carbohydrate moiety is oxidized by the oxidizing agent sodium periodate ($NaIO_4$).

17. A method of conjugating a polysialic acid (PSA) containing an active aminooxy group to an oxidized carbohydrate moiety of a blood coagulation protein, comprising contacting said oxidized carbohydrate moiety with at least one activated PSA under conditions that allow conjugation;

said blood coagulation protein selected from the group consisting of

(i) a blood coagulation protein with FIX biological activity; and

(ii) a blood coagulation protein with FVIII biological activity;

said carbohydrate moiety oxidized by incubation with a buffer comprising an oxidizing agent selected from the group consisting of sodium periodate ($NaIO_4$), lead tetraacetate ($Pb(OAc)_4$) and potassium perruthenate ($KRuO_4$); wherein an oxime linkage is formed between the oxidized carbohydrate moiety and the active aminooxy group on the PSA;

said modified blood coagulation protein having a specific activity of at least 50% relative to an unmodified blood coagulation protein.

18. The method of claim 17 wherein said blood coagulation protein is a blood coagulation protein with FIX biological activity, and wherein said modified blood coagulation protein has a specific activity of at least 60% relative to an unmodified blood coagulation protein.

19. The method of claim 17 wherein said blood coagulation protein is a blood coagulation protein with FVIII biological activity, and wherein said modified blood coagulation protein has a specific activity of at least 70% relative to an unmodified blood coagulation protein.

20. The method according to claim 17 wherein the PSA is comprised of about 10 - 300 sialic acid units.

21. The method of claim 17 wherein the PSA is comprised of 5-500 sialic acid units.

22. The method of claim 17 wherein the PSA has a molecular weight from 2,000 Da to 45,000 Da.

23. The method of claim 17 wherein the PSA has a molecular weight from 3,000 Da to 35,000 Da.

24. The method of claim 17 wherein the PSA has a molecular weight from 5,000 Da to 25,000 Da.

25. The method of any one of claims 17-24 wherein the oxidizing agent is sodium periodate ($NaIO_4$).

26. The method of any one of claims 17-25 wherein the oxidized carbohydrate moiety of the blood coagulation protein is located in the activation peptide of the blood coagulation protein.

27. The method of any one of claims 17-26 wherein the blood coagulation protein is a full-length blood coagulation protein.

28. The method of any one of claims 17-27 wherein the blood coagulation protein is FVIIa.

29. The method of any one of claims 17-27 wherein the blood coagulation protein is FVIII.

30. The method of any one of claims 17-27 wherein the blood coagulation protein molecule is a full-length blood coagulation protein with FVIII biological activity.

31. The method of any one of claims 17-27 wherein the blood coagulation protein is FIX.

32. The method of any one of claims 17-27 wherein the blood coagulation protein molecule is a full-length blood coagulation protein with FIX biological activity.

33. The method of any one of claims 17-32 wherein the polysialic acid (PSA) containing an active aminooxy group comprises 1-50 ethylene glycol units.

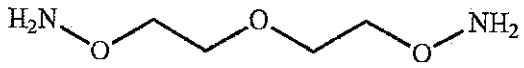
34. The method of claim 33 wherein the polysialic acid (PSA) containing an active aminooxy group has 2 or 4 ethylene glycol units.

35. The method of any one of claims 17-32 wherein the PSA has a molecular weight from 3,000 Da to 35,000 Da and comprises 1-50 ethylene glycol units, and wherein the oxidizing agent is sodium periodate ($NaIO_4$).

36. The method of any one of claims 17-32 wherein the PSA has a molecular weight from 3,000 Da to 35,000 Da and has 2 or 4 ethylene glycol units, and wherein the oxidizing agent is sodium periodate ($NaIO_4$).

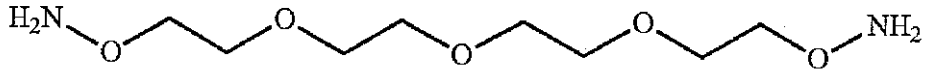
37. The method according to claim 17 wherein the PSA is prepared by reacting an activated aminooxy linker with oxidized PSA;

wherein the aminooxy linker is selected from the group consisting of:
(a) a 3-oxa-pentane-1,5-dioxyamine linker of the formula:



and

(b) a 3,6,9-trioxa-undecane-1,11-dioxyamine linker of the formula:



wherein the PSA is oxidized by incubation with a oxidizing agent to form a terminal aldehyde group at the non-reducing end of the PSA.

38 The method according to claim 37 wherein the aminooxy linker is 3-oxa-pentane-1,5-dioxyamine.

39. The method of any one of claims 17-38 wherein the contacting of the oxidized carbohydrate moiety with the activated PSA occurs in a buffer comprising a nucleophilic catalyst selected from the group consisting of aniline and aniline derivatives.

40. The method of any one of claims 17-39 further comprising the step of reducing an oxime linkage in the conjugated blood coagulation protein by incubating the conjugated blood coagulation protein in a buffer comprising a reducing compound selected from the group consisting of sodium cyanoborohydride ($NaCNBH_3$) and ascorbic acid (vitamin C).

41. The method of claim 40 wherein the reducing compound is sodium cyanoborohydride ($NaCNBH_3$).

42. Use of a blood coagulation protein according to any one of claims 1-16, in the preparation of a medicament for the treatment of a bleeding disorder.

43. The use according to claim 42, wherein the bleeding disorder is hemophilia A or hemophilia B.