CLAIMS

1. A method of targeting cell membrane phosphatidylserine (PtdS) comprising:

(a) providing an isolated polypeptide comprising a gamma-carboxyglutamic-acid (Gla) domain and lacking a protease or hormone-binding domain; and

(b) contacting said peptide with a cell surface,

wherein said polypeptide binds to PtdS on said cell membrane.

2. The method of claim 1, wherein said cell membrane is a cardiac cell membrane, a neuronal cell membrane, an endothelial cell membrane, a virus-infected cell membrane, an apoptotic cell membrane, a platelet membrane or a cancer cell membrane.

3. The method of claim 1, wherein said polypeptide further comprises an EGF binding domain.

4. The method of claim 1, wherein said polypeptide further comprises a Kringle domain.

5. The method of claim 1, wherein said polypeptide further comprises an aromatic amino acid stack domain.

6. The method of claim 1, wherein said Gla domain is a Gla domain from Factor II, Factor VII, Factor IX, Factor X, protein S or protein C.

7. The method of claim 1, wherein said polypeptide further comprises a detectable label.

8. The method of claim 7, wherein said detectable label is a fluorescent label, a chemilluminescent label, a radiolabel, an enzyme, a dye or a ligand.

9. The method of claim 1, wherein said polypeptide is 300 residues or less.

10. The method of claim 1, wherein said polypeptide is 200 residues or less.

1. A probe and/or therapeutic polypeptide suitable for targeting phosphatidylserine cell-surface expression both *in vitro* and *in vivo* said polypeptide comprising:

a protein S gamma-carboxyglutamic-acid (Gla) domain, and
an EGF domain,
wherein said polypeptide is fused to a proteinaceous sequence; and
wherein said polypeptide lacks a protease domain and also lacks a hormone-binding domain.

2. The polypeptide according to claim 1 comprising an EGF domain from protein S.

3. The polypeptide according to claim 2, wherein the GLA domain has the sequence shown in SEQ ID NO: 1.

4. The polypeptide according to any one of claims 1 to 3, wherein the polypeptide is 300 amino acids or less.

5. The polypeptide according to any one of claims 1 to 3, comprising SEQ ID NO: 6.

6. The polypeptide according to any one of claims 1 to 5, wherein the polypeptide further comprises an antibody Fc region.

7. A polypeptide according to any one of claims 1 to 6, for use in treatment.

8. A polypeptide according to claim 7, for use in treatment in a combination therapy.

9. Use of a polypeptide according to any one of claims 1 to 6, in the manufacture of a medicament for the treatment of cancer.

10. Use of a polypeptide according to any one of claims 1 to 6, in the manufacture of a medicament for the treatment of a viral infection.

11. Use according to claim 10, for the treatment of a viral infection selected from the group consisting of influenza, human immunodeficiency virus, dengue virus, West Nile virus, smallpox virus, respiratory syncytial virus, Korean hemorrhagic fever virus, chickenpox, varicella zoster virus, herpes simplex virus 1 or 2, Epstein-Barr virus, Marburg virus, hantavirus, yellow fever virus, hepatitis A, B, C or E, Ebola virus, human papilloma virus, rhinovirus, Coxsackie virus, polio virus, measles virus, rubella virus, rabies virus, Newcastle disease virus, rotavirus, HTLV-1 and -2.

12. Use of a polypeptide according to any one of claims 1 to 6, in the manufacture of a medicament for the treatment of hypercoagulation disorders.

~~11. The method of claim 1, wherein said polypeptide is 100 residues or less.~~

~~12. The method of claim 1, wherein said polypeptide comprises 5-15 Gla residues.~~

~~13. The method of claim 1, wherein said polypeptide comprises 9-13 Gla residues.~~

~~14. The method of claim 1, wherein said polypeptide comprises more than 13 Gla domains, but less than 30% total Gla residues.~~

~~15. The method of claim 1, wherein said polypeptide is between about 4.5 and 30 kD in size.~~

~~16. The method of claim 1, wherein said polypeptide comprises at least one disulfide bond.~~

~~17. The method of claim 1, wherein said polypeptide comprises 2-5 disulfide bonds.~~

~~18. The method of claim 1, wherein said polypeptide comprises protein S Gla domain.~~

~~19. The method of claim 1, wherein said polypeptide comprises protein S Gla domain and protein S EGF domain.~~

~~20. The method of claim 1, wherein said polypeptide comprises prothrombin Gla domain.~~

~~21. The method of claim 1, wherein said polypeptide comprises prothrombin Gla domain plus prothrombin Kringle domain.~~

~~22. The method of claim 1, wherein said polypeptide comprises protein Z Gla domain.~~

~~23. The method of claim 1, wherein said polypeptide comprises protein Z Gla domain plus prothrombin Kringle domain.~~

~~24. The method of claim 1, wherein said polypeptide comprises Factor VII Gla domain.~~

13. Use according to any one of claims 1 to 6, in the manufacture of a medicament for the treatment of autoimmune and/or an inflammatory disease state.

14. Use according to claim 13, wherein the disease state is selected from the group consisting of spondyloarthropathy, ankylosing spondylitis, psoriatic arthritis, reactive arthritis, enteropathic arthritis, ulcerative colitis, Crohn's disease, irritable bowel disease, inflammatory bowel disease, rheumatoid arthritis, juvenile rheumatoid arthritis, familial Mediterranean fever, amyotrophic lateral sclerosis, Sjogren's syndrome, early arthritis, viral arthritis, multiple sclerosis, systemic lupus erythematosus, psoriasis, vasculitis, Wegener's granulomatosis, Addison's disease, alopecia, antiphospholipid syndrome, Behcet's disease, celiac disease, chronic fatigue syndrome, ulcerative colitis, type I diabetes, fibromyalgia, autoimmune gastritis, Goodpasture syndrome, Graves' disease, idiopathic thrombocytopenic purpura (ITP), myasthenia gravis, pemphigus vulgaris, primary biliary cirrhosis, rheumatic fever, sarcoidosis, scleroderma, vitiligo, vasculitis, small vessel vasculitis, hepatitis, primary biliary cirrhosis, sarcoidosis, scleroderma, graft versus host disease (acute and chronic), aplastic anemia, and cyclic neutropenia.

15. Use of a polypeptide according to any one of claims 1 to 6, in the manufacture of a medicament for the treatment of sepsis.

25. The method of claim 1, wherein said polypeptide comprises Factor VII Gla domain plus prothrombin Kringle domain.

26. The method of claim 1, wherein said polypeptide further comprises an antibody Fc region.

27. A method of treating cancer in a subject comprising administering to said subject an isolated polypeptide comprising a gamma-carboxyglutamic-acid (Gla) domain and lacking a protease or hormone-binding domain.

28. The method of claim 27, where said cancer is breast cancer, brain cancer, stomach cancer, lung cancer, prostate cancer, ovarian cancer, testicular cancer, colon cancer, skin cancer, rectal cancer, cervical cancer, uterine cancer, liver cancer, pancreatic cancer, head & neck cancer or esophageal cancer.

29. The method of claim 27, further comprising treating said subject with a second cancer therapy.

30. The method of claim 28, wherein said second cancer therapy is an immunotherapy, a radiotherapy, a chemotherapy, a toxin therapy, a cytokine therapy or a hormone therapy.

31. A method of treating an autoimmune disease in a subject comprising administering to said subject an isolated polypeptide comprising a gamma-carboxyglutamic-acid (Gla) domain and lacking a protease or hormone-binding domain.

32. The method of claim 31, wherein said autoimmune disease is spondyloarthropathy, ankylosing spondylitis, psoriatic arthritis, reactive arthritis, enteropathic arthritis, ulcerative colitis, Crohn's disease, irritable bowel disease, inflammatory bowel disease, rheumatoid arthritis, juvenile rheumatoid arthritis, familial Mediterranean fever, amyotrophic lateral sclerosis, Sjogren's syndrome, early arthritis, viral arthritis, multiple sclerosis, systemic lupus erythematosus, psoriasis, vasculitis, Wegener's granulomatosis, Addison's disease, alopecia, antiphospholipid syndrome, Behcet's

~~disease, celiac disease, chronic fatigue syndrome, ulcerative colitis, type I diabetes, fibromyalgia, autoimmune gastritis, Goodpasture syndrome, Graves' disease, idiopathic thrombocytopenic purpura (ITP), myasthenia gravis, pemphigus vulgaris, primary biliary cirrhosis, rheumatic fever, sarcoidosis, scleroderma, vitiligo, vasculitis, small vessel vasculitis, hepatitis, primary biliary cirrhosis, sarcoidosis, scleroderma, graft versus host disease (acute and chronic), aplastic anemia, or cyclic neutropenia.~~

~~33. The method of claim 31, further comprising treating said subject with a second autoimmune disease therapy.~~

~~34. The method of claim 33, wherein said second autoimmune disease therapy is include prednisone, methylprednisone, Venipred, Celestone, hydrocortisone, triamcinoclone, Aristonpan Intra-Articular injection, Methapred, Rayos oral, betamethasone, or etanercept.~~

~~35. A method of treating a viral disease in a subject comprising administering to said subject an isolated polypeptide comprising a gamma-carboxyglutamic-acid (Gla) domain and lacking a protease or hormone binding domain.~~

~~36. The method of claim 35, wherein said viral disease is influenza, human immunodeficiency virus, dengue virus, West Nile virus, smallpox virus, respiratory syncytial virus, Korean hemorrhagic fever virus, chickenpox, varicella zoster virus, herpes simplex virus 1 or 2, Epstein-Barr virus, Marburg virus, hantavirus, yellow fever virus, hepatitis A, B, C or E, Ebola virus, human papilloma virus, rhinovirus, Coxsackie virus, polio virus, measles virus, rubella virus, rabies virus, Newcastle disease virus, rotavirus, HTLV-1 and -2.~~

~~37. The method of claim 35, further comprising treating said subject with a second anti-viral therapy.~~

~~38. The method of claim 37, wherein said second anti-viral therapy is Abacavir, Aciclovir, Acyclovir, Adefovir, Amantadine, Amprenavir, Ampligen, Arbidol, Atazanavir, Atripla, Boceprevirertet, Cidofovir, Combivir, Darunavir, Delavirdine,~~

~~Didanosine, Docosanol, Edoxudine, Efavirenz, Emtricitabine, Enfuvirtide, Entecavir, Entry inhibitors, Famciclovir, Fomivirsen, Fosamprenavir, Foscarnet, Fosfonet, Ganciclovir, Ibacitabine, Imunovir, Idoxuridine, Imiquimod, Indinavir, Inosine, Integrase inhibitor, Interferon type III, Interferon type II, Interferon type I, Interferon, Lamivudine, Lopinavir, Loviride, Maraviroc, Moroxydine, Methisazone, Nelfinavir, Nevirapine, Nexavir, Nucleoside analogues, Oseltamivir, Peginterferon alfa-2a, Penciclovir, Peramivir, Pleconaril, Podophyllotoxin, Protease inhibitor, Raltegravir, Reverse transcriptase inhibitor, Ribavirin, Rimantadine, Ritonavir, Pyramidine, Saquinavir, Stavudine, Synergistic enhancer (antiretroviral), Tea tree oil, Telaprevir, Tenofovir, Tenofovir disoproxil, Tipranavir, Trifluridine, Trizivir, Tromantadine, Truvada, Valaciclovir, Valganciclovir, Vicriviroc, Vidarabine, Viramidine, Zalcitabine, Zanamivir or Zidovudine.~~

~~39. A method of treating a hypercoagulation disorder in a subject comprising administering to said subject an isolated polypeptide comprising a gamma-carboxyglutamic-acid (Gla) domain and lacking a protease or hormone-binding domain.~~

~~40. The method of claim 39, further comprising treating said subject with a second anti-coagulant.~~

~~41. A method of modulating clotting in a subject comprising administering to said subject an isolated polypeptide comprising a gamma-carboxyglutamic-acid (Gla) domain and lacking a protease or hormone-binding domain.~~

~~42. The method claim 41, further comprising administering to said subject a clotting factor.~~

~~43. A method of treating sepsis in a subject comprising administering to said subject an isolated polypeptide comprising a gamma-carboxyglutamic-acid (Gla) domain and lacking a protease or hormone-binding domain.~~

~~44. A method of treating vaso-occlusive crisis in a sickle cell subject comprising administering to said subject an isolated polypeptide comprising a gamma-~~

~~carboxyglutamic-acid (Gla) domain and lacking a protease or hormone-binding domain.~~

~~45. A method treating a disorder characterized by pathologic expression of phosphatidylserine on the surface of a cell comprising administering to said subject an isolated polypeptide comprising a gamma-carboxyglutamic-acid (Gla) domain and lacking a protease or hormone-binding domain.~~