What is claimed is:

1. An isolated fusion protein comprising at least one human serpin polypeptide operably linked to a second polypeptide wherein the second polypeptide comprises at least one the following:

an immunoglobulin Fc polypeptide or an amino acid sequence that is derived from an immunoglobulin Fc polypeptide;

a cytokine targeting polypeptide or a sequence derived from a cytokine targeting polypeptide;

a WAP domain containing polypeptide or a sequence derived from a WAP domain containing polypeptide; or

an albumin polypeptide or an amino acid sequence that is derived from a serum albumin polypeptide.

2. An isolated fusion protein comprising at least one alpha-1 antitrypsin (AAT) polypeptide operably linked to a second polypeptide of at least one of the following:

an immunoglobulin Fc polypeptide;

a cytokine targeting peptide;

a human secretory leukocyte proteinase inhibitor (SLPI) polypeptide; and

an immunoglobulin Fc polypeptide and a human SLPI polypeptide, wherein the SLPI polypeptide comprises the WAP2 domain of human SLPI; or

a human serum albumin (HSA) polypeptide.

3. An isolated fusion protein comprising at least one alpha-1 antitrypsin (AAT) polypeptide operably linked to a second polypeptide of at least one of the following:

an immunoglobulin Fc polypeptide;

a cytokine targeting peptide;

a human Elafin polypeptide;

a human Elafin polypeptide and an immunoglobulin Fc polypeptide, wherein the Elafin polypeptide comprises the WAP domain of human Elafin; or

a human serum albumin (HSA) polypeptide.

4. The fusion protein of claim 1 wherein the human serpin polypeptide is a human alpha-1 antitrypsin (AAT) polypeptide or is derived from a human AAT polypeptide.

5. The isolated fusion protein of any one of claims 2-4, wherein AAT polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

6. The isolated fusion protein of any one of claims 2-4, wherein the AAT polypeptide comprises the reactive site loop of AAT comprising the amino acid sequence of SEQ ID NO: 1 or a mutated reactive site loop of AAT comprising the amino acid sequence of SEQ ID NO: 32 or 33.

7. The isolated fusion protein of any one of claims 2-4, wherein the immunoglobulin Fc polypeptide is a human Fc polypeptide.

8. The isolated fusion protein of claim 7, wherein human Fc polypeptide is a human IgM polypeptide or a human IgG Fc polypeptide.

9. The isolated fusion protein of claim 8, wherein the human IgG Fc polypeptide is a human IgG1 polypeptide, a human IgG2 Fc polypeptide, human IgG3 Fc polypeptide, or human IgG4 Fc polypeptide.

10. The isolated fusion protein of any one of claims 1-3, wherein the immunoglobulin Fc polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 3, 4, 5, 6, and 7.

11. The isolated fusion protein of claim 1, wherein the serpin polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

12. The isolated fusion protein of any one of claims 2-4, wherein the AAT polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

13. The isolated fusion protein of claim 11 or claim 12, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.

14. The isolated fusion protein of any one of claims 1-3, wherein the fusion protein comprises an amino acid sequence selected from SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, and SEQ ID NO: 21.

15. The isolated fusion protein of any one of claims 1-6, wherein the cytokine targeting polypeptide is a human cytokine receptor polypeptide or a derivative of a human cytokine receptor polypeptide, a cytokine targeting polypeptide that binds a cytokine receptor or a cytokine targeting polypeptide binds a human cytokine.

16. The isolated fusion protein of claim 15, wherein the human cytokine receptor polypeptide comprises multiple subunits.

17. The isolated fusion protein of claim 15 or claim 16, wherein the human cytokine receptor is a receptor for TNFα, IgE, IL-12, IL-23, IL-6, IL-1α, IL-1β, IL-17, IL-13, the p40 subunit of IL-12 and IL-23, IL-4, IL-10, IL-2, IL-18, IL-27, or IL-32.

18. The isolated fusion protein of claim 17, wherein the cytokine receptor is a receptor for human TNFα.

19. The isolated fusion protein of claim 15, wherein the human cytokine is TNFα, IgE, IL-12, IL-23, IL-6, IL-1α, IL-1β, IL-17, IL-13, the p40 subunit of IL-12 and IL-23, IL-4, IL-10, IL-2, IL-18, IL-27, or IL-32.

20. The isolated fusion protein of claim 19, wherein the cytokine is human TNFα.

21. The isolated fusion protein of claim 15, wherein the cytokine targeting polypeptide is an antibody or an antibody fragment.

22. The isolated fusion protein of claim 21, wherein the antibody or antibody fragment is chimeric, humanized, or fully human.

23. The isolated fusion protein of claim 1-6, where the fusion protein comprises an amino acid sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27.

24. The isolated fusion protein of claim 1, wherein the WAP domain containing polypeptide sequence comprises a SLPI polypeptide sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 8, 9 and 10.

25. The isolated fusion protein of claims 1, wherein the WAP domain containing polypeptide sequence comprises an elafin polypeptide sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 11, 12 and 13.

26. The isolated fusion protein of claim 1, wherein the fusion protein comprises a serpin polypeptide, a WAP domain-containing polypeptide and an immunoglobulin Fc polypeptide such that at least two of the serpin polypeptide, the WAP domain-containing polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

27. The isolated fusion protein of claim 2, wherein the fusion protein comprises an AAT polypeptide, a SLPI polypeptide and an immunoglobulin Fc polypeptide such that at least two of the AAT polypeptide, the SLPI polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

28. The isolated fusion protein of claim 3, wherein the fusion protein comprises an AAT polypeptide, an Elafin polypeptide and an immunoglobulin Fc polypeptide such that at least two of the AAT polypeptide, the Elafin polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

29. The isolated fusion protein of any one of claims 2-4, wherein the fusion protein comprises two AAT polypeptides and an immunoglobulin Fc polypeptide.

30. The isolated fusion protein of claim 29, wherein each of the two AAT polypeptides are operably linked to the immunoglobulin Fc polypeptide via a hinge region, a linker region, or both a hinge region and linker region such that the fusion protein has the structural arrangement from N-terminus to C-terminus as follows: AAT polypeptide-immunoglobulin Fc polypeptide-AAT polypeptide.

31. The isolated fusion protein of any one of claims 26-30, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.

32. The isolated fusion protein of claim 2, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 28.

33. The isolated fusion protein of claim 2, where the fusion protein comprises the amino acid sequence of SEQ ID NO: 29.

34. The fusion protein of claim 1, wherein the albumin polypeptide is a human serum albumin (HSA) polypeptide or is derived from a HSA polypeptide.

35. The isolated fusion protein of any one of claims 2, 3 or 34, wherein HSA polypeptide comprises the amino acid sequence of SEQ ID NO: 14 or the amino acid sequence of SEQ ID NO: 15.

36. The isolated fusion protein of any one of claims 2, 3 or 34, wherein the HSA polypeptide comprises domain 3 of HSA.

37. The isolated fusion protein of claim 34, wherein the serpin is operably linked to HSA via an albumin binding polypeptide.

38. The isolated fusion protein of claim 2 or claim 3, wherein the AAT polypeptide is operably linked to HSA via an albumin binding polypeptide.

39. The isolated fusion protein of claim 37 or 38, wherein the albumin binding polypeptide is an antibody or antibody fragment or derived from an antibody or antibody fragment.

40. The isolated fusion protein of claim 39, wherein the antibody or antibody fragment or chimeric, humanized, or fully human.

41. The isolated fusion protein of claims 37 or 38, wherein the albumin binding polypeptide is a peptide.

42. The isolated fusion protein of claims 47, wherein the albumin binding polypeptide is Domain 3 of *Streptococcal* Protein G or a sequence derived from Domain 3 of *Streptococcal* Protein G.

43. The isolated fusion protein of claim 1, wherein the serpin is covalently linked to a HSA polypeptide.

44. The isolated fusion protein of claim 1, wherein the serpin is non-covalently linked to a HSA polypeptide.

45. The isolated fusion protein any one of claims 1-3, where the fusion protein comprises the amino acid sequence of SEQ ID NO: 30 or 31.

46. The isolated fusion protein of any one of claims 1-3, wherein the immunoglobulin Fc polypeptide is modified to enhance FcRn binding.

47. The isolated fusion protein of any one of claims 1-3, wherein the immunoglobulin Fc polypeptide comprising at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser

48. A method of treating or alleviating a symptom of a disease or disorder associated with aberrant serine protease expression or activity in a subject in need thereof, the method comprising administering a fusion protein according to any one of the previous claims.

49. A method of treating or alleviating inflammation or a symptom of an inflammatory disease or disorder while reducing the risk of infection, in a subject in need thereof, the method comprising administering a fusion protein according to any one of the previous claims.

50. A method of reducing the risk of infection in a subject in need thereof, the method comprising administering a fusion protein according to any one of the previous claims.

51. The method of any one of claims 48-51, wherein the subject is a human.

52. The method of 49, wherein the inflammatory disease or disorder is selected from the following: emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), allergic asthma, cystic fibrosis, cancers of the lung, ischemia-reperfusion injury, ischemia/reperfusion injury following cardiac transplantation, myocardial infarction, rheumatoid arthritis, septic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, psoriasis, type I and/or type II diabetes, pneumonia, sepsis, graft versus host disease (GVHD), wound healing, Systemic lupus erythematosus, and Multiple sclerosis.

53. The method of 50, wherein the infection is selected from bacterial infections, fungal infections, or viral infections.

What is claimed is:

1. An isolated fusion protein comprising at least one human serpin polypeptide comprising a human alpha-1 antitrypsin (AAT) polypeptide comprising the amino acid sequence of SEQ ID NO: 1 operably linked to an immunoglobulin Fc polypeptide comprising the amino acid sequence of SEQ ID NO: 6.

2. The isolated fusion protein of claim 1, wherein AAT polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

3. The isolated fusion protein of claim 1, wherein the serpin polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

4. The isolated fusion protein of claim 3, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.

5. The isolated fusion protein of claim 4, wherein the peptide sequence comprises the amino acid sequence of SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, or SEQ ID NO: 46.

6. The isolated fusion protein of claim 1, wherein the fusion protein further comprises a WAP domain-containing polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 9-13.

7. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide is modified to enhance FcRn binding.

8. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide comprises at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser.

9. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide comprises at least one mutation at a position selected from the group consisting of: Met252, Ser254, Thr256, Met428, and Asn434.

10. An isolated fusion protein comprising at least one human alpha-1 antitrypsin (AAT) polypeptide comprising a human alpha-1 antitrypsin (AAT) polypeptide comprising the amino acid sequence of SEQ ID NO: 32 or SEQ ID NO: 33 operably linked to an immunoglobulin Fc polypeptide comprising the amino acid sequence of SEQ ID NO: 6.

11. The isolated fusion protein of claim 10, wherein the AAT polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

12. The isolated fusion protein of claim 10, wherein the fusion protein further comprises a SLPI polypeptide comprising the amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 10.

13. The isolated fusion protein of claim 11, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.

14. The isolated fusion protein of claim 10, wherein the immunoglobulin Fc polypeptide is modified to enhance FcRn binding.

15. The isolated fusion protein of claim 10, wherein the immunoglobulin Fc polypeptide comprises at least one mutation at a position selected from the group consisting of: Met252, Ser254, Thr256, Met428, and Asn434.

16. The isolated fusion protein of claim 10, wherein the immunoglobulin Fc polypeptide comprises at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser.

17. A method of treating or alleviating a symptom of a disease or disorder associated with aberrant serine protease expression or activity in a subject in need thereof, the method comprising administering a fusion protein according to claim 1 or claim 10.

18. The method of claim 17, wherein the subject is a human.

19. A method of treating or alleviating inflammation or a symptom of an inflammatory disease or disorder while reducing the risk of infection, in a subject in need thereof, the method comprising administering a fusion protein according to claim 1 or claim 10.

20. The method of claim 19, wherein the inflammatory disease or disorder is selected from the following: emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), allergic asthma, cystic fibrosis, cancers of the lung, ischemia-reperfusion injury, ischemia/reperfusion injury following cardiac transplantation, myocardial infarction, rheumatoid arthritis, septic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, psoriasis, type I and/or type II diabetes, pneumonia, sepsis, graft versus host disease (GVHD), wound healing, Systemic lupus erythematosus, and Multiple sclerosis.

21. A method of reducing the risk of infection in a subject in need thereof, the method comprising administering a fusion protein according to claim 1 or claim 10.

22. The method of claim 21, wherein the infection is selected from bacterial infections, fungal infections, or viral infections.