~~Claims~~

~~1. An isolated fusion protein comprising at least one human serpin polypeptide operably linked to a human immunoglobulin Fc polypeptide comprising the amino acid sequence of SEQ ID NO: 60, wherein the immunoglobulin Fc polypeptide comprises mutations at positions S228, L235, M252, and M428 (Kabat numbering system), and wherein the human serpin polypeptide is a human alpha 1 antitrypsin (AAT) polypeptide comprising the amino acid sequence of SEQ ID NO:80.~~

~~2. The isolated fusion protein of claim 1, wherein the fusion protein further comprises an additional polypeptide selected from the group consisting of:~~

~~a cytokine targeting polypeptide;~~

~~a whey acidic protein (WAP) domain containing polypeptide; or~~

~~an albumin polypeptide.~~

~~3. The isolated fusion protein of claim 1, wherein the AAT polypeptide comprises a mutated reactive site loop of AAT comprising the amino acid sequence of SEQ ID NO: 32.~~

~~4. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide comprises the amino acid sequence of SEQ ID NO: 73.~~

~~5. 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.~~

~~6. The isolated fusion protein of claim 5, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.~~

~~7. The isolated fusion protein of claim 1, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 79.~~

~~8. The isolated fusion protein of claim 1, wherein the mutations at positions S228, L235, M252, and M428 comprise S228P, L235E, M252Y, and M428L~~

~~9. Use of the fusion protein according to any one of claims 1-8 in the manufacture of a medicament for treating or alleviating a disease or disorder associated with aberrant serine protease expression or activity in a subject in need thereof, wherein the disease or disorder associated with aberrant serine protease expression or activity is alpha-1-antitrypsin deficiency.~~

~~10. Use of the fusion protein according to any one of claims 1-8 in the manufacture of a medicament for treating or alleviating inflammation or an inflammatory disease or disorder while reducing the risk of infection, in a subject in need thereof.~~

~~11. Use of the fusion protein according to any one of claims 1-8 in the manufacture of a medicament for reducing the risk of infection in a subject in need thereof.~~

~~12. The use of claim 11, wherein the subject is a human.~~

~~13. The use of claim 10, 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.~~

~~14. The use of claim 11, 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 operably linked to a modified human IgG4 Fc polypeptide, wherein the modified human IgG4 Fc polypeptide comprises the amino acid sequence of SEQ ID NO: 60, SEQ ID NO: 69, or SEQ ID NO: 70, and wherein the modified human IgG4 Fc polypeptide comprises a mutation at position M252 (residue 34 of SEQ ID NO: 60) and at position M428 (residue 210 of SEQ ID NO: 60), wherein the human serpin polypeptide is a human alpha-1 antitrypsin (AAT) polypeptide comprising an amino acid sequence according to SEQ ID NO: 80.

2. The isolated fusion protein of claim 1, wherein the fusion protein further comprises an additional polypeptide selected from the group consisting of:

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.

3. The isolated fusion protein of claim 1, wherein AAT polypeptide comprises a 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.

4. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide comprises the amino acid sequence of SEQ ID NO: 73.

5. The isolated fusion protein of claim 1 or claim 3, wherein the serpin polypeptide and the modified human IgG4 Fc polypeptide are operably linked via a linker region, optionally wherein the linker region comprises a peptide sequence.

6. The isolated fusion protein of claim 1, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 79.

7. The isolated fusion protein of claim 1, wherein the modified human IgG4 Fc polypeptide comprises a mutation at position T256 (residue 38 of SEQ ID NO: 60).

8. Use of a fusion protein of any one of claims 1 to 7 in the manufacture of a medicament for treating or alleviating a symptom of a disease or disorder associated with aberrant serine protease expression or activity in a subject in need thereof.

9. Use of a fusion protein of any one of claims 1 to 7 in the manufacture of a medicament for 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.

10. Use of a fusion protein of any one of claims 1 to 7 in the manufacture of a medicament for reducing the risk of infection in a subject in need thereof.

11. The use of claim 9, 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.

12. The use of claim 9 or 10, wherein the infection is selected from bacterial infections, fungal infections, or viral infections.