

## 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 one or more mutations at a position selected from S228, L235, M252, M258, M428 (Kabat numbering system), and combinations thereof 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 modified human IgG4 Fc polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 61, 62, 65, 66, 67, 68, 69, 70, 71, 72, and 73.
9. The isolated fusion protein of claim 8, 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.
10. The isolated fusion protein of claim 1 or claim 9, wherein the modified human IgG4 Fc polypeptide comprises one or more mutations at a position selected from M252 (residue 34 of SEQ ID NO: 60), T256 (residue 38 of SEQ ID NO: 60), M428 (residue 210 of SEQ ID NO: 60), and combinations thereof.
11. The isolated fusion protein of claim 1 or claim 9, 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).
12. Use of the fusion protein according to any one of claims 1-11 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.
13. Use of the fusion protein according to any one of claims 1-11 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.
14. Use of the fusion protein according to any one of claims 1-11 in the manufacture of a medicament for reducing the risk of infection in a subject in need thereof.
15. The use of claim 14, wherein the subject is a human.

16. The use of claim 14, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 79.

17. The use of claim 13, 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.

18. The use of claim 14, wherein the infection is selected from bacterial infections, fungal infections, or viral infections.