CLAIMS:

1. A modified membrane type serine protease 1 (MT-SP1) polypeptide or catalytically active fragment thereof, comprising an amino acid replacement in an MT-SP1 polypeptide, wherein:

the amino acid replacement is T98P or both T98P and F99L, based on chymotrypsin numbering in an unmodified MT-SP1 polypeptide;

the mutant MT-SP1 polypeptide and catalytically active fragment, which contains the amino acid replacement(s), exhibit increased substrate specificity for a complement protein target substrate compared to the MT-SP1 polypeptide not containing the amino acid replacement(s).

2. The modified MT-SP1 polypeptide or catalytically active fragment thereof of claim 1, comprising the amino acid replacement T98P.

3. The modified MT-SP1 polypeptide or catalytically active fragment thereof of claim 1 or claim 2, comprising an amino acid replacements T98P and F99L.

4. The MT-SP1 polypeptide or catalytically active fragment thereof of any of claims 1-3, wherein:

the unmodified MT-SP1 polypeptide comprises the sequence of amino acids set forth in SEQ ID NO:253 or 515; and the catalytically active portion comprises the sequence of amino acids set forth in SEQ ID NO: 505 or 507; or

MT-SP1 polypeptide has 95% or more sequence identity with a the MT-SP1 polypeptide set forth in SEQ ID NO:253, or a catalytically active portion thereof set forth in SEQ ID NO:505.

5. The modified MT-SP1 polypeptide or catalytically active fragment thereof of any of claims 1-4, wherein the MT-SP1 polypeptide or catalytically active portion thereof comprises up to 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid replacements compared to the MT-SP1 set forth in SEQ ID NO:253 or 505.

6. The modified MT-SP1 polypeptide or catalytically active fragment thereof of any of claims 1-5, wherein the unmodified MT-SP1 consists of the sequence of amino acids set forth in SEQ ID NO:507 or 515, whereby the modified MT-SP1 polypeptide comprises an amino acid replacement corresponding to the amino acid replacement C122S, based on chymotrypsin numbering.

7. The modified MT-SP1 polypeptide or catalytically active portion thereof of any of claims 1-6, wherein the modifications increase one or both of specificity for a C2 complement protein or activity towards C2 complement protein.

8. A pharmaceutical composition, comprising a modified protease or catalytically active portion thereof of any of claims 1-7 in a pharmaceutically acceptable excipient.

9. The pharmaceutical composition of claim 8, wherein the pharmaceutical composition is formulated for systemic, oral, nasal, pulmonary, local or topical administration.

10. A nucleic acid molecule, comprising a sequence of nucleotides that encodes a modified protease or catalytically active portion thereof of any of claims 1-9.

11. A vector, comprising the nucleic acid molecule of claim 10.

12. A cell, comprising the vector of claim 11.

13. A pharmaceutical composition, comprising a modified MT-SP1 polypeptide or catalytically active portion thereof of any of claims 1-7 for use in treatment of an inflammatory disease or condition or a disease or condition with an inflammatory component.

14. Use of a modified MT-SP1 polypeptide or catalytically active portion thereof of any of claims 1-7 for formulation of a medicament for treatment of an inflammatory disease or condition or a disease or condition with an inflammatory component.

15. The use of claim 14, wherein complement protein C2 is cleaved, resulting in decreased complement activation to thereby reduce inflammation.

16. The use of claim 14 or 15, wherein the disease or condition is selected from among autoimmune diseases, sepsis, Rheumatoid arthritis (RA), membranoproliferative glomerulonephritis (MPGN), Multiple Sclerosis (MS), Myasthenia gravis (MG), asthma, inflammatory bowel disease, immune complex (IC)-mediated acute inflammatory tissue injury, Alzheimer's Disease (AD), Ischemia-reperfusion injury, rejection of a transplanted organ, macular degeneration, and Guillain-Barre syndrome.

17. The use of claim 16, wherein the disease or condition is ischemia-reperfusion injury that is caused by an event or treatment selected from among myocardial infarct (MI), stroke, angioplasty, coronary artery bypass graft, cardiopulmonary bypass (CPB), and hemodialysis.

18. The pharmaceutical composition of claim 13, wherein the disease or condition is selected from among autoimmune diseases, sepsis, Rheumatoid arthritis (RA), membranoproliferative glomerulonephritis (MPGN), Multiple Sclerosis (MS), Myasthenia

gravis (MG), asthma, inflammatory bowel disease, immune complex (IC)-mediated acute inflammatory tissue injury, Alzheimer's Disease (AD), Ischemia-reperfusion injury, rejection of a transplanted organ, macular degeneration, and Guillain-Barre syndrome.

19. The pharmaceutical composition of claim 18, wherein the disease or condition is ischemia-reperfusion injury that ischemia-reperfusion injury is caused by an event or treatment selected from among myocardial infarct (MI), stroke, angioplasty, coronary artery bypass graft, cardiopulmonary bypass (CPB), and hemodialysis.

CLAIMS:

1. A modified matrix type serine protease-1 (MT-SP1) polypeptide or catalytically active fragment thereof, comprising an amino acid replacement in an MT-SP1 polypeptide, wherein:

the amino acid replacement is one or both of T98P and F99L, based on chymotrypsin numbering;

the mutant MT-SP1 polypeptide and catalytically active fragment, which contains the amino acid replacement(s), exhibit increased substrate specificity for a complement protein target substrate compared to the MT-SP1 polypeptide not containing the amino acid replacement(s).

2. The modified MT-SP1 polypeptide or catalytically active fragment thereof of claim 1, comprising the amino acid replacement T98P.

3. The modified MT-SP1 polypeptide or catalytically active fragment thereof of claim 1 or claim 2, comprising an amino acid replacement F99L.

4. The modified MT-SP1 polypeptide or catalytically active fragment thereof of any of claims 1-3, further comprising an amino acid replacement at Y60g.

5. A modified matrix type serine protease-1 (MT-SP1) polypeptide or a catalytically active portion thereof, comprising an amino acid replacement at a position corresponding to 60(g), based on chymotrypsin numbering, whereby substrate specificity or activity is altered compared to the MT-SP1 polypeptide not containing the amino acid replacement.

6. The MT-SP1 polypeptide or catalytically active fragment thereof of any of claims 1-5, wherein:

the unmodified MT-SP1 polypeptide comprises the sequence of amino acids set forth in SEQ ID NO:253 or 515; and the catalytically active portion comprises the sequence of amino acids set forth in SEQ ID NO: 505 or 507; or

MT-SP1 polypeptide has 95% or more sequence identity with a the MT-SP1 polypeptide set forth in SEQ ID NO:253, or a catalytically active portion thereof set forth in SEQ ID NO:505.

7. The modified MT-SP1 polypeptide or catalytically active fragment thereof of any of claims 1-6, wherein the MT-SP1 polypeptide or catalytically active portion thereof comprises up to 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid replacements compared to the MT-SP1 set forth in SEQ ID NO:253 or 505.

8. The modified MT-SP1 polypeptide or catalytically active fragment thereof of any of claims 1-7, wherein the unmodified MT-SP1 consists of the sequence of amino acids set forth in SEQ ID NO:507 or 515, whereby the modified MT-SP1 polypeptide comprises an amino acid replacement corresponding to the amino acid replacement C122S, based on chymotrypsin numbering.

9. The modified MT-SP1 polypeptide or catalytically active portion thereof of any of claims 1-8, wherein the modifications increase one or both of specificity for a C2 complement protein or activity towards C2 complement protein.

10. A pharmaceutical composition, comprising a modified protease or catalytically active portion thereof of any of claims 1-9 in a pharmaceutically acceptable excipient.

11. The pharmaceutical composition of claim 10, wherein the pharmaceutical composition is formulated for systemic, oral, nasal, pulmonary, local or topical administration.

12. A nucleic acid molecule, comprising a sequence of nucleotides that encodes a modified protease or catalytically active portion thereof of any of claims 1-9.

13. A vector, comprising the nucleic acid molecule of claim 12.

14. A cell, comprising the vector of claim 13.

15. A pharmaceutical composition, comprising a modified MT-SP1 polypeptide or catalytically active portion thereof of any of claims 1-9 for use in treatment of an inflammatory disease or condition or a disease or condition with an inflammatory component.

16. Use of a pharmaceutical composition comprising a modified MT-SP1 polypeptide or catalytically active portion thereof of any of claims 1-9 for treatment of an inflammatory disease or condition or a disease or condition with an inflammatory component.

17. The pharmaceutical composition of claim 15 or the use of claim 16, wherein complement protein C2 is cleaved, resulting in decreased complement activation to thereby reduce inflammation.

18. The pharmaceutical composition or use of any of claims 15-17, wherein the disease or condition is selected from among autoimmune diseases, sepsis, Rheumatoid arthritis (RA), membranoproliferative glomerulonephritis (MPGN), Multiple Sclerosis (MS), Myasthenia gravis (MG), asthma, inflammatory bowel disease, immune complex (IC)-mediated acute inflammatory tissue injury, Alzheimer's Disease (AD), Ischemia-reperfusion injury, rejection of a transplanted organ, macular degeneration, and Guillain-Barre syndrome.

19 The pharmaceutical composition or use of claim 18, wherein the ischemia-reperfusion injury is caused by an event or treatment selected from among myocardial infarct (MI), stroke, angioplasty, coronary artery bypass graft, cardiopulmonary bypass (CPB), and hemodialysis.