

62/713,804; 62/646,788; 62/613,545; and 62/613,564, incorporated herein by reference in their entirety for all purposes.

SUMMARY

[0006] Provided herein are antibodies that specifically bind human Tissue Factor (TF), anti-TF antibody-drug conjugates, and related methods. Provided herein are methods for treating inflammatory diseases by administering an antibody or ADC of the present disclosure.

[0006a] In one aspect, disclosed herein is a use of an antibody in the manufacture of a medicament for the treatment of an inflammatory disease in a subject in need thereof, wherein the antibody binds to the extracellular domain of human Tissue Factor (TF), wherein the antibody binds human TF at a human TF binding site that is distinct from a human TF binding site bound by human FVIIa.

[0007] In one aspect, provided herein is a method of treating an inflammatory disease in a subject in need thereof comprising administering to the subject an isolated antibody wherein the antibody binds to the extracellular domain of human Tissue Factor (TF), wherein the antibody binds human TF at a human TF binding site that is distinct from a human TF binding site bound by human FVIIa.

[0008] In some embodiments, the viral infection is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In some embodiments, the inflammatory disease is selected from: colitis, inflammatory bowel disease, arthritis, acute lung injury, acute respiratory distress syndrome (ARDS), and Respiratory Syncytial Virus (RSV). In some embodiments, the inflammatory disease is colitis. In some embodiments, the inflammatory disease is inflammatory bowel disease (IBD). In some embodiments, the inflammatory disease is arthritis. In some embodiments, the inflammatory disease is acute lung injury. In some embodiments, the inflammatory disease is ARDS. In some embodiments, the inflammatory disease is RSV. In some embodiments, the inflammatory disease is a cardiovascular disease or injury. In some embodiments, the cardiac disease or injury is myocardial infarction. In some embodiments, the inflammatory disease is a cardiovascular disease associated with upregulation of protease-activated receptor 2 (PAR-2).

[0009] In some embodiments, the antibody does not inhibit human thrombin generation as determined by thrombin generation assay (TGA). In some embodiments, the isolated human antibody does not inhibit or inhibits human thrombin generation to a lesser extent, as determined by thrombin generation assay (TGA), compared to a reference antibody comprising a V_H sequence of SEQ ID NO:821 and a V_L sequence of SEQ ID NO:822. In

some embodiments, binding between the isolated antibody and a variant TF extracellular domain comprising a mutation at amino acid residue 149 of the sequence shown in SEQ ID NO:810 is less than 50% of the binding between the isolated antibody and the extracellular domain of TF of the sequence shown in SEQ ID NO:810, as determined by the median fluorescence intensity value of the isolated antibody relative to an isotype control in a live