We claim:

1. An isolated antibody, or antigen-binding fragment thereof, that binds to the apple 2 (A2) domain of coagulation factor XI (FXI), wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable region (HCVR) comprising a heavy chain complementarity determining region (HCDR) 1, HCDR2, and HCDR3, and a light chain variable region (LCVR) comprising a light chain complementarity determining region (LCDR) 1, LCDR2, and LCDR3, wherein

(a) the HCDR1 comprises an amino acid sequence of SEQ ID NO: 5;

(b) the HCDR2 comprises an amino acid sequence of SEQ ID NO: 7;

(c) the HCDR3 comprises an amino acid sequence of SEQ ID NO: 9;

(d) the LCDR1 comprises an amino acid sequence of SEQ ID NO: 15;

(e) the LCDR2 comprises an amino acid sequence of SEQ ID NO: 17; and

(f) the LCDR3 comprises an amino acid sequence of SEQ ID NO: 19; or

wherein

(a) the HCDR1 comprises an amino acid sequence of SEQ ID NO: 33;

(b) the HCDR2 comprises an amino acid sequence of SEQ ID NO: 35;

(c) the HCDR3 comprises an amino acid sequence of SEQ ID NO: 37;

(d) the LCDR1 comprises an amino acid sequence of SEQ ID NO: 15;

(e) the LCDR2 comprises an amino acid sequence of SEQ ID NO: 17; and

(f) the LCDR3 comprises an amino acid sequence of SEQ ID NO: 19.

2. The isolated antibody, or antigen-binding fragment thereof, of claim 1, wherein the HCVR comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 3, and wherein the LCVR comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 13, or

wherein the HCVR comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 31, and wherein the LCVR comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 13.

3. The isolated antibody, or antigen-binding fragment thereof, of claim 2, wherein the HCVR comprises an amino acid sequence comprising SEQ ID NO: 3, and wherein the LCVR comprises an amino acid sequence comprising SEQ ID NO: 13, or

wherein the HCVR comprises an amino acid sequence comprising SEQ ID NO: 31, and wherein the LCVR comprises an amino acid sequence comprising SEQ ID NO: 13.

4. An isolated antibody, or antigen-binding fragment thereof, that binds to the apple 2 (A2) domain of coagulation factor XI (FXI), wherein the antibody, or antigen-binding fragment thereof, comprises

a heavy chain variable region (HCVR) comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 3 and a light chain variable region (LCVR) comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 13, or

a heavy chain variable region (HCVR) comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 31 and a light chain variable region (LCVR) comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 13.

5. The isolated antibody, or antigen-binding fragment thereof, of claim 4, wherein the HCVR comprises an amino acid sequence comprising SEQ ID NO: 3, and wherein the LCVR comprises an amino acid sequence comprising SEQ ID NO: 13, or

wherein the HCVR comprises an amino acid sequence comprising SEQ ID NO: 31, and wherein the LCVR comprises an amino acid sequence comprising SEQ ID NO: 13.

6. The isolated antibody, or antigen-binding fragment thereof, of claim 4 or claim 5, comprising:

(a) a HCDR1 comprising an amino acid sequence of SEQ ID NO: 5;

(b) a HCDR2 comprising an amino acid sequence of SEQ ID NO: 7;

(c) a HCDR3 comprising an amino acid sequence of SEQ ID NO: 9;

(d) a LCDR1 comprising an amino acid sequence of SEQ ID NO: 15;

(e) a LCDR2 comprising an amino acid sequence of SEQ ID NO: 17; and

(f) a LCDR3 comprising an amino acid sequence of SEQ ID NO: 19; or

comprising

(a) the HCDR1 comprises an amino acid sequence of SEQ ID NO: 33;

(b) the HCDR2 comprises an amino acid sequence of SEQ ID NO: 35;

(c) the HCDR3 comprises an amino acid sequence of SEQ ID NO: 37;

(d) the LCDR1 comprises an amino acid sequence of SEQ ID NO: 15;

(e) the LCDR2 comprises an amino acid sequence of SEQ ID NO: 17; and

(f) the LCDR3 comprises an amino acid sequence of SEQ ID NO: 19.

7. The isolated antibody or antigen-binding fragment of any one of the previous claims, wherein the antibody, or antigen-binding fragment thereof, binds human FXI with a K_D of less than about 1,000 pM as measured by surface plasmon resonance at 25ºC or 37ºC.

8. The isolated antibody or antigen-binding fragment of claim 7, wherein the antibody, or antigen-binding fragment thereof, binds human FXI with a K_D selected from the group consisting of less than about 800 pM, less than about 500 pM, less than about 100 pM, or less than about 50 pM as measured by surface plasmon resonance at 25ºC or 37ºC.

9. The isolated antibody or antigen-binding fragment of any one of the previous claims, wherein the antibody, or antigen-binding fragment thereof, binds human FXI with a dissociative half-life (t½) selected from the group consisting of greater than about 10 minutes, greater than about 60 minutes, greater than about 500 minutes, or greater than about 1,000 minutes as measured by surface plasmon resonance at 25ºC or 37ºC.

10. The isolated antibody or antigen-binding fragment of claim 1, wherein the antibody, or antigen-binding fragment thereof, inhibits activation of human coagulation factor X (FX) with an IC_{50} of less than about 10 nM.

11. The isolated antibody or antigen-binding fragment of any one of the previous claims, wherein the antibody, or antigen-binding fragment thereof, inhibits activation of human coagulation factor X (FX) with an IC_{50} of less than about 40 pM.

12. The isolated antibody or antigen-binding fragment of any one of the previous claims, wherein the antibody, or antigen-binding fragment thereof, increases by at least two-fold activated partial thromboplastin time (aPTT).

13. The isolated antibody or antigen-binding fragment of claim 12, wherein the antibody, or antigen-binding fragment thereof, does not increase prothrombin time (PT).

14. The isolated antibody or antigen-binding fragment of any one of the previous claims, wherein the antibody, or antigen-binding fragment thereof, inhibits FXIa-mediated thrombin activity by at least 5%, by at least 10%, by at least 15%, or by 5%-15%.

15. The isolated antibody or antigen-binding fragment of any one of the previous claims, wherein the antibody, or antigen-binding fragment thereof, prolongs aPTT by at least two-fold in human plasma at a concentration ≤100nM, ≤75nM, or ≤50nM.

16. The isolated antibody or antigen-binding fragment of claim 15, wherein the antibody, or antigen-binding fragment thereof, does not prolong PT.

17. The isolated antibody, or antigen-binding fragment thereof, of any one of the previous claims, wherein the antibody, or antigen-binding fragment thereof, inhibits thrombin production or activation via the intrinsic coagulation pathway in human plasma at a concentration of at least 10 nM, at least 25 nM, or at least 50 nM without affecting thrombin production or activation via the extrinsic coagulation pathway.

18. An isolated antibody, or antigen-binding fragment thereof, which competes for binding with the antibody, or antigen-binding fragment thereof, of any one of the previous claims.

19. An isolated antibody, or antigen-binding fragment thereof, which binds the same epitope as the antibody, or antigen-binding fragment thereof, of any one of the previous claims.

20. A pharmaceutical composition comprising the antibody, or antigen-binding fragment thereof, of any one of the previous claims, and a pharmaceutically acceptable carrier or diluent.

21. An isolated nucleic acid molecule comprising a polynucleotide sequence that encodes the antibody, or antigen-binding fragment thereof, according to any one of claims 1-19.

22. A vector comprising the nucleic acid molecule of claim 21.

23. A cell comprising the vector of claim 22 or the nucleic acid molecule of claim 21.

24. A method for inhibiting a biological activity mediated by FXI, the method comprising:

contacting FXI or FXIa with a biologically effective amount of the antibody, or antigen-binding fragment thereof, of any one of claims 1-19 or the pharmaceutical composition of claim 20.

25. The method of claim 24, wherein the biological activity is thrombogenesis, and wherein thrombogenesis is inhibited upon contact of FXI with the antibody, or antigen-binding fragment thereof.

26. The method of claim 25, wherein the contact results in prolonging aPTT or reducing thrombin activity in plasma.

27. Use of the antibody, or antigen-binding fragment thereof, of any one of claims 1-19 or the pharmaceutical composition of claim 20 in the manufacture of a medicament for treating or preventing a disease or disorder associated with FXI activity or expression, or for ameliorating at least

one symptom associated with the disease or disorder associated with FXI activity or expression, in a subject in need of such treatment.

28. The use of claim 27, wherein the disease or disorder is a disease or disorder of blood coagulation or a disease or disorder that provides an increased risk of thrombogenesis in the subject.

29. The use of claim 28, wherein the disease or disorder is atrial fibrillation.

30. The antibody, or antigen-binding fragment thereof, of any one of claims 1-19 or the pharmaceutical composition of claim 20 for use in therapy.