[00102] In one embodiment, the antibody, or antigen-binding fragment thereof, specifically binds human FXI.

[00103] In one embodiment, the disease or disorder to be treated with an anti-FXI antibody of the disclosure is thrombosis, and any complication resulting from thrombosis.

[00104] It is envisioned that any disease or disorder associated with FXI activity or expression is amenable to treatment with an antibody of the disclosure. These disorders may include any disease or condition in which harmful clot formation is a risk, especially, but not limited to, those conditions in which intrinsic clotting and hemostasis are a risk to the patient.

[00104a] In one aspect, the present disclosure refers to 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.

[00104b] In another aspect, the present disclosure refers to 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.

[00104c] In another aspect, the present disclosure refers to an isolated antibody, or antigen-binding fragment thereof, which competes for binding with the antibody, or antigen-binding fragment thereof, as described herein.

[00104d] In another aspect, the present disclosure refers to an isolated antibody, or antigen-binding fragment thereof, which binds the same epitope as the antibody, or antigen-binding fragment thereof, as described herein.

[00104e] In another aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody, or antigen-binding fragment thereof, as described herein, and a pharmaceutically acceptable carrier or diluent.

[00104f] In another aspect, the present disclosure refers to an isolated nucleic acid molecule comprising a polynucleotide sequence that encodes the antibody, or antigen-binding fragment thereof, as described herein.

[00104g] In another aspect, the present disclosure refers to a vector comprising the nucleic acid molecule as described herein.

[00104h] In another aspect, the present disclosure refers to a cell comprising the vector as described herein or the nucleic acid molecule as described herein.

[00104i] In another aspect, the present disclosure refers to 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, as described herein or the pharmaceutical composition as described herein.

[00104j] In yet another aspect, the present disclosure refers to use of the antibody, or antigen-binding fragment thereof, as described herein or the pharmaceutical composition as described herein 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.

[00104k] In yet another aspect, the present disclosure refers to the antibody, or antigen-binding fragment thereof, as described herein or the pharmaceutical composition as described herein for use in therapy.

[00105] Other embodiments will become apparent from a review of the ensuing detailed description.

BRIEF DESCRIPTION OF THE FIGURES

[00106] FIG. 1 depicts a line graph showing fold change in aPTT as a function of log concentration of antibody. Filled pyramids depict either an isotype control antibody (apex at top) or an FXI A2 antibody of the invention, REGN9933 (apex at bottom, labeled as H4H29790P2). Filled circles depict a comparator antibody that binds FXI A2.

[00107] FIG. 2 depicts a line graph showing thrombin activity as a function of concentration of isotype control antibody (REGN1945) over time.

[00108]FIG. 3 depicts a line graph showing thrombin activity as a function of concentration of subject antibody (REGN9933) that binds FXI A2 over time.

[00109]FIG. 4 depicts a line graph showing thrombin activity as a function of concentration of comparator antibody (COMP3448) that binds FXI A2 over time.

[00110]FIG. 5 depicts a line graph showing thrombin activity as a function of concentration of isotype control antibody (REGN1945) over time.

[00111]FIG. 6 depicts a line graph showing thrombin activity as a function of concentration of subject antibody (REGN9933) that binds FXI A2 over time.

[00112]FIG. 7 depicts a line graph showing thrombin activity as a function of concentration of comparator antibody (COMP3448) that binds FXI A2 over time.

[00113]FIG. 8A depicts a line graph showing fold change in activated partial thromboplastin time (aPTT) as a function of log concentration of antibody. The dark shade depicts an isotype control. The light shade depicts the subject antibody, REGN9933, that binds FXI A2. In the aPTT clotting assay, human donor plasma was incubated with 2-fold serial dilutions of either REGN9933 or an IgG4P isotype control 19nM to 1200nM followed by the addition of ellagic acid (EA), a specific activator of the intrinsic coagulation pathway. **FIG. 8B** depicts a line graph showing fold change in prothrombin time (PT) as a function of log concentration of antibody. In the PT clotting assay, human donor plasma was incubated with either REGN9933 or an IgG4P isotype control at 600nM and 1200nM followed by the addition of tissue factor (TF), a specific activator of the extrinsic coagulation pathway. **FIG. 8B** shows overlapping lines for REGN9933 and the IgG4P isotype control for the PT clotting assay;