Supplemental Data

Figure S1. The blocking FXI antibody, 1A6, which inhibits the FXI activation by α-FXIIa, does not inhibit the activation of FXI by thrombin.

FXI activation was quantified in a purified system following addition of 5 nM α-FXIIa (black bars) or 30 nM α-thrombin (white bars) to 50 nM FXI in presence of vehicle or 50 μg/ml 1A6. FXIa generation was measured with a chromogenic substrate. Data are mean ± SE (n = 3).

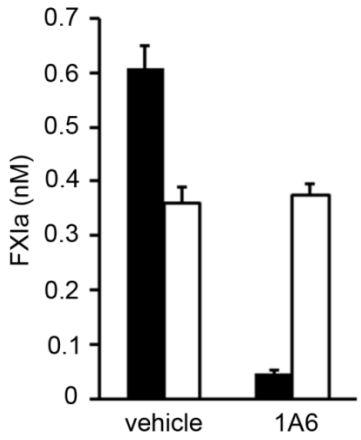

Figure S2. Clotting time. Long polyP was added to citrated plasma supplemented with 30 nM FVa in the presence of vehicle (◇), 20 μg/ml 14E11 (■) or CTI plus 14E11 (▲). Clotting was initiated with 10 pM α-thrombin. Data are mean ± SE (n = 3)

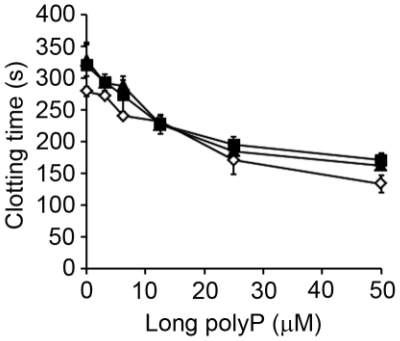

Figure S3. Role of FXIIa in the activation of FIX, FX and prothrombin. (**A**) FIX activation in a purified system following the addition of 100 nM FIX in the presence of 5 nM FXIa, 50 nM kallikrein or 50 nM FXIIa for 1 hour at 37 ^{o}C. FXIa generation was measured by western blot. (**B**) FX activation was measured in a purified system following the addition of 10 nM FXIa (○), FXIa plus 1A6 (20 μg/ml) (●), or 50 nM α-FXIIa (□) to 150 nM FX. FXa generation was measured with a chromogenic substrate. (**C**) Prothrombin activation was measured in a purified system following the addition of 50 nM FXa (○), 50 nM α-FXIIa (●) or 50 nM FXIa (□) to 1 μM prothrombin. Thrombin generation was measured with a chromogenic substrate. (**D**) Prothrombin activation was measured in a purified system following the addition of 10 nM FXIIa (●,○) or 10 nM kallikrein (■, □) to 1 μM prothrombin in the presence (●, ■) or absence of Ca^{2+} (○, □). (**E**) FXIIa can activate prothrombin. The initial rates of prothrombin activation were quantified in a purified system following additon of 25 nM (●), 50 nM (▲), 100 nM (■) α-FXIIa, or 100 nM α-FXIIa plus CTI (◇). Thrombin generation was measured with a chromogenic substrate. Data are mean ± SE (n = 3).

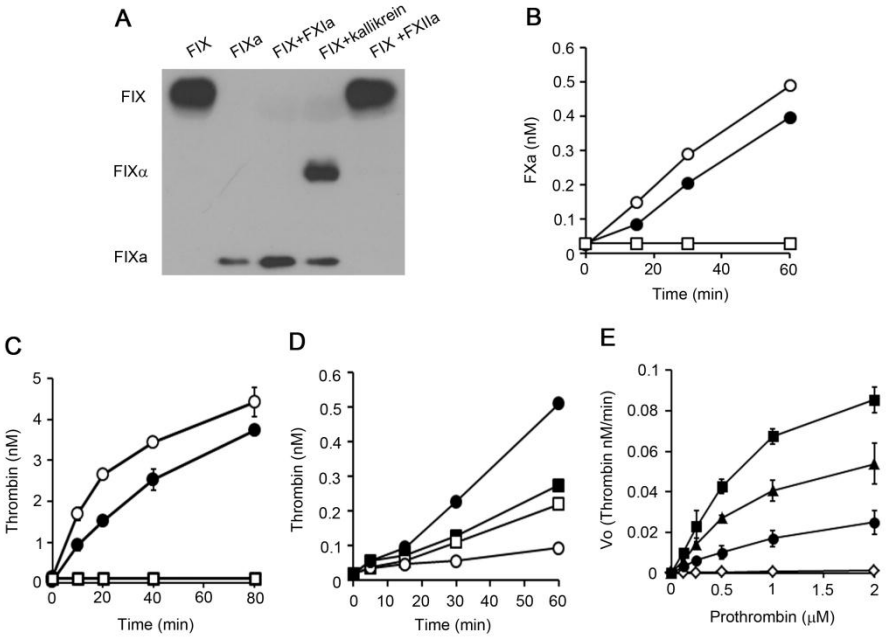

Figure S4. FXII autoactivation and FXI activation by FXIIa in the presence of dextran sulfate or long polyP. (**A**) Activation of purified FXII (200 nM) was analyzed in the presence of vehicle (◇), dextran sulfate (●; 2 ug/ml) or long polyP (▲; 10 μM). Data are mean ± SE (n = 3). (**B**) FXI activation following addition of 30 nM FXI and 5 nM FXIIa in the presence of vehicle (◇), 10 μM long polyP (▲) or 2 μg/ml dextran sulfate (●). (**C**) FXI activation following addition of 30 nM FXI, 200 nM FXII, 50 nM PK and 50 nM HK in the presence of vehicle (◇), 10 μM long polyP (▲) or 2 μg/ml dextran sulfate (●). FXIa generation was measure with a chromogenic substrate. Data are mean ± SE (n = 3).