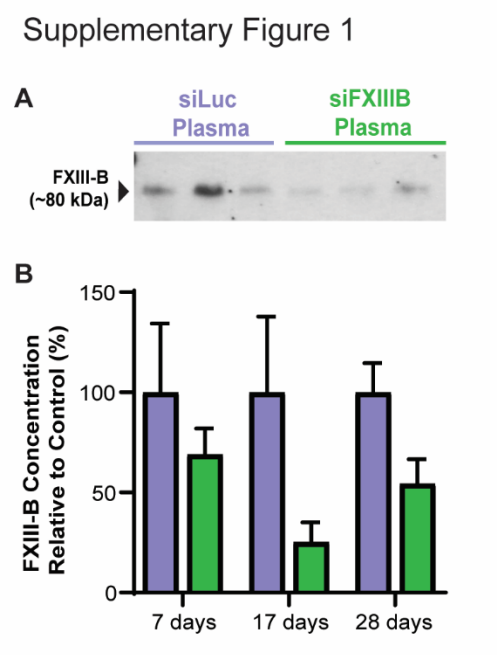
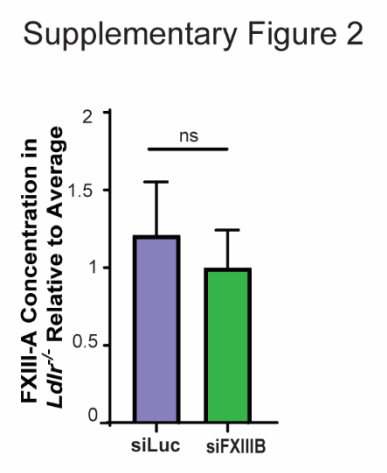
Supplementary Information

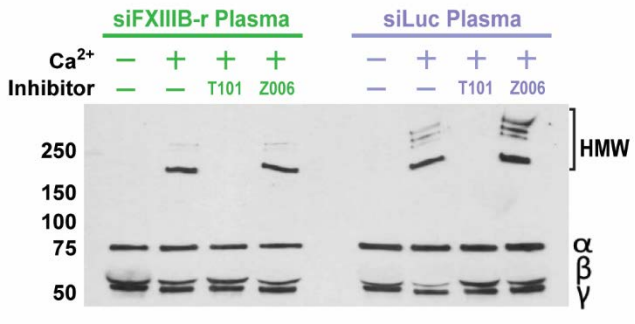


Supplementary Figure 1: FXIII-B protein is decreased in plasma by siFXIIIB. A) Western blot of plasma taken from mice 17 days after siLuc or siFXIIIB were administered. The blots were prepared with a primary antibody against FXIII-B (1:1000; HPA003827-100UL; from Sigma Aldrich, St Louis, MS, USA). **B)** Quantification of western blots against FXIII-B in plasma from mice 7, 17, and 28 days post administration of siLuc (lavender) or siFXIIIB (green); graph shows mean ± SEM.



Supplementary Figure 2: siRNA has no effect on FXIII levels in *Ldlr*$^{-/-}$ mice. Plasma FXIII-A quantified from western blots of plasma collected 14 days after *Ldlr-/-* mice were treated with siLuc or siFXIIIB. Graph represents the mean ± SEM, N = 9 mice per group.

Supplementary Figure 3



Supplementary Figure 3: Crosslinking of fibrin is decreased for weeks after administration of siFXIIIB. Western blot against fibrin, comparing the high molecular weight (HMW) fibrin species in plasma that was collected 42 days after rabbits were treated with siFXIIIB-r or siLuc. Plasma was recalcified and incubated with bovine thrombin (70 nM) for 60 min at 37°C. Non-recalcified plasma was used as a control for unactivated FXIII. Addition of an inhibitor of FXIII-A* (T101, 0.8 mM) abolished fibrin crosslinking. Plasma containing an inhibitor specific to tissue transglutaminase that does not inhibit FXIII-A* (Z006, 0.8 mM) maintained a similar amount of fibrin crosslinking as samples without inhibitor.