

Independent Anti-Angiogenic Capacities of Coagulation Factors X and Xa

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Knockout models have shown that the coagulation system has a role in vascular development and angiogenesis. Herein, we report for the first time that zymogen FX and its active form (FXa) possess anti-angiogenic properties. Both the recombinant FX and FXa inhibit angiogenesis in vitro using endothelial EA.hy926 and human umbilical cord vascular endothelial cells (HUVEC). This effect is dependent on the Gla domain of FX. We demonstrate that FX and FXa use different mechanisms: the use of Rivaroxaban (RX) a specific inhibitor of FXa attenuated its anti-angiogenic properties but did not modify the anti-angiogenic effect of FX. Furthermore, only the anti-angiogenic activity of FXa is PAR-1dependent. Using in vivo models, we show that FX and FXa are anti-angiogenic in the zebrafish intersegmental vasculature (ISV) formation and in the chick embryo chorioallantoic

membrane (CAM) assays. Our results provide further evidence for the non-hemostatic functions of FX and FXa and demonstrate for the