

## **Mechanisms Regulating Platelet FXIII Release**

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### **ABSTRACT**

Blood coagulation factor (F)XIII, located in plasma and platelets, stabilizes blood clots by crosslinking fibrin chains. Plasma FXIII is an efficient crosslinker, but the function of platelet FXIII is unclear, mainly because the mechanisms behind platelet FXIII-A release and fate are unclear. Platelets from STIM1-, fibrinogen-, plasminogen-, or FXIII-A-deficient mouse platelets and their respective controls were unstimulated or stimulated by convulxin (CVX) and thrombin or by calcium ionophore (A23187). Centrifugation was performed to separate platelet pellet and releasate, and FXIII-A in these two fractions was determined by immunoblotting. To investigate the effect of platelets on exogenous FXIII, mouse FXIII was added to FXIII-deficient mouse platelets and then activated by CVX+thrombin. We showed that CVX+thrombin-activated STIM1-deficient platelets released less FXIII-A compared to control platelets, platelet FXIII-A release was unaffected in fibrinogen- and plasminogen-deficient mice, and exogenous FXIII was not protected from proteolysis by platelets. These results suggest STIM1 signaling plays a role in the release of platelet FXIII, and only platelet-derived and associated FXIII-A can be protected from thrombin cleavage. Further characterization of platelet FXIII physiology may help understand its function and develop therapeutic treatments for thrombosis.