G13 is an essential mediator of platelet activation in hemostasis and thrombosis.

Abstract:
Platelet activation at sites of vascular injury is essential for primary hemostasis, but also underlies arterial thrombosis leading to myocardial infarction or stroke. Platelet activators such as adenosine diphosphate, thrombin or thromboxane A(2) (TXA(2)) activate receptors that are coupled to heterotrimeric G proteins. Activation of platelets through these receptors involves signaling through G(q), G(i) and G(z) (refs. 4-6). However, the role and relative importance of G(12) and G(13), which are activated by various platelet stimuli, are unclear. Here we show that lack of Galpha(13), but not Galpha(12), severely reduced the potency of thrombin, TXA(2) and collagen to induce platelet shape changes and aggregation in vitro. These defects were accompanied by reduced activation of RhoA and inability to form stable platelet thrombi under high shear stress ex vivo. Galpha(13) deficiency in platelets resulted in a severe defect in primary hemostasis and complete protection against arterial thrombosis in vivo. We conclude that G(13)-mediated signaling processes are required for normal hemostasis and thrombosis and may serve as a new target for antiplatelet drugs.