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Strong Binding of Platelet Integrin αiIbβ3 to Fibrin Clots: Potential Target to Destabilize Thrombi

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Abstract

© 2017 The Author(s). The formation of platelet thrombi is determined by the integrin αIIbβ3-mediated interactions of platelets with fibrinogen and fibrin. Blood clotting in vivo is catalyzed by thrombin, which simultaneously induces fibrinogen binding to αIIbβ3 and converts fibrinogen to fibrin. Thus, after a short time, thrombus formation is governed by αIIbβ3 binding to fibrin fibers. Surprisingly, there is little understanding of αIIbβ3 interaction with fibrin polymers. Here we used an optical trap-based system to measure the binding of single αIIbβ3 molecules to polymeric fibrin and compare it to αIIbβ3 binding to monomeric fibrin and fibrinogen. Like αIIbβ3 binding to fibrinogen and monomeric fibrin, we found that αIIbβ3 binding to polymeric fibrin can be segregated into two binding regimes, one with weaker rupture forces of 30-60 pN and a second with str onger rupture forces > 60 pN that peaked at 70-80 pN. However, we found that the mechanical stability of the bimolecular αIIbβ3-ligand complexes had the following order: fibrin polymer > fibrin monomer > fibrinogen. These quantitative differences reflect the distinct specificity and underlying molecular mechanisms of αIIbβ3-mediated reactions, implying that targeting platelet interactions with fibrin could increase the therapeutic indices of antithrombotic agents by focusing on the destabilization of thrombi rather than the prevention of platelet aggregation.

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