Novel role of the membrane-bound chemokine fractalkine in platelet activation and adhesion.

Abstract:
Chemokines released by the endothelium have proaggregatory properties on platelets. Fractalkine, a recently discovered membrane-bound chemokine with a transmembrane domain, is expressed in vascular injury; however, the effects of fractalkine on platelets have not yet been investigated. Blood was taken from healthy Wistar-Kyoto rats and the expression of the fractalkine receptor on platelets was demonstrated. The modulation of surface expression of P-selectin was assessed by flow cytometry. P-selectin expression was significantly enhanced by in vitro stimulation with recombinant rat fractalkine compared with baseline levels. Selectively inhibiting the function of recombinant fractalkine by an antagonizing antibody or the disruption of the G-protein-coupled intracellular signaling cascade of the fractalkine receptor by pertussis toxin (PTX) completely prevented fractalkine-mediated platelet activation. Preincubation with apyrase significantly attenuated the fractalkine-induced degranulation. In a flow chamber model of platelet adhesion, stimulation with fractalkine significantly enhanced platelet adhesion to collagen and fibrinogen. Similar to P-selectin expression, enhanced adhesion could be prevented by the antagonizing antibody or preincubation of platelets with PTX. Fractalkine, which is overexpressed in atherosclerosis and vascular injury, contributes to platelet...
activation and adhesion and hence is likely to play a pathophysiologically important role for increased thrombogenesis in vascular diseases.