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Endothelial C-Reactive Protein Increases Platelet Adhesion Under Flow Conditions

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Background: While data regarding the pathogenetic role of C- reactive protein (CRP) in atherothrombosis is accumulating it is still controversial whether local CRP secretion is of any pathobiological significance. The present study examined whether endothelial-derived CRP modulates an autocrine prothrombotic activity.
Methods and Results: Endothelial cells were isolated from hearts of mice transgenic to human CRP (CRPtg) and grown in primary cultures. Human CRP expression was confirmed in these cells as compared with no expression in cultures derived from wildtype congenes. Adhesion of human platelets to endothelial cells was studied in the "cone and plate" flow system. Platelet adhesion to cells expressing CRP was significantly increased as compared with controls ($n=6$, $p<0.01$). The pro-adhesive effect of CRP was significantly suppressed in mouse heart endothelial cells and in human umbilical vein endothelial cells following treatment with SiRNA for human CRP. Adhesion was modulated by an increase in p-selectin; blocking P-selectin with neutralizing antibody significantly decreased the adhesion of platelets to CRP-expressing cells (40.4±10.5 to 9.4±6.9 platelets / high power field , $n=5-6$, $p<0.01$).
Conclusions: human CRP that is locally produced in endothelial cells increases platelet adhesion to endothelial cells under normal shear flow conditions. These findings support the notion that the presence of CRP at the "scene of the crime" can indicate "evidence of guilt"; ie, CRP exerts a local effect on endothelial cells, via p-selectin expression that promotes platelet adhesion and subsequent thrombus formation.