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Titel des Beitrags:
Impact of glycoprotein VI and platelet adhesion on atherosclerosis--a possible role of fibronectin.

Abstract:
Glycoprotein VI (GPVI) mediates binding of platelets to subendothelial collagen during acute arterial thrombosis. GPVI interactions with the activated atherosclerotic vascular endothelium during early atherosclerosis, however, are not well understood. In ApoE-/- mice, platelet adhesion to atherosclerotic arteries was increased, as measured by intravital microscopy. This platelet adhesion was significantly inhibited by IV injection of GPVI-Fc (1 mg/kg body weight). Atherosclerosis in ApoE-/- mice was attenuated both after 7 and 10 weeks of treatment with the anti-GPVI antibody JAQ1 (2 mg/kg body weight i.p. twice weekly). Binding of GPVI-Fc (1 mg/kg IV) occurred to deeper layers, but also to the luminal site of plaques in atherosclerotic rabbits, but not to the vessel wall of healthy littermates. Gene transfer of GPVI-Fc to the carotid vascular wall significantly attenuated athero-progression and endothelial dysfunction in atherosclerotic rabbits in vivo. Specific binding of the soluble GPVI receptor (GPVI-Fc) to fibronectin was found in vitro to coated ELISA plates. Platelet adhesion to fibronectin was significantly inhibited both by GPVI-Fc and by the anti-GPVI antibody 5C4 ex vivo in flow chamber experiments. GPVI plays a role in platelet adhesion to atherosclerotic endothelium in the absence of plaque rupture. Inhibition of GPVI both via GPVI-Fc and anti-GPVI-antibodies
results in protection against atherosclerosis in both cholesterol-fed rabbits and ApoE⁻/⁻ mice. This novel mechanism of GPVI-mediated platelet adhesion—possibly via fibronectin—could relevantly contribute to platelet-triggered atheroprogession.

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