Inhibitory mechanisms of activated matrix metalloproteinase-9 on platelet activation.

許準榕
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Abstract

The intracellular mechanisms underlying the signaling pathways of activated matrix metalloproteinase-9 (MMP-9) in platelets are not yet completely understood. Therefore, the aim of this study was to further examine the effects of activated MMP-9 in preventing platelet aggregation. In this study, activated MMP-9 time-dependently (3-60 min) inhibited platelet aggregation in washed human platelet suspensions stimulated by agonists. However, activated MMP-9 had no significant effect on the binding of FITC-triflavin to the platelet glycoprotein IIb/IIIa complex. Triflavin is a specific antagonist of the glycoprotein IIb/IIIa complex purified from snake venom. Moreover, activated MMP-9 (21 and 90 ng/ml) markedly decreased the fluorescence intensity of platelet membranes tagged with diphenylhexatriene. The thrombin-evoked increase in pHi was inhibited in the presence of activated MMP-9 (21 and 90 ng/ml). In addition, activated MMP-9 (21 and 90 ng/ml) markedly reduced the electron spin resonance (ESR) signal intensity of hydroxyl radicals in collagen (1 mug/ml)-activated platelets. These results indicate that the antiplatelet activity of activated MMP-9 may involve the following pathways: (1) activated MMP-9 may initially induce conformational changes in platelet membranes and hydroxyl radical formation, leading to inhibition of platelet aggregation; and (2) activated MMP-9 also inhibits the Na(+)/H(+) exchanger, leading to reduced intracellular Ca(2+) mobilization, and ultimately to inhibition of platelet aggregation. This study further provides new insights concerning the effects of activated MMP-9 on platelet aggregation.