Interaction of thrombin-activated platelets with extracellular matrices (fibronectin and vitronectin): comparison of the activity of arg-gly-asp-containing venom peptides and monoclonal antibodies again glycoprotein IIb/IIIa complex.

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摘要

Abstract

Platelets adhere to fibronectin and vitronectin substrates following activation with physiological concentrations of thrombin. Adhesion of activated-platelets to either substrate is dependent upon the amount of fibronectin and vitronectin, and the duration of the adhesion assay. In this study, we showed that the Arg-Gly-Asp-containing peptides (including naturally occurring polypeptides, triflavin, trigramin and rhodostomin, synthetic peptides GRGDS, GRGDSPK, GRGDF, and GRGD and monoclonal antibodies, 7E3, 10E5 and AP2, raised against glycoprotein IIb/IIIa complex, inhibited the adhesion of activated-platelets to fibronectin and vitronectin-coated plates in a dose-dependent manner. In fibronectin-coated plates, GRGDF was shown to be much more efficient than GRGDS, GRGDSPK and GRGD at inhibiting the adhesion of activated-platelets to immobilized fibronectin. On the other hand, there were no marked differences in the abilities of these three peptides (GRGDF, GRGDS and GRGDSPK) to inhibit platelet adhesion to immobilized vitronectin. Furthermore, the RGD-containing venom peptide, triflavin was more effective than rhodostomin and trigramin at inhibiting the adhesion of activated-platelets to either substrates. The monoclonal antibodies raised against glycoprotein IIb/IIIa complex (i.e., 7E3, 10E5 and AP2) inhibited platelet adhesion to fibronectin and vitronectin in a similar dose-dependent manner. Interestingly, we found

that 7E3 was more efficient than 10E5 and AP2 in this reaction. These studies suggest that the glycoprotein IIb/IIIa complex, present on activated-platelets, may interact with fibronectin and vitronectin substrates through the Arg-Gly-Asp-dependent mechanism. Since fibronectin and vitronectin are present in the subendothelial matrix, they may be involved in platelet-vessel wall interaction. The Arg-Gly-Asp containing peptide, especially triflavin, is an ideal therapeutic agent for inhibiting thrombus formation by interrupting platelet-platelet and platelet-subendothelium interactions