Staphylokinase-Annexin XI Chimera Exhibited Efficient in Vitro Thrombolytic activities

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摘要

Abstract

Annexins (ANXs) are a family of calcium dependent phospholipid binding proteins. Phospholipids such as phosphatidylserine are rapidly exposed on the surfaces of injured endothelial cells, activated platelets, and apoptotic cells in a large number of disorders. In this study, annexin V and XI (ANXV and ANXXI) were individually fused to the C-terminal of staphylokinase (SAK), a fibrin-selective thrombolytic protein, to form chimeras for evaluation of their in-vitro thrombolytic activities. The two chimeras were found to have plasminogen activation activity of comparable efficiency. When the chimeras were challenged under higher concentrations of plasmin for 1h, hydrolysis of them into moieties was not seen on SDS-PAGE. In two thrombolytic assays, SAK-ANXXI was found to resolve both platelet rich plasma (PRP) clots and platelet poor plasma (PPP) clots with an efficiency similar to that of SAK. However, SAK-ANXV showed significantly reduced efficiency. With regard to anticoagulation ability, SAK-ANXXI was also found to have a stronger effect on dose-dependent extension of clotting time among the four tested proteins. The unique long N-terminal tail of ANXXI, composed of 202 residues, in contrast to the 16 residues of ANXV, probably served successfully to dispatch two moieties to function properly in a complicated microenvironment. Hence, a new option other than the most committed ANXV for the ANX based chimera without elaboration of linker construction is presented.