Localization and characterization of a novel secreted protein SCUBE1 in human platelets

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摘要

Abstract

OBJECTIVE: The aim of the study was to investigate the protein expression and function of a novel secreted protein in the vascular system, named SCUBE1 for signal peptide, CUB (Complement proteins C1r/C1s, Uegf, and Bmp1) and epidermal growth factor-like (EGF)-like domain containing protein 1. METHODS AND RESULTS: Immunohistochemical analysis demonstrated that the SCUBE1 staining is mainly confined to the intravascular platelet-rich thrombus in vascular tissue samples. While quantitative real-time RT-PCR verified that the SCUBE1 mRNA is expressed in human platelets, numerous immunolocalization techniques revealed that the preformed SCUBE1 protein is stored in the alpha-granules and translocated to the surface upon platelet stimulation. A smaller SCUBE1 fragment, possibly formed by limited proteolysis after being released from the storage granules, was detected in thrombus lysate by Western blot analysis. Interestingly, deposition of SCUBE1 into the subendothelial matrix of the atherosclerotic plagues was evidenced by immunohistochemistry. In addition, studies of platelet adhesion and ristocetin-induced platelet agglutination showed that fragments containing the amino-terminal EGF-like repeats were able to support platelet adhesion and enhance the ristocetin-induced platelet agglutination, respectively. CONCLUSION: These data suggest that platelet-derived SCUBE1 could function as a novel adhesive molecule and its matrix-bound and soluble fragments may play critical (patho)physiological roles in cardiovascular biology