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Vascular Gas6 contributes to thrombogenesis and promotes tissue factor upregulation following vessel injury in mice

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Gas6 (growth-arrest specific gene 6) plays a role in thrombus stabilization. Gas6 null (-/-) mice are protected from lethal venous and arterial thromboembolism through platelet signalling defects induced only by 5 μM ADP and 10 μM of the thromboxane analogue, U46619. This subtle platelet defect, despite a dramatic clinical phenotype, raise the possibility that Gas6 from a source other than platelets contributes to thrombus formation. Thus, we hypothesize that Gas6 derived from the vascular wall plays a role in venous thrombus formation. Bone marrow transplantation and platelet depletion/reconstitution experiments generating mice with selective ablations of Gas6 from either the hematopoietic or non-hematopoietic compartments demonstrate an approximately equal contribution by Gas6 from both compartments to thrombus formation. Tissue factor expression was significantly reduced in the vascular wall of Gas6-/- mice as compared to WT. In vitro, thrombin-induced tissue factor expression was reduced in Gas6-/- endothelial cells as compared to WT endothelium. Taken together, these results demonstrate that vascular Gas6 contribute to thrombus formation in vivo and can be explained by the ability of Gas6 to promote tissue factor expression and activity. These findings support the notion that vascular wall derived Gas6 may play a pathophysiologic role in venous thromboembolism.

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