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LSC 3 - Life Sciences Centre

2350 Health Sciences Mall

12-1pm



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“Role of gas6 in vascular biology”

Gas6 is a gamma-carboxylated secreted protein that binds to a series of receptor tyrosine kinase receptors of the TAM (Tyro3, Axl, Mer) family. Although homologous to protein S, it has no role in the generation of thrombin but rather plays a vital role in blood clot stabilization through platelet receptor activation. Gas6 null mice are protected from lethal thromboembolism and do not suffer from excessive bleeding making gas6 an attractive antithrombotic target. Gas6 binds to TAM receptors on vascular endothelium protecting these cells from apoptosis through classical intracellular signalling pathways. The survival function of gas6 is dependant on proper gamma-carboxylation underlying novel potential roles of the commonly used anticoagulant, warfarin, a gamma carboxylation inhibitor. Although the prothrombotic role of gas6 was initially demonstrated to occur through the platelet activation defect, recent data has shown a prothrombotic effect through other cell types such as endothelial cells and monocytes. Endothelial cell expression of tissue factor is upregulated by gas6 through Axl trafficking to lipid rafts and Akt activation. Finally, monocytes, shown to be important in the pathophysiology of venous thrombosis, promote thrombosis through gas6 upregulation of important chemokines and adhesion molecules. These latter effects underlie other novel effects of gas6 on the vasculature in promoting thrombosis. In summary, gas6 has a multitude of effects on platelets, endothelium, and monocytes during venous thrombosis making it a novel target for the treatment of venous thromboembolism.

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