Title

Neuropilin-1 prevents endothelial activation and interacts with TGFBR2 and VE-cadherin to promote adherens junction stability.

Authors

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Abstract

Endothelial homeostasis maintains the semi-permeable, anti-inflammatory properties of the endothelium. Here, we investigate the homeostatic role of NRP1 in endothelial cells (ECs) exposed to flow, in endothelium-specific NRP1 knockout mice and in a mouse model of atherosclerosis. We demonstrate that NRP1 is a constituent of adherens junctions, interacting with VE-cadherin and promoting its association with p120 catenin, stabilizing adherens junctions and promoting cytoskeleton remodeling. We show that NRP1 interacts with Transforming Growth Factor β (TGFβ) receptor II (TGFBR2) and inhibits the plasma membrane localization of TGFBR2 in puncta and TGFβ signaling. NRP1 downregulation increases the expression of pro-inflammatory cytokines and adhesion molecules resulting in increased leukocyte rolling and atherosclerotic plaque size. These findings elucidate a novel homeostatic role of endothelial NRP1 and reveal a mechanism by which NRP1 reduction in ECs contributes to vascular disease by destabilizing adherens junction and promoting TGFβ signaling and inflammation.