

A Role for the Glycocalyx in Angiogenesis

Patricia A. D'Amore, PhD, MBA

Department of Ophthalmology, Schepens Eye Research Institute, Harvard Medical School, Boston, MA

The endothelial glycocalyx is a network of apically-localized membrane-bound glycoproteins proteoglycans. Soluble factors derived from both the endothelium and the plasma are bound to this matrix. Only recently has the physiological contribution of the glycocalyx been revealed with roles for glycocalyx components demonstrated in mechanotransduction, hemostasis, signaling, and blood cell-vessel wall interactions. We have focused on endomucin (EMCN), one component of the vascular glycocalyx that is expressed by venous and capillary endothelial cells but not by most arterial endothelium. Intravitreal injection of siEMCN into eye of P5 mice lead to disrupted vascular development, indicating a role of EMCN in angiogenesis. In vitro studies using human retinal capillary endothelial cells (HRCEC) demonstrated that knockdown of EMCN suppressed VEGF-induced proliferation, migration, and tube formation. Mechanistic studies showed that the absence of EMCN prevented the internalization of VEGFR2 by clathrin-mediated endocytosis, an event necessary for success VEGF signaling. While the presence of EMCN permitted VEGFR2 internalization, EMCN was not similarly internalized. The requirement for EMCN appears to be specific to VEGFR2 as FGFR1 internalization is not affected by EMCN knockdown. EMCN represents a novel endothelial-specific target for the blockage of angiogenesis.