Endoglin in adhesion between endothelial and mural cells

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The interaction and interplay between endothelial cells (ECs) and mural cells (such as vascular smooth muscle cells -VSMCs- and pericytes) play a pivotal role in vascular biology. Endoglin is an RGD-containing ligand of β1 integrins highly expressed by ECs during angiogenesis. Our working hypothesis is that endothelial endoglin acts as an adhesion molecule via integrin recognition motifs, allowing the interaction between ECs and mural cells. We find that suppression of endoglin expression or addition of soluble endoglin inhibits the adhesion between ECs and VSMCs as shown by tubulogenesis assays on matrigel. The EC-VSMC adhesion was also abolished by an antiintegrin α5β1 inhibitory antibody, whereas it was markedly enhanced by the integrin activators $MnCl_2$ or CXCL12. The CXCL12-dependent cell adhesion was abolished in the presence of soluble endoglin or a derived pentapeptide containing the RGD motif. Adhesion of cells overexpressing different endoglin mutant constructs, allowed the specific mapping of the endoglin RGD motif as involved in adhesion to VSMCs. Binding of soluble endoglin to VSMCs was markedly enhanced by MnCl2 and CXCL12 and this increase was inhibited by the RGD peptide. Moreover, transgenic mice overexpressing soluble endoglin show podocyturia and lower number of glomerular podocytes, suggesting that soluble endoglin induced the detachment of podocytes from glomerular capillaries. These results suggest a critical role for endoglin in integrin-mediated adhesion of mural cells and provide a better understanding on the mechanisms of vessel development and maturation in normal physiology as well as in pathologies such as preeclampsia, cancer or hereditary hemorrhagic telangiectasia.

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