CHARACTERIZATION OF PERICYTE INVASIVE RESPONSES AND PERICYTE-INDUCED VASCULAR MORPHOGENESIS IN 3D MATRICES: DISTINCTIONS WITH VASCULAR SMOOTH MUSCLE CELLS

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During vascular morphogenic events, mural cells are recruited to developing endothelial tubes to aid in stabilization and maturation of the new vessels. There are two known types of mural cells, pericytes and vascular smooth muscle cells (VSMCs). Their different locations within the vasculature (capillaries versus larger vessels, respectively) suggest that there may be distinct vessel recruitment mechanisms or factors, however, these issues remain unresolved. Platelet-derived growth factor (PDGF) is known to be released from endothelial cells during morphogenic events and has been shown to influence mural cell functions. In this study, we investigate the ability of PDGF isoforms to regulate pericyte versus VSMC invasive behaviors and recruitment to EC monolayers or developing vascular tubes. Using a novel invasion system developed in our lab, we show that PDGF isoforms with affinity for PDGFRβ selectively induce pericyte, but not VSMC, invasion toward an EC monolayer. Coculture studies have allowed us to examine the effect of this recruitment on vessel stabilization and maturation while also providing us the ability to define pericyte versus VSMC functional behaviors. Also, when ECs are seeded as a monolayer on top of 3D collagen gels containing pericytes, we show enhancement of monolayer stability compared to when ECs are seeded alone. Coculture studies also reveal pericyte-induced EC tube sprouting that is sustained over time compared to EC only cultures or EC/VSMC cocultures. This work demonstrates marked functional differences between pericytes versus VSMCs in recruitment to developing EC tubes and stimulation of EC tube sprouting during vascular morphogenesis.