Col-IV: An Indicator of Vascular Formation and Pericyte Recruitment

Karri, Abhinav (School: Roanoke Valley Governor's School for Science and Technology)

Stroke, a leading cause of disability, causes brain tissue to become abruptly hypoxic. Acute hypoxia stimulates destabilization of the extracellular matrix (ECM) and damages the cellular microenvironment. Following a stroke, hypoxic cells drive vascular changes by up-regulating pro-angiogenic pathways targeting endothelial cells (EC) and pericytes (PC). Angiogenesis proceeds via PC-EC communication and involves the ECM for migration, signaling, and vessel stabilization. Therefore, understanding how hypoxia destabilizes the ECM and impacts the microvasculature during vessel formation is vital for treating vascular-related pathologies by developing new drug targets and lays the foundations for next-generation proactive therapy then modern medicine’s reactive therapy. In the current study, we sought to determine how hypoxia may disrupt the ECM and thus impair PC recruitment to ECs. We utilized a murine embryonic stem cell (ESC) model to investigate how hypoxia affects Type IV Collagen (Col-IV) and Type III Collagen (Col-III) synthesis and PC-EC interactions during vascularization. ESCs were differentiated over 10 days (D10); during this time cells were placed in a hypoxia chamber for 12hrs or 24hrs. At D10, ESC-derived vessels were fixed, stained, and imaged. A general increase of Col-III and Col-IV after 12 hours of hypoxia, however, protein volume decreased after 24 hours of hypoxia suggesting hypoxia-mediated disruption of the ECM. Furthermore, pericyte presence was decreased in both periods.

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