Elevated transgelin reduces function of endothelial colony forming cells from gestational diabetic pregnancies

Kaela M. Varberg[1,2], Rashell O. Garretson[2], Emily K. Blue[2,3], Laura S. Haneline[2,3]

[1]Department of Cellular and Integrative Physiology, Indiana University School of Medicine, Indianapolis, IN, [2]Herman B. Wells Center for Pediatric Research, Indianapolis, IN, [3]Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN

Fetal exposure to maternal diabetes predisposes children to future complications including hypertension and cardiovascular disease. A key mechanism by which these complications are thought to occur and persist is through the functional impairment of vascular progenitor cells, including endothelial colony forming cells (ECFCs). Previously, we showed that ECFCs exposed to gestational diabetes exhibit functional deficits, such as impaired vessel formation, but also differential gene expression compared to uncomplicated controls. One gene that was confirmed to be significantly upregulated in ECFCS from diabetic pregnancies was transgelin, an actin-binding smooth muscle protein. However, the functional consequences of increased transgelin in ECFCs are unknown. Therefore, to determine if transgelin is sufficient and required to induce dysfunction of ECFCs from diabetic pregnancies, transgelin protein levels were manipulated using genetic methods. Specifically, lentiviral overexpression and siRNA knockdown techniques were used in ECFCs from control and diabetic pregnancies respectively. Network formation assays and trans-well migration assays were performed to assess whether alteration of transgelin levels impact ECFC vasculogenesis and migration. Decreasing transgelin expression in diabetes-exposed ECFCs increased network formation ($n=15$, $p<0.05$) and cell migration ($n=12$, $p<0.05$). Conversely, overexpression of transgelin in ECFCs from uncomplicated pregnancies decreased network formation ($n=12$, $p<0.05$). Additional studies are underway to further elucidate intracellular signaling altered as a result of increased transgelin expression in diabetes-exposed ECFCs. Delineating the mechanisms underlying ECFC functional deficits will aid in the understanding of how and why chronic vascular complications persist in children born to mothers with diabetes.