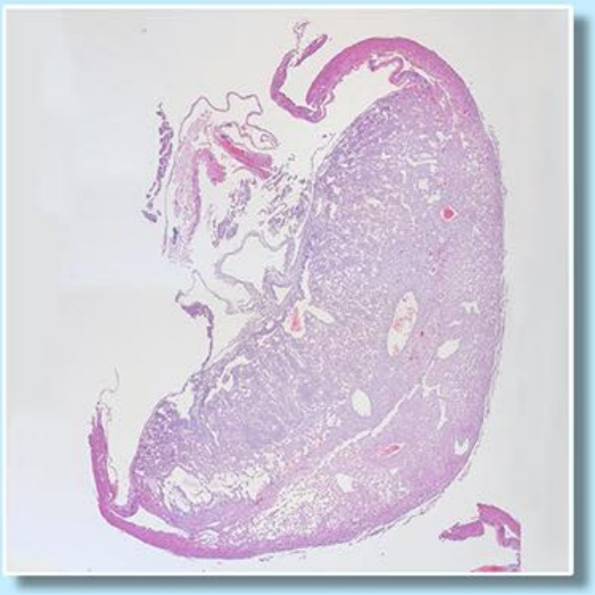
ANNALEIGH POWELL

Faculty Research Mentor: Dr. Kathleen Caron
Department of Cell Biology and Physiology



H&E staining of *Calcrl$^{fl/fl}$; Wt1-Cre* placenta

Investigation of Placental Phenotype in *Calcrl$^{fl/fl}$; Wt1-Cre* Mice

The placenta is a crucial organ for pregnancy that mediates the exchange of nutrients and gases between the fetus and mother. Calcitonin receptor-like receptor (CLR, *Calcrl*) is a G-protein coupled receptor involved in fetal-maternal blood circulation and feto-placental development. The importance of *Calcrl* in proper placental development is well supported by literature. *Calcrl* global knockouts exhibit placental phenotypes similar to preeclampsia, a disease in which placental arteries are formed abnormally. During cardiac development, *Wilms Tumor 1 (Wt1)* expression in endothelial cells regulates proper vascular growth and could therefore have similar implications in establishing vascular networks in the placenta. To further elucidate the role of CLR in placental development, our study investigated the possibility of *Wt1* driven Cre activity, and subsequent Calcrl knockout in the placenta of *Calcrl$^{fl/fl}$; Wt1-Cre* mice. We identified that *Calcrl$^{fl/fl}$; Wt1-Cre* mice are embryonic lethal at embryonic (e) day 13.5, a critical time point of artery remodeling. We therefore hypothesized that placental deformities contribute to lethality in *Calcrl$^{fl/fl}$; Wt1-Cre* mice. By utilizing immunofluorescence staining to observe Cre activity in *Calcrl$^{fl/fl}$; Wt1-Cre* placentas, we found that Wt1 is active in the junctional zone of the placenta. In placental tissue of *Calcrl$^{fl/fl}$; Wt1-Cre* e12.5 embryos, minor anatomical abnormalities were observed in the junctional zone. Furthermore, cytokeratin, a fetal derived trophoblast cell marker, was more highly expressed in *Calcrl$^{fl/fl}$; Wt1-Cre* placentas compared to wild type controls. *Calcrl$^{fl/fl}$; Wt1-Cre* placentas contained an increased abundance of uNK cells which infiltrate spiral arteries, and initiate spiral artery remodeling. From this research, we have identified a possible role of CLR in endothelial cells of the placenta, which when deleted, may lead to physiological changes in trophoblast and uNK cells in *Calcrl$^{fl/fl}$; Wt1-Cre* placentas, resulting in possible fetal death. Placental defects often result in gestational complications and mortality, such as preeclampsia and preterm birth. Understanding placental development has clinical implications for diagnosing and treating fetal complications.