"Effects of PCB mixtures on gene expression in distinct cell types of the Rett syndrome mouse model brain"

Mutations in the MECP2 gene encoding Methyl CpG Binding Protein 2 (MeCP2) has been found to be the cause of 80-90% of Rett Syndrome (RTT) cases. The MeCP2 protein binds to methylated CpG sites in DNA and acts as transcriptional regulator by either repressing or activating gene expression. While it is clear that MeCP2 function is very important for normal neurological function, it is unclear how molecular signatures of disease progression in distinct brain cell types interact with environmental toxicants such as persistent organic pollutants (POPs). Polychlorinated biphenyls (PCBs) are POPs that are identified as probable environmental risk factors for neurodevelopmental disorders (NDD). Dr. Pam Lein’s lab has developed a “MARBLES mix” of the mixture of PCB congeners found in the MARBLES cohort. I propose to investigate the gene expression patterns of RTT mouse pup brains at the single-cell level during critical developmental time points after exposing the Mecp2e1-/+ dams to this MARBLES mix. We will address these questions using single-cell 5' RNA-seq technology and phenotyping the pups for disease progression. Our preliminary findings establish a baseline for single cell gene expression in the brains of wild-type mice that will be used to gain insight into pharmacological treatments for RTT.