Alternative splicing is a mechanism that allows cells to produce multiple transcripts from a single gene. Alternative splicing plays a significant role in development and is regulated by RNA binding proteins (RBPs). Abnormal expression of RBPs in the ventricles can contribute to a reversion to fetal splicing patterns and cardiovascular abnormalities, affirming the role of RBPs in cardiac maturation. Similar research has yet to be performed in the atria, which has a unique proteome. We hypothesize that differentially expressed atrial RBPs may be vital for proper postnatal maturation through the regulation of age-specific splicing networks

We performed RNA-sequencing studies on atrial RNA samples isolated from FVB mice of various developmental stages. We identified Rbfox1 and Fmr1 as candidate RBPs differentially expressed across atrial development. We performed quantitative real time PCR assays to validate mRNA expression, western blotting to observe protein expression, and reverse transcriptase PCR assays to evaluate splicing patterns throughout atrium development. Additionally, Fmr1 was depleted in atrial HL-1 cells to observe splicing and expression changes.

We found that Rbfox1 (mRNA and protein) is upregulated during atrial development while Fmr1 is downregulated. We also found Fmr1 itself is alternatively spliced with increased long isoform inclusion throughout atrium and ventricle development. Additionally, we observed that expression of the FMR1 homolog, FXR1, is unaffected in the absence of FMR1. Our next step is to investigate Fmr1 splicing targets and protein interactions. We will also observe changes in $Fmr1^{flox}$ and $Rbfox1^{flox}$ Cre-lox mouse lines to analyze the functional impact of these RBPs.