THE ROLE OF ALTERNATIVE SPLICING IN LEFT vs RIGHT VENTRICLE DURING NEONATAL MOUSE HEART MATURATION

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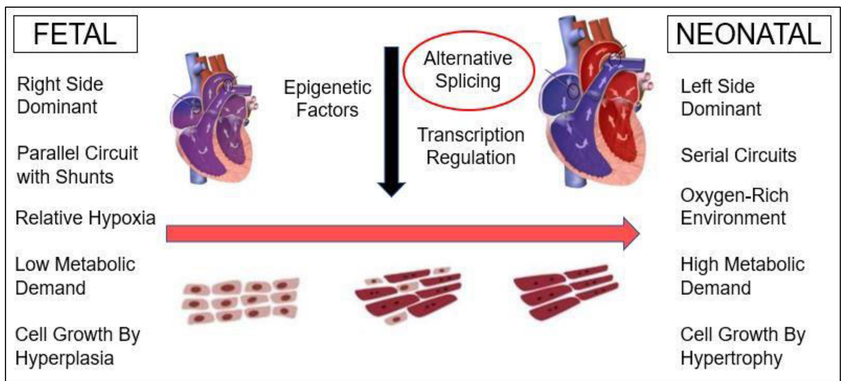
BACKGROUND

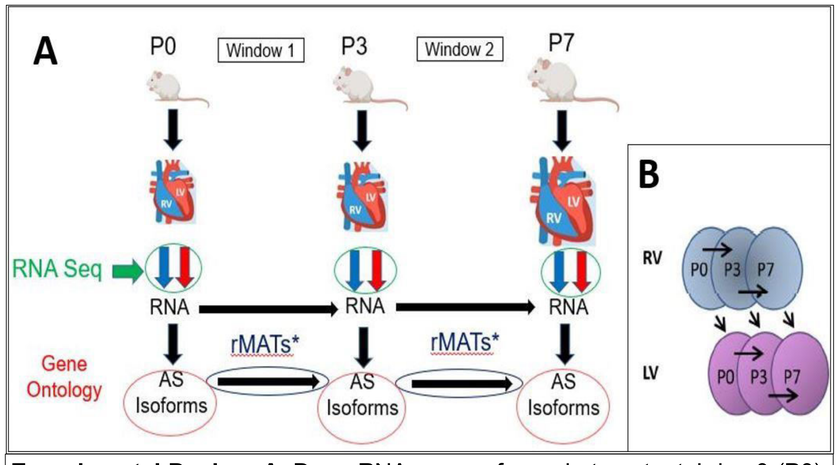


Perinatal Circulatory Transition. Schematic representation of major changes in hemodynamics, environment, morphology, respiration and cardiomyocyte phenotype during fetal to neonatal transition

OBJECTIVES

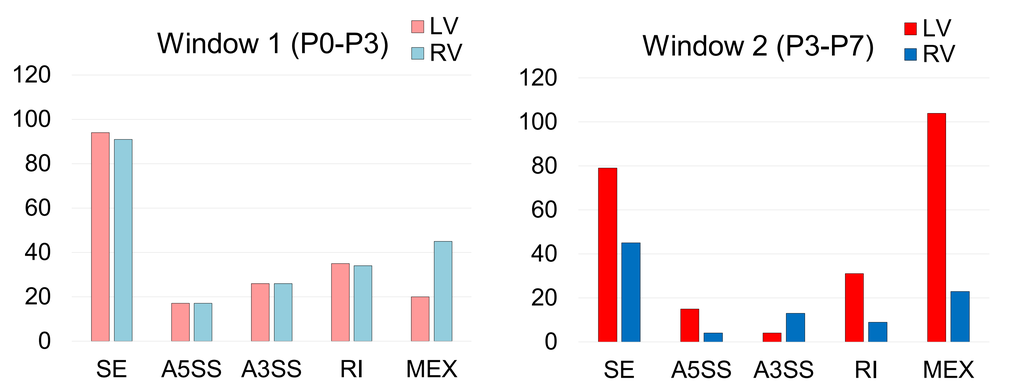
- Profile genes that are alternatively spliced during perinatal heart maturation
- Elucidate the functional role of alternative splicing (AS) in left vs right ventricle
- Identify key splicing regulators in left vs right ventricle

METHODS

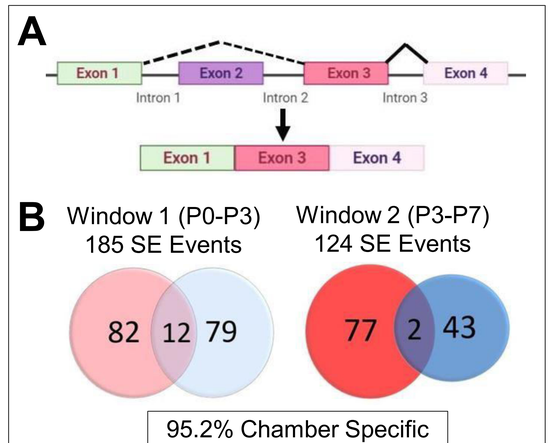


Experimental Design. A. Deep RNA-seq performed at postnatal day 0 (P0), P3 and P7. AS analysis performed using rMATS (robust Multivariate Analysis of Transcript Splicing). **B.** Pair-wise comparisons of AS events in two schemes: Developmental & chamber-specific

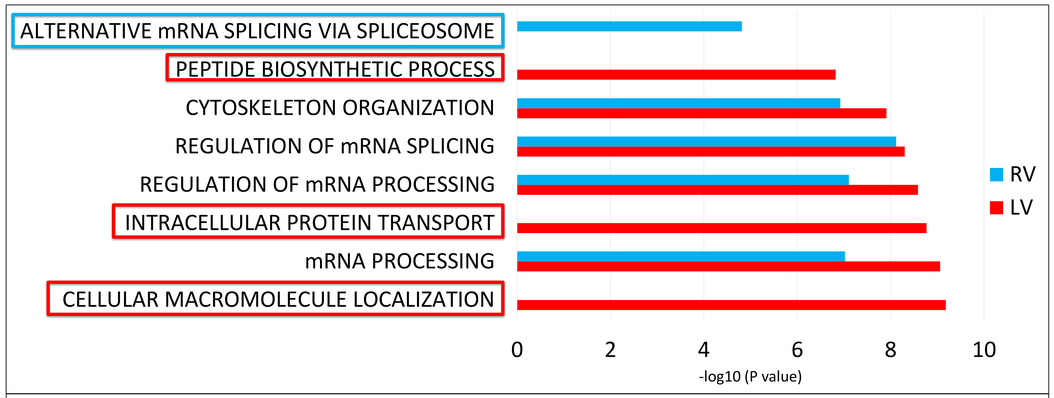
RESULTS



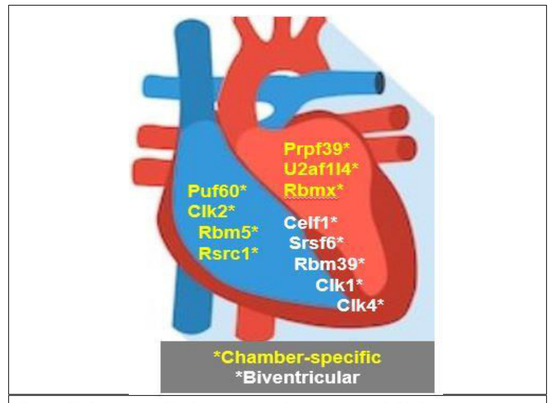
Chamber-Specific Distribution of Significant* AS Events During Perinatal Heart Maturation.
SE, Skipped Exon; A5SS, Alternative 5' Splice Site; A3SS, Alternative 3' Splice Site
RI, Retained Intron; MEX, Mutually Exclusive Exon.
*Differential exon usage > 20%; False Discovery Rate < 0.05



Distribution of Skipped Exon (SE) Events.
A. Schematic representation of SE event.
B. Venn diagrams depict chamber-specific distribution of SE events



Gene Ontology Analysis (Functional Terms) of AS Genes in LV vs RV. Significant chamber-specific enrichment of important biological processes (adj $P \leq 0.05$)



Candidate splicing regulators exhibit differential exon usage in LV vs RV

CONCLUSIONS

- Alternative splicing during perinatal heart maturation is largely chamber-specific and may play an important role in chamber-specific transcriptome regulation.
- Splicing regulation and intracellular transport are enriched functional categories in the alternatively spliced genes.
- Key splicing regulators may contribute to chamber specificity during perinatal heart maturation.
- Future studies of these AS regulators in LV vs RV may lead to chamber-specific approaches for neonatal/congenital heart disease

ACKNOWLEDGEMENTS

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