Title: Understanding the Role of microRNAs in the Post-Transcriptional Regulation of RNPS1 gene

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Abstract: RNA-binding protein with serine-rich domain 1, RNPS1, is an essential regulator of splicing activity. Transcriptome-wide studies revealed deficiency of RNPS1 causes mis-splicing due to the de-repression of cryptic splice sites, indicating the critical role of RNPS1 in maintaining splicing fidelity. The crucial role of RNPS1 in splicing activity raises a fundamental question, whether the expression of RNPS1 is altered to orchestrate differential splicing activity observed during cellular differentiation and organism development. Here we investigate the role of microRNAs in regulating the expression of RNPS1. We identified miR-6893-3p and miR-490-3p are negative regulators of RNPS1 in humans. Ectopic expression of miR-6893-3p or miR-490-3p reduced the endogenous mRNA and protein levels of RNPS1. In contrast, knockdown of miR-6893-3p elevates the level of endogenous RNPS1. miR-6893-3p mediated regulation of RNPS1 is dependent on the binding of miR-6893-3p to a microRNA response element in the 3'UTR of RNPS1 mRNA. We found that targeted negative regulation of RNPS1 by miR6893-3p occurs via enhanced mRNA degradation.