

Biological Sciences Seminar

D'Ambra Auditorium ~ Life Science Building ~ University at Albany

January 17, 2012 ~ 4:00pm

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“MicroRNA regulation of alternative splicing networks during heart development and disease”

ABSTRACT: Recent genome wide studies have revealed a previously unexpected level of mRNA complexity within metazoan transcriptomes. Amongst the various RNA processing events, alternative pre-mRNA splicing is the most prominent mechanism to generate mRNA complexity. The functional outcomes of alternative splicing are increased proteome diversity, introduction of premature termination codons to degrade mRNAs by nonsense-mediated decay, and variability in the untranslated regions (UTRs) to affect mRNA translation efficiency, stability and localization (5). We have identified a conserved program of alternative splicing regulation in vertebrates that is important for postnatal heart development. Computational and expression analyses coupled with genetic studies were used to identify *cis* elements and *trans*-acting RNA binding proteins (the CELF and MBNL family of splicing factors) that drive over half of these postnatal splicing transitions. We also discovered a regulatory hierarchy in which a rapid increase in microRNA expression results in the down-regulation of multiple splicing factors to coordinate the postnatal switch in splicing. More recently, We found that loss of this regulatory hierarchy re-activates the embryonic gene expression program in adult hearts of patients with myotonic dystrophy type I (DM1), a neuromuscular disorder, which affects heart, skeletal muscle, and brain.

