

Neuron-specific regulation of alternative pre-mRNA splicing

Sika Zheng

University of California, Riverside, USA

Families of alternative splicing regulators often contain multiple paralogs presumed to fulfill different functions. Polypyrimidine tract binding proteins *Ptbp1* and *Ptbp2* exhibit dynamic stage-specific expression and program developmental pre-mRNA splicing in neurons, but how and why their regulatory actions differ are not understood. To compare their targeting, we generated a knockin mouse allele that conditionally expresses *Ptbp1*. Bred to a *Ptbp2* knockout, the transgene allowed us to compare the developmental and molecular phenotypes of mice expressing only *Ptbp1*, only *Ptbp2*, or neither protein in the brain. This knockin *Ptbp1* rescued a forebrain-specific, but not a pan-neuronal, *Ptbp2* knockout, demonstrating both redundant and distinct roles for the proteins. Using comprehensive approaches of biochemistry, RNA-Seq, and CLIP-Seq to probe their targeting and protein-RNA interactions, we found that

many developmentally regulated exons exhibited different sensitivities to *Ptbp1* and *Ptbp2*. Nevertheless, the two paralogs displayed similar RNA binding across the transcriptome, indicating that their differential targeting does not derive from their RNA interactions, but from possible different cofactor interactions.

Speaker Biography

Sika Zheng is an expert in studying RNA binding proteins and alternative splicing. His lab combines Biochemistry, Molecular Biology, Cell Biology, Neurobiology, Genetics, Genomics, and Computational Biology to understand the activity, mechanism, function and dysfunction of gene regulation at the RNA level in the nervous system focusing on *Ptbp1* and *Ptbp2* two RNA binding proteins programming neuron-specific alternative splicing. He has made seminal contributions revealing the roles of alternative splicing for neuronal development and the mechanisms of *Ptbp1/2* controlling neuron-specific alternative splicing events.

e: sika.zheng@ucr.edu

 Notes: