



Barbara Vivash Award in Molecular Genetics

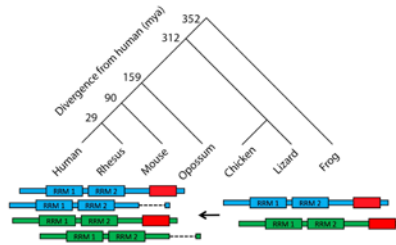
Seminar and Award Presentation

2016-2017 Recipient:

Dr. Serge Gueroussov

Postdoctoral Associate

Broad Institute of MIT and Harvard



Functional Consequences of Mammalian-Specific Alternative Splicing Events in RNA Binding Proteins

Alternative splicing (AS) patterns diverged rapidly in vertebrates, but the functions of most species- and lineage-specific isoforms remain unknown. Using a combination of targeted and transcriptome-wide analyses, I characterized the mammalian-specific isoforms of multiple RNA binding proteins. I showed that mammalian-specific AS in the PTBP1 gene alters its activity, and engineered AS of the orthologous exon in chicken is sufficient to induce mammalian-like regulatory changes. AS of this exon during neurogenesis was found to significantly impact differentiation timing in mice. Subsequent analysis of all mammalian-specific exons revealed they are enriched in glycine/tyrosine-rich disordered domains, such as those of HNRNPA and D genes. Evolution of skipping involved formation of intramolecular RNA duplexes. At the protein level, inclusion of such exons facilitates higher-order assemblies on substrate pre-mRNAs required for AS regulation. This work demonstrates how splice isoform evolution in RNA binding proteins can impact development and expand the regulatory capabilities of mammalian cells.

Host: Dr. Leah Cowen

Date: Friday February 16th, 2018

Time: 2:00PM

Place: Donnelly Centre CCB, Red Seminar Room, 160 College Street