CENTER FOR RNA BIOMEDICINE

RNA Innovation Seminar
Monday, October 15th at 3:00pm
ABC Seminar rooms, Biomedical Research Science Building (BSRB), 109 Zina Pitcher

John Moldovan, Ph.D. is a postdoctoral research fellow in the John Moran Lab. His primary research project is focused on how LINE-1 retrotransposons mobilize other cellular RNAs such as mRNA, Alu elements, and U6 snRNA. He developed an in vitro RNA ligation assay and used RNA-seq to identify a new mechanism for chimeric U6 snRNA/LINE-1 pseudogene formation. He collaborated on a multi-disciplinary project to investigate how somatic mutations caused by mobile genetic element insertions may contribute to schizophrenia.

"RNA ligation precedes U6 snRNA/LINE-1 retrotransposition"

Abstract: Long INterspersed Element-1 (LINE-1 or L1) retrotransposons constitute approximately 17% of human DNA and are the only known active autonomous retrotransposons in the human genome. L1 amplifies throughout the genome via retrotransposition and active L1s encode two proteins (ORF1p and ORF2p) that bind their encoding transcript to promote retrotransposition in cis. ORF1p and/or ORF2p also promote the retrotransposition of Small INterspersed Element RNAs, non-coding RNAs, and messenger RNAs in trans. Some L1-mediated retrotransposition events consist of a copy of U6 small nuclear RNA conjoined to a variably 5'-truncated L1, but how U6/L1 chimeras are formed requires elucidation. Here, we report that: U6/L1 chimeric RNAs are present in human cell lines; the RNA 2',3'-cyclic phosphate ligase RtcB can join U6 RNAs ending in a 2',3'-cyclic phosphate to L1 RNAs containing a 5'-OH group in vitro; and retrotransposition of U6/L1 RNAs leads to U6/L1 pseudogene formation. Thus, we have uncovered a novel mechanism for U6/L1 chimera formation.