CENTER FOR RNA BIOMEDICINE

RNA Innovation Seminar

Monday, December 3, 2018 at 3:00pm
ABC Seminar rooms, Biomedical Research Science Building (BSRB), 109
Zina Pitcher

Meredith Purchal
PhD candidate
Mentors: Markos Koutmos and Kristin Koutmou

"Deciphering the Structure and Function of mRNA-Modifying Pseudouridine Synthases"

Abstract: Pseudouridine (Ψ) is among the most abundant post-transcriptional RNA modifications in cells and has long been known to make important contributions to tRNA structure and function. While traditionally pseudouridine was only thought to occur in non-coding RNAs, recent efforts in mapping pseudouridylation across the transcriptome have identified a multitude of sites consistently pseudouridylated across mRNA and dynamically modified under stress conditions. As appreciation for the complexity of the role of this modification increases, a deeper understanding of the enzymes that catalyze the incorporation of this modification is necessary. Our goal is to describe the sequence and structural elements that cooperatively determine the specificity of pseudouridine synthase (Pus) enzymes towards their mRNA targets. We solved the first crystal structure of *S. cerevisiae* Pus7, a pseudouridine synthase that primarily modifies mRNA under cellular stress. Furthermore, we developed binding and kinetic assays to interrogate wild-type and mutant Pus7 pseudouridylation activity. Our biochemical work reveals several residues important to Pus7 function (K61, F307, F67, and D256). Ultimately, the combination of biophysical and biochemical techniques will allow us to dissect the features determining substrate recognition, and help to lay the foundation for a deeper understanding of RNA post-transcriptional regulation.