Landon Clark

Identification of Proteins that Regulate CRISPR DNA Uptake of *Pyrococcus furiosus*

The CRISPR-Cas (Clustered Regularly Interspace Short Palindromic Repeats–CRISPR associated) system is a prokaryotic, adaptive immune system used by bacterial and archaeal organism to fight infections by viruses and other harmful invasive DNAs. These prokaryotic CRISPR-Cas immune systems have been exploited as powerful genome editing tools that work many different organisms and cells including humans. The newly developed CRISPR-based technologies are transforming medicine and science and have been used in research applications for developing cures for certain cancers, HIV, hemophilia, etc. The function of the CRISPR-Cas systems follow three basis steps: (1) adaptation (invading DNA is integrated into the host genome at CRISPR locus), (2) crRNA biogenesis (the CRISPR locus creates mature CRISPR RNAs (crRNA)), and (3) invader silencing (mature crRNAs are associated with Cas protein nucleases that silence future foreign invaders). This research focuses on the molecular mechanisms of the first step in the pathway, adaptation. It is known that two proteins, Cas1 and Cas2, are universally conserved among all active CRISPR-Cas systems and are involved in adaptation, specifically the integration of DNA into the CRISPR locus. By using the model organism *Pyrococcus furiosus*, a hyperthermophilic archaeaon, this research tests potential roles for many candidate proteins that are hypothesized to regulate DNA acquisition and/or modulate the uptake of properly sized and oriented DNA fragments into the CRISPR genome. Identifying proteins that control uptake of DNA and CRISPR loci contribute to CRISPR-Cas systems to aid in the applications it provides, such as its molecular timeline and the genomic editing for diseases.