UC RIVERSIDE

BCH 252 Seminar Series

Matthew Tippin, BCMB Graduate Student Researcher, Department of Biochemistry, UC Riverside

Seminar Title: "The Molecular Basis of the Human Mitochondrial Lon Protease Binding to DNA"

Biography: The human mitochondrial Lon protease homolog Isoform 1, LonP1, is a universally conserved Protein Quality Control ATP-dependent serine protease associated with a variety of cancers and neuronal disorders such as ALS. While current investigation of Lon is focused primarily on drug discovery of its protease domain (and protease inhibitor analogs) due to Lons stabilization of the mitochondria and oxidative phosphorylation in many aggressive cancers, there has been little reported about human Lon's conserved single-stranded DNA-binding interactions, including a lack of structure of Lon bound to DNA. Previous work has demonstrated Lon prefers G-rich regions of DNA and suggested that these are G-quadruplex forming regions of DNA and little has progressed on this front in fifteen years. My project is an investigation into this particular interaction, its biological significance, and identifying the crucial residues involved in this protein DNA secondary structure interaction. While demonstrating that Lon binds to a variety of G-quadruplex forming sequences found in the mitochondria, including tetramolecular and unimolecular G-quadruplexes, my work also demonstrates that these DNA structures attenuate Lon's proteolytic activity through interaction with its ATPase domain in addition to identifying some of the key DNA-interacting residues involved. Continued investigation of these DNA-protein interactions and the residues involved will ideally lead to a new domain target for drug discovery and iteration in Lon overexpressed cancers, representing a new avenue of therapeutic design while simultaneously elucidating key mitochondrial features.

Tuesday, May 14th, 2024 12:00 p.m. - 12:50 p.m. PST

In-Person: Genomics Auditorium 1102A

Host: Dr. Maria Ninova