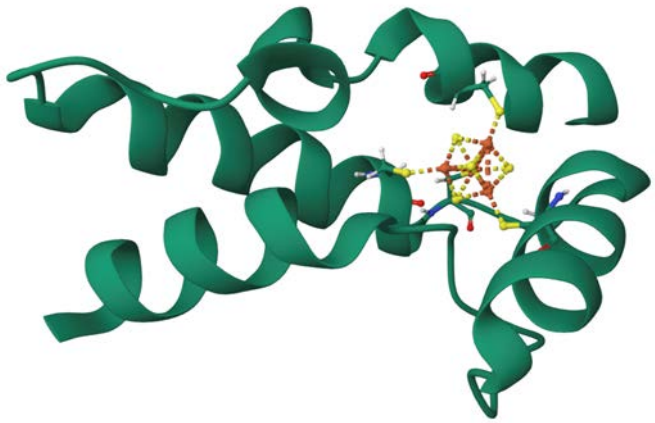
CHEMISTRY SEMINAR

Understanding the Functional Mechanisms of WhiB1 in *M. tuberculosis*

By Jess McThomas ’24 BMB

11:30 a.m. **April 25, 2024** **Darrah Auditorium**
McCreary 101

Abstract:
Multidrug-resistant tuberculosis (MDR TB) is a pathogenic respiratory infection that does not respond, or responds ineffectively, to many of the antimicrobial therapies currently available. There is a need for new antibiotics that target MDR TB survival and virulence, in which the use of transition metals has become a powerful tool with current emphasis on Fe-S redox sensors. The White-B like (Wbl) protein family consists of seven transcription factors found in actinobacteria, including *Mycobacterium tuberculosis*, that contain a [4Fe-4S] cluster anchored by four conserved cysteine residues and a succeeding β-turn with a GXWXG motif. One member of the protein family, WhiB1, is essential for cell growth, making it a potential target for MDR TB antibiotics. The structure of WhiB1 has recently been mapped, yet the functional motifs and mechanisms are still poorly understood. Absorbance spectroscopy was performed for chimeric growth assays of WhiB1 with other proteins in the family, WhiB2 and WhiB3, to investigate its functional motifs for antibiotic targeting. Additional assays were performed to test the oxidant reactivity of the [4Fe-4S] cluster of WhiB1 and a potential role of WhiB1 within the TCA cycle.



Protein structure of WhiB1 protein in *M. tuberculosis*. PDB ID: 6ONO

CHEMISTRY SEMINAR

Development and Synthesis of Novel Cyanuric Chloride-Based, Structurally Diverse, Lipids

By Emily Sullivan ’24 BMB

11:30 a.m. **April 25, 2024** **Darrah Auditorium**
McCreary 101

Abstract:
Molecular delivery (proteins, RNA, DNA, drugs, and other organic materials) in a targeted fashion using lipid nanoparticles (LNPs), also known as transfection, has gained popularity in the recent years. At the heart of the science behind transfection is the use of LNPs as protection of the materials from getting degraded in the cell before entry and localization of the molecules, and thus LNP structure and function is vital to proper transfection. However, the structure and function of these LNPs are primarily due to the structure of the lipids that make up the LNP. Lipids are generally comprised of a hydrophilic headgroup and a hydrophobic tail group which are connected via a molecular linker. LNPs have been comprised of both naturally occurring and synthetic lipids, and the ability to modify the structure of a synthetic lipid to be used in gene transfection remains vital to understanding the structure-function relationship between the lipid and the LNP, but also potentially tailor the LNP function by using a specific structurally modified lipid. The ability to create new and structurally diverse lipids has been critical to understanding and furthering these efforts. Venditto *et al.* has published numerous works, as well as other groups, outlining the use of cyanuric chloride as a molecular linker in which to build various lipid libraries from. Venditto *et al.* has even gone further to demonstrate successful transfection properties using LNPs comprised from cyanuric chloride-based lipids.

This work builds off of Venditto’s work to highlight improved synthetic methods and synthesis of a more structurally diverse lipid library that differs in both headgroup and tail group structure/length as well as details a synthetic method that has a consistent headgroup but variable tail groups, attached to the headgroup/cyanuric structure using ester-linkages, a biodegradable functional group. This work will aid in the understanding of the structure-function relationship between lipids and LNPs as transfection agents and hopefully comprise LNPs that can function in gene transfection and other delivery of molecular cargo in the future.