CHEMISTRY SEMINAR

Characterization of Vanadium Binding to Due Ferri Proteins

By Bonnie Coley, Chemistry '25

11:30 am **Thursday, October 12, 2023** **Science Center Room 300**

Abstract:
First-row transition metals are abundant and less costly than other metals in industrial settings, but their unwanted reactivity in aqueous conditions can be a problem. Vanadium is a transition metal that can undergo unwanted reactivity in an aqueous environment, but nature has found ways to control these undesired reactions. In the Buettner lab, we seek to capitalize on the systems nature has developed to overcome these reactions using the Due Ferri single chain (DFsc) system. The DFsc proteins are computationally designed proteins that were developed to mimic the way nature protects iron from its unwanted reactions with water. The active site of DFsc is easily modifiable to look like a variety of natural enzyme binding sites, and recently, we developed a series of new protein constructs that mimic vanadium haloperoxidases by incorporating a series of arginine residues in the active site. Vanadium haloperoxidases are enzymes found in algae that play a crucial role in the biosynthesis and ecological cycling of halogenated organic compounds. This haloperoxidase reactivity is only able to be carried out in aqueous conditions by these enzymes, making them a good target to mimic. The presence of arginine in the active site makes the binding site more positively charged, thereby increasing the binding of the vanadate ion. To understand the effect of these arginine residues, we are using circular dichroism to probe the thermal stability of the metal-bound proteins and cyclic voltammetry to probe how the proteins affect the redox potential of the metal. Thermal melts on the CD have shown that vanadium-bound proteins can maintain their structure at higher temperatures when compared to non-metal-bound proteins. Vanadium-bound proteins have been shown to affect the redox potentials of vanadium.

CHEMISTRY SEMINAR

A Molecule Modulator of Cardiac Myosin Targets the Sarcomere Hypercontractility of Hypertrophic Cardiomyopathy

By Audrey Moroz, Chemistry '25

11:30 am **Thursday, October 12, 2023** **Science Center Room 300**

Abstract:
Hypertrophic cardiomyopathy (HCM) is one of the most common hereditary cardiovascular disorders, as it affects about 1 in every 500 individuals. HCM causes thickening of the left ventricular wall, which is the main pumping chamber of the heart. This makes the left ventricle stiff and rigid, which in turn makes it extremely difficult for the heart to take in and pump blood throughout the body. Mavacamten has been recently discovered to be a novel small-molecule modulator of cardiac myosin that can target the underlying sarcomere hypercontractility of HCM. MyoKardia, Inc. conducted research in 2017 to look into the molecular mechanism of mavacamten to see how it affects different kinds of myosin. Cardiac myosin is the motor that powers the contraction of the heart. It converts chemical energy from ATP hydrolysis into a mechanical force. MyoKardia hypothesized that a molecule that could decrease the ATPase activity of cardiac myosin might improve the overall contractile properties of a heart with HCM. Transient kinetic experiments were conducted in order to learn more about the mechanism of mavacamten.

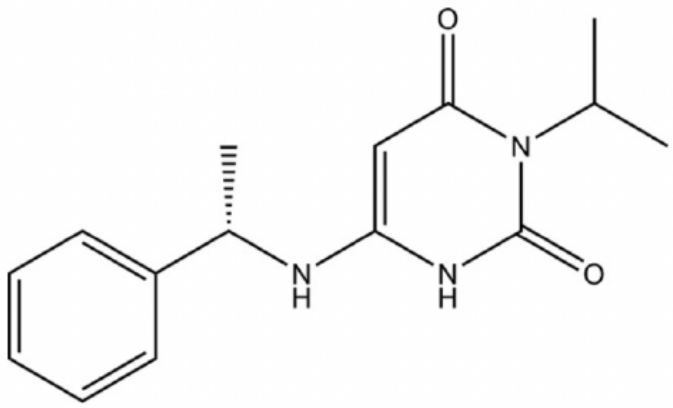

Figure 1: Chemical Structure of Mavacamten

Kawas, Raja F., et al. "A small-molecule modulator of cardiac myosin acts on multiple stages of the myosin chemomechanical cycle." *Journal of Biological Chemistry*, vol. 292, no. 40, 2017, pp. 16571–16577, https://doi.org/10.1074/jbc.m117.776815.