**ABSTRACT**

Toxic metal exposure is linked to a variety of health issues including cardiovascular disease and diabetes. It is known that toxic metals are capable of mimicking essential metals for binding sites in proteins. Toxic metal exposure is linked to a variety of health issues including cardiovascular disease and diabetes. It is known that toxic metals are capable of mimicking essential metals for binding sites in proteins. The recent events in Flint Michigan highlight the persistent problem of lead toxicity in the United States. While the use of Pb was banned from paint and gasoline products in the mid-1970s, researchers are finding new areas of possible exposure. Studies conducted by the NC Department of Public Health (2018) and the New York City Department of Health and Mental Hygiene (2019) both suggested that spices can also be a cause of lead exposure. In 2018, researchers at Johns Hopkins first reported the high concentration of toxic metals present in e-cigarettes.

**MOTIVATION AND METHODS**

It has been found that both divalent cadmium (Cd\(^{2+}\)) and lead (Pb\(^{2+}\)) can disrupt Ca\(^{2+}\) signaling pathways. However, little else is known about how this happens at the molecular level. Research in the Spuches Lab is geared towards understanding metal toxicity from a thermodynamic and structural perspective. In this project, I will investigate Pb\(^{2+}\) binding to human cardiac troponin C (hcTnC), a Ca\(^{2+}\) binding protein that is responsible for heart muscle contraction. Isothermal titration calorimetry (ITC) will provide the following: 1. Stoichiometry of Pb\(^{2+}\) binding to the protein 2. The affinity, K\(_a\), or how strong the interaction is between Pb\(^{2+}\) and the protein. 3. Provide us with the important thermodynamic parameters (G, H, and TS) that can then be compared to other metals such as Ca\(^{2+}\) and Cd\(^{2+}\).

**ISOTHERMAL TITRATION CALORIMETRY (ITC)**

ITC analysis provides a full thermodynamic analysis of a ligand-binding system, including the enthalpy, binding constant, and ligand stoichiometry.

**CIRCULAR DICHROISM (CD)**

Cyclic dichroism is a spectroscopic technique that uses linearly polarized light to probe the secondary structure of proteins. Representative CD spectra of the structural curves for protein solutions containing mostly alpha helices (--), anti-parallel beta sheets (--), beta (-----), or random coiled structures (-----).

**REFERENCES**


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