



Department of Chemistry

UNIVERSITY OF CENTRAL FLORIDA

Department of Chemistry Seminar Series – Fall 2020

Exploring the mechanistic and structural role of metalloenzymes in disease: A synthetic-inorganic, biomimetic chemistry approach



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Host: Prof. Jonathan Caranto

October 30, 2020 **10:00 AM** – Zoom

Meeting Room: <https://ucf.zoom.us/j/95787434425> Passcode: 184066

In our group we are interested in the role that metalloenzymes play in disease. Our approach is to use biomimetic modeling of the active sites of metalloenzymes. This strategy provides an effective route to understanding structure-function property relationships of transition metal coordination compounds at the active site of enzymes. The understanding of these relationships gives us insight into enzyme function and links molecular level chemistry with protein structure and function. Our talk will focus on two metalloenzymes with such implications, *Acireductone dioxygenase (ARD)* and *human superoxide dismutase (SOD1)*.

ARD is an essential enzyme in the methionine salvage pathway in plants and bacteria. It was recently found in mammals and the human form has now been found to be expressed in a variety of in-vitro studies of certain cancer cell lines. However, there is no known role of *ARD* in humans. Many questions remain about *ARD*'s unique mechanism of substrate activation, as well as its involvement in disease states. This talk will discuss our efforts to model the active site of *ARD*, and introduce the synthesis and characterization of a new family of structural and functional model complexes that aim at understanding the mechanism of substrate activation promoted by *ARD*.

SOD1 promotes the detoxification of the cell from superoxide radical. *SOD1* has been implicated in the development and proliferation of the neurodegenerative disease amyotrophic lateral sclerosis (ALS). We will discuss our initial efforts at understanding how structural distortions at the active site of superoxide dismutase might result in aberrant gain of function and loss of structure ultimately connected with ALS. We will discuss our proof of principle efforts at modeling the active site of *SOD1* using a set of copper complexes recently developed in our laboratory.