

JOSEPH F. FOSTER MEMORIAL CHEMICAL BIOLOGY AND BIOCHEMISTRY SEMINAR

Monday, February 19th, 2024
3:30 PM, BRWN 4102



KHAI PHAM

Ph.D. Candidate
Dr. Tian's Lab Group

Abstract:

The substrate binding to a protein often leads to conformational changes that enhance catalytic efficiency, a key principle in many enzymes essential for various biological functions. These enzymes usually undergo small conformational shifts, particularly in the geometry of catalytic residues, with changes typically below 1 Å. In this research, we analyzed the cryo-electron microscopy (cryoEM) structures of cobalamin-dependent lysine 5,6-amino mutase in both its inactive 'Open' and active 'Closed' states following substrate binding. The binding triggers a significant conformational shift, including a 75-degree rotation of the Rossmann-like domain. Simultaneously, the 5'-deoxyadenosylcobalamin (Ado) cofactor moves over 20 Å, bringing it close to the substrate-bound pyridoxal phosphate (PLP) cofactor. We identified a critical hydrogen bond network involving Lys371 and Asp299, which keeps the Ado moiety positioned for substrate interaction and protects the Ado• radical from unintended side reactions. These findings highlight the complex and dynamic interplay between protein conformation and radical-based chemical reactions within the enzyme's structure.

“Catalysis in Motion: Large-Scale Domain Shift Enables Co-C Bond Homolysis.”



Department of Chemistry