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**Structural Studies of Bacterial Metallo-Beta-Lactamases**

D. Tierney (U. of Mexico), M. Crowder (U. of Miami)

Beamline(s): X9B

The aim of the work is to use x-ray absorption spectroscopy (XAS) to characterize stable resting states and catalytic intermediates relevant to metallo-beta-lactamase catalyzed hydrolysis. These enzymes, capable of binding two equivalents of Zn at their active sites, confer bacterial resistance to penicillin-type antibiotics. One of the metal binding site presents a ligand set as carbonic anhydrase (CA site), while the other is a ligand set analogous to that of the farnesyl transferases (FT site). The goal is to aid the development of pharmaceuticals capable of metallo-beta-lactamase inhibition, and, in long term, to develop detailed understanding of the factors controlling reactivity that are determined by the second metal ion.

Preliminary work done on X9B for Co-substituted forms of beta-lactamases L1, CcrA and imiS establish the validity of the substitution of Co for Zn in the active sites of these enzymes. Furthermore, imiS reconstructed with either one or two equivalents of Co show that the first equivalent of metal bound to imiS occupies the FT-site, and not the CA-site as had been predicted. Further measurements involve looking at a potential inhibitor binding to the metallo-beta-lactamases, both Zn and Co forms, characterization Co Schiff base complexes and set of samples prepared at the extrema of pH vs. activity for CcrA.