Inorganic Chemistry of the Cell: Transition Metal Homeostasis in Bacterial Pathogens

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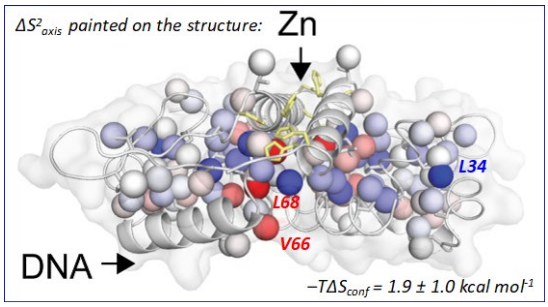

First-row late *d*-block metals from Mn to Zn play distinct roles in cellular metabolism. In bacterial pathogens, metalloregulation of transcription drives physiological adaptation to host-mediated transition metal starvation and toxicity, required to maintain metal homeostasis. We are currently working on two separate aspects of this problem. In the first, we are employing global multi- 'omics strategies to elucidate metabolic adaptation to host-mediated transition metal starvation. In the second, we are employing advanced NMR approaches to understand transition metal sensing at the physicochemical level. In bacterial zinc (Zn) homeostasis, for example, a pair of metal-sensing transcriptional repressors regulate the transcription of metal uptake and efflux transporters, where Zn allosterically activates or inhibits DNA operator-promoter binding. I will present the results of recent comprehensive NMR-based investigations of metal-mediated allostery in a number of metal-sensing transcriptional repressors in an effort to elucidate general features of metal sensing, inducer specificity and evolution of distinct biological outputs that function at the host-microbial pathogen interface.