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**Molecular Mechanisms of Bacterial Signaling: from O2 Sensing to Cyclic Nucleotides**

Bacteria sense and respond to numerous signals in their environment to adapt to changing conditions, such as external stressors or entering a host. Nucleotide-based second messengers are often used to transduce the external signals into changes in intracellular pathways, resulting in alteration of transcription, translation, and/or enzymatic activity. Work in my group is focused on elucidating the molecular mechanisms of bacterial cyclic nucleotide signaling pathways, from novel signaling molecules and proteins to physiological effects. To do so, we are investigating a family of oxygen-sensing proteins, termed globin coupled sensors, that synthesize cyclic dimeric guanosine monophosphate (c-di-GMP), a bacterial second messenger best known for regulating biofilm formation. Our studies have yielded new insights into the mechanism by which ligand binding to the heme alters enzymatic activity, including key amino acid residues, the role of heme deformation, and protein conformational changes. In addition, we have identified effects of globin coupled sensor signaling *in vivo*, including O2-dependent effects on virulence, motility, and metabolism. We also have identified atypical cellular 2’,3’-cyclic nucleotide monophosphates (2’,3’-cNMPs) as novel bacterial signaling molecules and have determined the biomolecules responsible for synthesis and roles for these atypical cyclic nucleotides in stress responses. Using bio/chemical tools developed within the group, we are investigating the molecular mechanisms underpinning the effects of 2’,3’-cNMP levels on the transcriptome, regulation of translation, and bacterial phenotypes. By identifying and investigating novel signaling proteins and small molecules, we can identify new targets/methods to modulate phenotypes, such as virulence and biofilm formation, that could potentially be developed into anti-bacterial therapies.