

Oxygen sensing in humans is crucial for normal growth and development. The Knapp Group is interested in further understanding how the two oxygen sensing enzymes, PHD and FIH, function and their roles in hypoxia sensing. These enzymes control transcription of over 100 genes, including those important to angiogenesis, erythropoiesis and cell metabolism.

We use methods of enzymology, spectroscopy and mass spectrometry to investigate the mechanism of these two enzymes. The key question is how does HIF binding initiate hydroxylation chemistry. We study how the structure of the enzymes control oxygen access and reactivity, the role of hydrogen bonding networks within the active site and the conformational changes these enzymes undergo. We also are interested in selectively inhibiting PHD and FIH with small molecules. Further characterization of these enzymes and understanding their roles in hypoxia sensing can give insights to fighting diseases such as ischemia, arthritis, diabetes and cancer.

