Biophysical studies of the HIF-asparaginyl hydroxylase, FIH

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Cellular sensing of hypoxia, or low [O_2], is central to normal tissue development, as well as playing a crucial role in cancer and cardiovascular disease. The *Hypoxia Inducible Factor* (HIF) is the human transcription factor which controls the hypoxic response. HIF is post-translationally modified by the *HIF-asparaginyl hydroxylase* (called FIH), a non-heme Fe^{2+} hydroxylase which uses O_2 to hydroxylate HIF, leading to reduced transcriptional efficiency for a variety of genes. We report on FIH structural dynamics and cofactor binding, as these are two criteria dictating FIH activity. Backbone amide exchange rates will be presented as a probe of FIH structural dynamics for both metal-free and metal-bound FIH. Thermodynamic and spectroscopic studies of the metal site of FIH will be presented.