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Department of Chemistry

Dow Lecture Series

9:45 a.m. Thursday, February 12, 2015 • 331 Smith Hall



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Professor

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Pennsylvania State University

Demystifying the Chemical Magic of Non-heme-iron Enzymes in Natural Product Biosynthesis

Research concerns proteins that contain complex clusters of metal ions and inorganic ligands at their active sites.

Website: <http://bmb.psu.edu/directory/jmb21>

Abstract

Non-heme-iron (NH-Fe) enzymes activate O₂ for an array of biomedically, agriculturally, and environmentally important oxidation reactions. Our past decade's work has characterized iron(IV)-oxo (ferryl) complexes in several such NH-Fe enzymes.¹ In five of these enzymes, the ferryl complexes generate substrate radicals by abstracting hydrogen (H•) from aliphatic carbons,²⁻⁶ leading to formation of new C–O,²⁻⁴ C–Cl/Br,^{5,6} or C–S bonds.¹ Motivated by our success in rationalizing the divergent outcomes of the NH-Fe 2-(oxo)glutarate-dependent aliphatic hydroxylases and halogenases,⁷ we now seek both to exploit the ferryl manifold for novel, unnatural carbon-functionalization reactions⁸ and to explain the structural and mechanistic bases for several other natural reaction types, including 1,3-dehydrogenation of an alcohol to epoxide,⁹ stereo-inversion of a chiral carbon,¹⁰ and desaturation and cleavage of C–C bonds, that are initiated by ferryl complexes in other NH-Fe enzymes. Insight obtained will inform combinatorial design of new antibiotic and anticancer drugs.

¹ Krebs, C., et al. *Acc. Chem. Res.*, **2007**, *40*, 484-492.

² Price, et al. *Biochemistry*, **2003**, *42*, 7497-7508.

³ Price, et al. *J. Am. Chem. Soc.*, **2003**, *125*, 13008-13009.

⁴ Hoffart, et al. *Proc. Natl. Acad. Sci. USA*, **2006**, *103*, 14738-14743.

⁵ Galonic, et al. *Nat. Chem. Biol.*, **2007**, *3*, 113-116.

⁶ Matthews, et al. *Biochemistry*, **2009**, *48*, 4331-4343.

⁷ Matthews, et al. *Proc. Natl. Acad. Sci. USA*, **2009**, *106*, 17723-17728.

⁸ Matthews, et al. *Nat. Chem. Biol.*, **2014**, *10*, 209-215.

⁹ Wang, et al. *Science*, **2013**, *342*, 991-995.

¹⁰ Chang, et al. *Science*, **2014**, *343*, 1140-1144.

Host: Professor Lawrence Que Jr.
Refreshments will be served prior to the seminar.