BIOCHEMISTRY SEMINAR

Structural and Mechanistic Bases for Promotion of Diverse Reaction Outcomes by Iron(II)- and 2-Oxoglutarate-Dependent Oxygenases

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Iron(II)- and 2-oxoglutarate-dependent (Fe/2OG) oxygenases install synthetically useful and bioactivity-conferring chemical functionality, including hydroxyl, chloro/bromo, azido, nitro, (iso)cyanato, oxa/aza/carbo-cycle, and olefin groups, in the biosynthesis of valuable natural products and important drugs. Understanding how a simple mononuclear iron cofactor and largely conserved protein architecture can elicit such a remarkable array of chemically quite distinct reactivities has been a longstanding goal of our multi-investigator team here at Penn State. In the first part of my presentation, I will summarize recent progress toward that understanding in select enzymes that promote different reaction types. In the second part, I will focus on a single Fe/2OG oxygenase known as ethylene forming enzyme (EFE), which catalyzes a reaction that sets it apart from the rest of the enzyme superfamily. In this reaction, all four oxidizing equivalents of O2 are unleashed upon 2OG, fragmenting it to ethylene (from C3 and C4) and three fully oxidized C1 equivalents (from C1, C2, and C5), while the would-be "prime substrate" (L-arginine), which would ordinarily be targeted for oxidation, escapes unmodified. The mechanism of this reaction involves several previously unprecedented steps, which could only have been correctly deduced by a hand-over-hand cooperation of experimental and computational chemists. I will outline our current understanding of the reaction, which has revealed that EFE has potential to support industrial bioprocesses not only to ethylene, the most prolifically manufactured organic compound on earth, but also to larger alkenes (propylene, isobutylene) and the valuable plastics monomer, 3-hydroxypropionic acid.

Professor J. Martin (Marty) Bollinger, Jr. obtained a B.S. degree in Chemistry from Penn State University in 1986 and a Ph.D. in Biochemistry from the Massachusetts Institute of Technology in 1993, where he studied the enzyme ribonucleotide reductase under Prof. JoAnne Stubbe. After postdoctoral training at Harvard Medical School with Christopher T. Walsh, he joined the faculty of Penn State in 1995, where he helped to assemble a world-class team of bioinorganic chemists. His joint research group with Carsten Krebs elucidates mechanisms by which metalloenzymes harness the oxidizing power of O2 and its reduced forms, superoxide and peroxide, to transform biomolecules. He has earned a number of honors, including the Nobel Laureate Signature Award for Graduate Education in Chemistry from the American Chemical Society (ACS), the ACS Division of Biological Chemistry's Abeles and Jencks Award for the Chemistry of Biological Processes, and the William C. Rose Award, for outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists, from the American Society of Biochemistry and Molecular Biology (ASBMB).

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