

Crystallographic snapshots of natural product biosynthesis

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Halogenated natural products are medically valuable and include antibiotics (vancomycin), antitumor agents (rebeccamycin), and hormones (thyroxine). Scientists have wondered about the mechanism by which proteins halogenate natural products, since the analogous reactions by total chemical synthesis pose multiple challenges. In many cases, the moiety to be halogenated is completely nonreactive, requiring employment of a powerful catalyst. The first crystal structure of a non-heme iron halogenase, SyrB2 from *Pseudomonas syringae*, revealed a novel coordination environment for the catalytic iron and the presence of a naturally occurring iron-chloride bond [1]. The active site architecture suggests a mechanism by which nature can harness the catalytic prowess necessary to perform the most chemically challenging of halogenation reactions. Findings from our studies on SyrB2 and other non-heme iron halogenases will be presented.

[1]. Blasiak, L. C., Vaillancourt, F. H., Walsh, C. T., and Drennan, C. L. (2006) Crystal structure of the non-haem iron halogenase SyrB2 in syringomycin biosynthesis *Nature* 440, 368-71.