Many biochemical reactions, particularly oxidations, appear to require cofactors: small molecules that associate with protein active sites and catalyze key reaction steps. However, classes of microbial enzymes have been discovered that do not require cofactors. Such “protein-only” reactions have the engineering advantage of not requiring the apparatus to assemble, insert, and protect cofactors in order to retain catalytic activity. Our lab is studying a half-dozen examples of reactions of this type, several catalyzed by members of the same protein structural family. The substrates span a range of chemical types, including the very activated metallosubstrate coproheme. In this seminar, structure-based mechanism for the oxidative decarboxylation of coproheme will be described.