

**NON-TECHNICAL ABSTRACT:** *(State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project.)*

The specific and selective insertion of an oxygen atom into an unactivated C-H bond remains one of the most challenging reactions in organic chemistry. Nature has evolved enzymes into finely tuned biocatalysts capable of performing such reaction utilizing molecular dioxygen and reducing equivalents. Cytochromes P450 are a unique superfamily of heme-thiolate proteins that catalyze the insertion of an oxygen atom, derived from molecular dioxygen, into a C-H bond of a variety of organic substrates, often with high degrees of regio- and stereoselectivity. Recent interests in these proteins arise from the desire to harness their synthetic potential. However, the slow electron delivery to the active site and the rapid protein deactivation due to reactive oxygen species have hampered the use of P450 systems as efficient biocatalysts in biotechnological applications.

We propose to develop novel hybrid P450 enzymes capable of selectively inserting an oxygen atom into unactivated C-H bonds upon light activation. This hybrid enzyme is composed of a photosensitizer covalently attached to a P450 heme domain mutant. Our preliminary results are evidence that the novel hybrid enzymes can oxidize long chain fatty acids under constant visible light irradiation. Our first aim will focus on optimizing the conditions for the photocatalytic reactions. In our second aim, we will investigate the encapsulation of the hybrid enzymes into macrocapsules to improve their stability and the reusability of the hybrid enzymes, a proven cost effective advantage for biotechnological applications.