Dissertation Abstract

Heme is a ubiquitous molecule that is vital for an array of cellular processes. Within bacteria and eukaryotes there are two heme biosynthesis pathways each using a different terminal enzyme, ferrochelatase and coproheme decarboxylase. Both enzymes show significant diversity within their enzyme family. Ferrochelatases show significant sequence variation, but most notably, some have been shown to carry a [2Fe-2S] cluster, whereas other do not. The purpose of the microbial [2Fe-2S] remains unknown, as its removal does not impact catalysis. We have used a bioinformatics approach to assess the distribution of the [2Fe-2S] and have found a significant prevalence of the cluster within a small subset of phyla. Further analysis of the habitats of the cluster containing species also revealed a potential tie between aerobic metabolism and the presence of the cluster. The coproheme decarboxylase is an enzyme family that has only upon its recent discovery been tied to heme biosynthesis. Interestingly the enzyme uses its substrate as a simultaneous co-factor for catalysis. Although the mechanism of this reaction has been elucidated, we show that the activity is regulated by protein-protein interaction in actinobacteria. Overall, this body of work has identified that regulation of terminal steps of heme biosynthesis is more complex than previously assessed.