Structure and Function for Novel Proteins from an Extremophilic Iron Oxidizing Community

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As information from proteomic and genomic analyses rapidly escalates, the number of genes and proteins of unknown function continually expands. Yet methods to understanding these novel proteins, often key to understanding unique aspects of niche adaptation, are only just emerging. Because extreme environments are geochemically distinct and biologically limiting, low complexity ecosystems like that of acid mine drainage are ideal for such studies. Genomic and proteomic analysis of samples collected from the Richmond Mine in Iron Mountain (Redding, CA) have provided an initial survey of the genes and proteins that function within the community; however, it remains unclear how the numerous unique proteins facilitate survival under these conditions. With integrated metagenomic and proteomic datasets as a foundation[2], we are using a combination of computational and experimental methods to determine the structure and function of the several hundred proteins of unknown function within our model system.

Initial studies center on a high-throughput computational approach for predicting structure and function for 421 novel proteins from the dominant species in the community. We have developed a structural modeling system to compare these proteins to those of known structure (AS2TS)[2], resulting in the assignment of structures to 360 proteins (85%) and functional information for up to 75% of the modeled proteins. Detailed examination of the modeling results reveals the roles of many of the novel proteins within the microbial community. Protein classes (e.g., hydrolases, oxidoreductases) and families (metalloproteins, tetratricopeptide [TPR] repeats) that are highly represented in the community are now being targeted in experimental work. Complementing structure-function studies are biochemical and molecular biological techniques. Affinity chromatography has enabled enrichment of novel proteins with specific functions or active sites moieties. Environmental DNA clone libraries have facilitated screening of bacterial colonies for hydrolytic enzymes, including proteases, phosphatases, amylases, and lipases. Further to this molecular approach, a bacterial two-hybrid screen has been established to identify proteins interacting with our novel proteins, such as a novel iron oxidizing cytochrome and 27-repeat TPR protein.

1 Ram et al, 2005, *Science* 308:1915-20, “Community Proteomics of a Natural Microbial Biofilm”

2 Zemla et al, 2005, *Nucleic Acids Res* 33 (Web Server issue):W111-5, “AS2TS system for protein structure modeling and analysis”

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