Protein-DNA Interactome of Oxidative-Stress Transcription Factors OxyR1 and OxyR2 in Aliivibrio fischeri

The Lys-R type transcriptional regulators (LTTRs) comprise the largest prokaryotic family of transcription factors. Transcription factors (TFs) are sequence-specific DNA-binding proteins that dictate cell function by controlling selective usage of genomic information. The conservation of LTTRs within the genomes of extremely diverse bacteria means that they have evolved a regulatory role over genes with similarly diverse functions, whose products can be involved in metabolism, cell division, quorum sensing, virulence, nitrogen fixation, and oxidative stress. OxyR is a transcription factor that functions as a defense mechanism against hydrogen peroxide-induced oxidative stress in bacteria. It has been noted that *A. fischeri*'s genome, a bacterium that lives in a symbiotic association with the bobtail squid *Euprymna scolopes,* encodes for OxyR1 and OxyR2 (OxyRs). The OxyRs share functional and sequence similarities across different bacterial species, but respond differently depending on the present concentration of hydrogen peroxide. Studying the OxyR protein-DNA interactomes will allow us to identify key differences, regarding their sequence-specific DNA interactions and putative target genes. Currently, we are working on over-expressing and purifying full-length and DNA binding domain of OxyR1 and OxyR2. To determine their protein-DNA interactomes of the OxyRs, High-Throughput Systematic Evolution of Ligands by Exponential Enrichment (HT-SELEX) will be used. HT-SELEX provides information regarding the in vitro DNA-binding preferences of a target TF. The determined DNA-binding specificities will be used to bioinformatically predict the genomic targets of OxyR1 and OxyR2. Uncovering the molecular mechanisms by which the OxyRs function, will contribute to novel biomedical applications. Understanding how alterations in the TFs-genome interactions reduces an organism's survivability may contribute to deciphering novel ways of directing the death of antibiotic resistant bacteria by targeting their molecular-defense mechanism against hydrogen peroxide-induced oxidative stress.