STRUCTURAL BASIS OF SUBSTRATE RECOGNITION AND INACTIVATION IN PHOSPHATASES

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ABSTRACT

Phosphatases are ubiquitous enzymes that catalyze the transfer of phosphoryl group to water. In addition to being one of the most important and fundamental reactions in biological systems, phosphatases are critical to cellular processes such as metabolism, energy balance, nucleotide pool regulation, signal transduction pathways, and sequestration of inorganic phosphate. In bacteria, phosphatases are not only implicated in virulence but also are important vaccine candidates. In humans, phosphatases play crucial roles in disease and metabolism. For instance, human prostatic acid phosphatase has been shown to suppress pain by generating adenosine from extracellular adenosine 5' monophosphate whereas protein tyrosine phosphatase 1B is a drug target against type II diabetes. The larger context of the research described in this dissertation addresses the structural basis of substrate preferences and recognition by *Francisella tularensis* histidine acid phosphatase, class C prototype acid phosphatases from *Haemophilus influenzae*, *Pasteurella multocida* acid phosphatase, *Mycoplasma bovis* acid phosphatase and structural basis of H_2O_2/$KHCO_3$ mediated inactivation of PTP1B. Finally, this thesis addresses the structural context of oligomerization in class C acid phosphatases using small angle x-ray scattering and analytical ultracentrifugation methods.