Public Abstract
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Title:STRUCTURAL BASIS OF SUBSTRATE RECOGNITION AND INACTIVATION IN PHOSPHATASES

Hydrolysis of phosphomonoesters by phosphatases is an important biological phenomenon and is involved in critical processes such as energy metabolism, metabolic regulation of nucleotides and various signal transduction pathways. In bacteria, phosphatases are not only implicated in virulence but also are important vaccine candidates. For example acid phosphatases from a category A pathogen Francisella tularensis, has been suggested to play role in the pathogenesis. Another phosphatase that is known as P4, from an opportunistic pathogen Haemophilus influenzae, has been shown to be a promising vaccine candidate. Furthermore in humans, recent studies suggested that the human prostatic acid phosphatase (hPAP) could act as a pain-suppressing enzyme. Broadly these phosphatases are categorized as nonspecific phosphatases implying that these enzymes have broad substrate preferences. Therefore, a detailed understanding on how these enzymes recognize different substrate molecules is crucial in understanding the structure and function of phosphatases. The larger context of the research described in this dissertation addresses the structural basis of substrate preferences and recognition by different nonspecific acid phosphatases from pathogenic bacteria such as Francisella tularensis, Haemophilus influenzae, Pasteurella multocida, and Mycoplasma bovis. Finally, this dissertation provides information on the structural basis of inactivation of human protein tyrosine phosphatase 1B (PTP1B) using KHCO3/H2O2. PTP1B is a major drug target against type II diabetes. The findings described in this dissertation can help better understand the role of phosphatases in different pathogenic bacteria and subsequently may aid in vaccine development, efficient enzyme engineering, and drug development.