Public Abstract
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Biochemistry
Structural Studies of PMM/PGM From *Pseudomonas aeruginosa*
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The human pathogen *Pseudomonas aeruginosa* is a leading cause of hospital-acquired infections and poses a significant threat to individuals with compromised immune systems. *P. aeruginosa* expresses a variety of cell surface polysaccharides, including alginate, lipopolysaccharide, and rhamnolipid which contribute to its virulence and are believed to protect the organism from antibiotic therapy, and the host's immune response. Understanding the production of these polysaccharides may lead to the development of novel, potent therapeutics.

The enzyme phosphomannomutase/phosphoglucomutase (PMM/PGM) is required for the production of these molecules. Our goal is to understand the enzyme at the atomic level to develop inhibitors using the three-dimensional information provided by X-ray crystallography. Eventually, if PMM/PGM in *P. aeruginosa* can be inhibited, then the production of alginate by the bacteria may be greatly reduced, making the organism more vulnerable to conventional antibiotics.

The three-dimensional structure of PMM/PGM was determined in our laboratory showing that the protein has four domains organized in a "heart shape," with the active site in a deep cleft formed by residues from each domain. We have determined the structures of PMM/PGM bound to its two substrates, two products, and an intermediate at 2.0 Å resolution or higher. These structures reveal how the enzyme is able to recognize diverse ligands, and can serve as templates for future inhibitor design efforts.