Poster Presentation

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Structural Studies of an Novel Sugar Nucleotide Pyranose-Furanose Mutase

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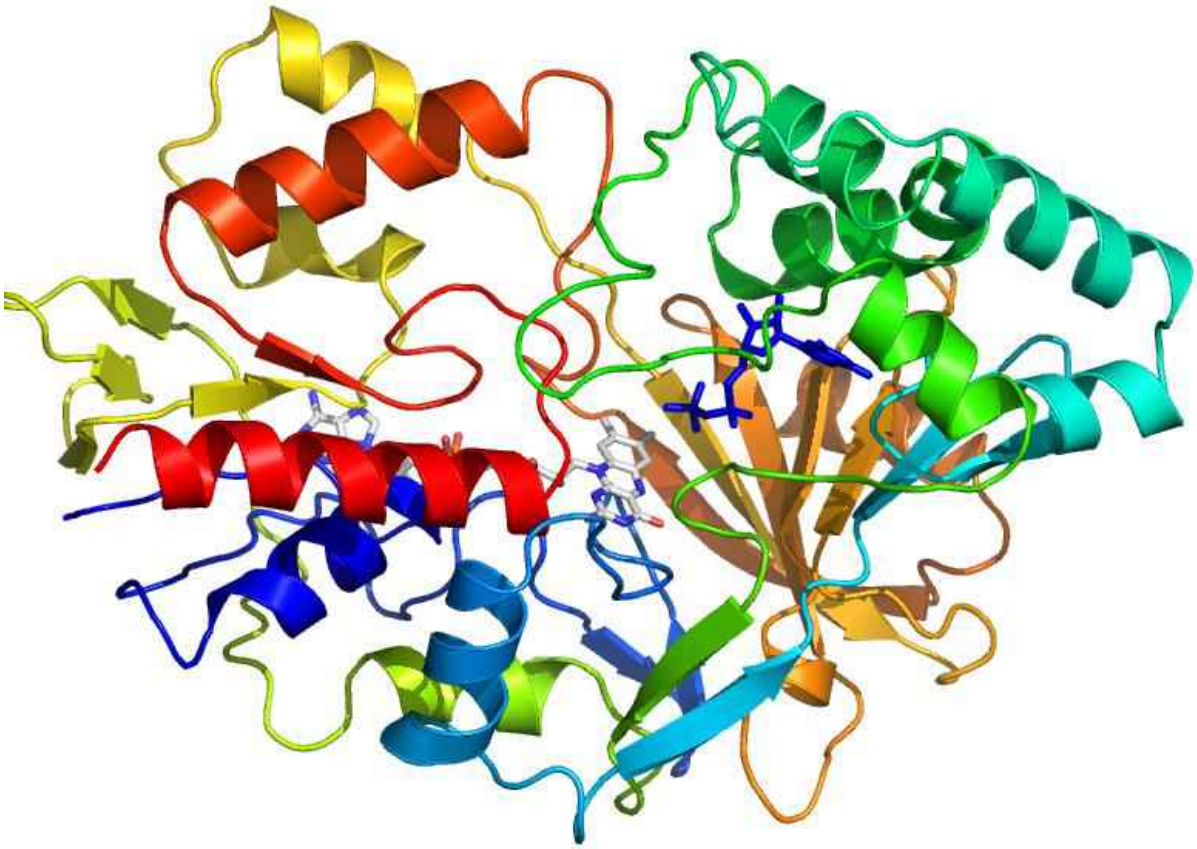
Campylobacter jejuni (Cjj) is the leading cause of gastroenteritis in humans, its glycoconjugates are known to include sugars in the furanose ring conformation. In particular, Cjj HS:41 strains are associated with the development of Guillian-Barré syndrome (GBS) and produce a key virulence factor of the bacterium, namely furanose-based capsular polysaccharides (CPS). To date, the enzymes responsible for furanose biosynthesis in Cjj HS:41 CPS are poorly understood. CPS sequencing has revealed three genes, annotated as glf1-3 via homology to known bacterial UDP-D-galactopyranose mutase (UGM), could be involved in the biosynthetic pathways. Our laboratories are interested in the structure-function relationship behind recognition and discrimination within such pyranose-furanose mutases. Enzymology studies have shown Glf1 is a flavoprotein responsible for isomerization between GDP-6d-D-altro-heptopyranose and GDP-6d-D-altro-heptofuranose, the latter being a major component of CPS. This GDP-altro-heptopyranose mutase (GaHM) activity is the first example of a heptose-recognizing mutase. Given that many of the UGM active site and FAD binding site residues are conserved in GaHM, the catalytic mechanism is likely similar to that of UGM. In order to establish key features of the enzyme, detailed structural information is required. We report here on the structure of Cjj GaHM, which has been co-crystallized with GDP, in both oxidized and reduced states. Due to low sequence identity with bacterial UGMs, Se-MET SAD phasing was ultimately employed to solve the structure. We will also discuss our recent crystallization efforts with Cjj GaHM in the presence of GDP-sugar substrate derivatives. Ultimately, the structural information gleaned from this study could lead to the identification of a new inhibitors targeting the CPS biosynthetic pathway.



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