Structural and functional characterization of the glycosyltransferase PglA from Campylobacter concisus

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Glycoconjugates represent a class of macromolecules relevant for bacterial viability and virulence, as they play a key role in host adherence. Despite the capability to synthesize a diverse set of glycoconjugates, bacteria share common mechanisms, such as en bloc glycoconjugate synthesis. The biosynthesis involves transfer of glycan moieties from a nucleotide activated sugar to a lipid acceptor undecaprenyl phosphate (Und-P). The glycan-based macromolecules are diversified through the action of glycosyltransferases, which vary in their donor-molecule selectivity. Understanding the factors influencing selectivity of glycosyltransferases could lead to the development of novel highly selective antibiotics, in the light of the emerging threat of antibiotic resistance. In this work we report the first structural characterization of a Type-B glycosyltransferase, PglA, from Campylobacter concisus, involved in the N-linked glycosylation pathway. Using X-ray crystallography, we have determined a 2.5 Å structure of PglA, bound to its native donor substrate, uridine 5′-diphospho-N-acetylgalactosamine (UDP-GalNac). Guided by this structural information we designed a series of site-directed variants in order to gain understanding of the factors influencing PglA substrate specificity.