MurJ Is The Flippase Of Lipid-Linked Precursors Of Peptidoglycan Biogenesis

Dr Chris Sham
Postdoctoral Researcher
Dr Thomas G Bernhardt’s Lab
Department of Microbiology and Immunobiology
Harvard Medical School

Abstract
Bacteria produce a variety of surface exposed polysaccharides important for biofilm formation, evading the host immune response, and promoting host adherence. The pathways responsible for producing these polysaccharides are often similar. First, the repeating units of the sugar polymer are assembled at the inner face of the cytoplasmic membrane on the lipid carrier undecaprenyl-phosphate. The resulting lipid-linked precursors are then transported across the cytoplasmic membrane by dedicated flippases, after which they are polymerized by synthases at the outer surface of the cytoplasmic membrane. Most of the flippases of lipid-linked precursors belong either to the ABC transporter or the MOP (Multidrug/Oligosaccharidyl-lipid/Polysaccharide) superfamly. While ABC transporters are relatively well studied, little is known about the mechanism by which MOP family transporters “flip” their substrates or how they identify the appropriate substrates for transport. We therefore performed Mut-seq analysis of the Escherichia coli lipid II flippase MurJ to identify all residues critical for function. Additionally, we developed a genetic selection to identify variants of the E. coli colonic acid precursor flippase WzcX that lose specificity and gain the ability to transport the lipid II peptidoglycan precursor. The combination of these studies has identified a potential substrate-binding region within MOP-family transporters and suggests a mechanism for the determination of transport specificity.

Selected Publications for Reference
