

## Microsymposium

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*Analysis of bacterial cell-wall synthesis to combat antibiotic resistance*

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The peptidoglycan biosynthetic pathway is one of the most important processes in the bacterial cell to be exploited as a target for the design of antimicrobial drugs to combat infection and pathogenesis. This pathway, unique to bacteria, utilizes over twenty enzymes, likely in concert, with reactions that proceed from the cytoplasm, across the membrane and into the periplasmic space culminating in the production of the mesh-like structure composed of polymerized glycan and cross-linked peptide components that form the major structural component of the essential bacterial protective barrier known as the cell wall. Work in our group has aimed at understanding the structural and kinetic properties of several of these enzymes including the glycosyltransferase/transpeptidase activity of a family of enzymes known historically as the penicillin binding proteins (PBPs). As the name implies, these enzymes are also the target of beta-lactam antibiotics, and molecular modifications to transpeptidase variants have been shown to be linked to increased antibiotic resistance in superbugs such as Methicillin Resistant Staphylococcal aureus (MRSA). In parallel, highly disseminated plasmid-encoded beta-lactamase enzymes, with structural and mechanistic ties to the transpeptidases, have also arisen in many of the clinically important bacterial pathogens, leading to further widespread beta-lactam antibiotic resistance. The molecular details of these critical enzymatic reactions in bacterial viability and drug resistance will be presented.

**Keywords:** antibiotic resistance