

CONFÉRENCE

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Lipoprotein cofactors located in the outer membrane activate bacterial cell wall synthases

To fortify their cytoplasmic membrane and protect it from osmotic lysis, bacterial cells typically surround themselves with a crosslinked polysaccharide meshwork called peptidoglycan (PG). The major cellular PG synthases are thought to be the penicillin binding proteins (PBPs), the targets of penicillin and related antibiotics. Although PBPs have been well characterized *in vitro*, surprisingly little is known about how these enzymes build the PG *in vivo*.

Using *Escherichia coli* as a model organism, we developed a genetic screen to directly identify factors essential for the *in vivo* activity of the PBPs. We identified two outer membrane lipoproteins of previously unknown function as critical PG assembly factors. These proteins have been named LpoA and LpoB for lipoprotein modulators of PBP function from the outer membrane. We demonstrated that LpoA and LpoB form specific trans-envelope complexes with their cognate PBP and are essential for PBP function *in vivo*. Furthermore, we confirmed that the lipoproteins directly activate their cognate PBP *in vitro*. These results indicate that essential PBP accessory proteins play a central role in PG biogenesis, and like the PBPs they work with, these factors are attractive targets for antibiotic development.

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Pavillon Claire McNicoll, salle Z-255

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