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Studies on cell wall recycling and modification in Gram-negative bacteria

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Akademisk avhandling

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Abstract
The bacterial cell wall is made from peptidoglycan (PG), which forms a bag-like exoskeleton that envelopes the cell. PG is composed of chains of alternating sugars, *N*-acetylglucosamine (GlcNAc) and *N*-acetylmuramic acid (MurNAc) crosslinked by short peptide chains and is constantly remodelled during growth and division and in response to environmental stimuli. Decades of study of this process have focused largely on a select few model organisms, leaving the diversity of these processes poorly understood. In this thesis, I present studies on different aspects of PG recycling and modification in several Gram-negative models, with a particular focus on the plant pathogen *Agrobacterium tumefaciens*, a model of the Hyphomicrobiales group of the Alphaproteobacteria which includes several species of medical and environmental interest. It is shown that *A. tumefaciens* encodes a novel peptidoglycan transporter, which is vital for cell wall integrity and resistance to β-lactam antibiotics, and widely conserved in the Hyphomicrobiales and Rhodobacterales orders. Growth defects caused by the loss of the transporter are suppressed by mutations in a novel glycopolymer, which is hypothesized to play a role in sequestering metal ions and thereby lowering periplasmic oxidative stress. Next, in collaboration, it is shown that PG recycling in the best studied model, *Escherichia coli*, is more complicated than previously thought. Rather than depending mostly on the MFS-family transporter AmpG, *E. coli* uses an ABC transporter, MppA-OppBCDF or AmpG depending on the growth phase and conditions. Finally, two studies on modification of PG by deacetylation are presented. First, *A. tumefaciens* is shown to encode a novel anhydroMurNAc deacetylase, which intriguingly seems to deacetylate specifically the PG chain termini. Then, it is shown that the causative agent of Legionnaires' disease, *Legionella pneumophila*, depends on deacetylation of its PG during infection for defense against host lysozyme and correct polar placement of its type IV secretion system.

Keywords
Peptidoglycan recycling, bacterial cell wall, antibiotics, *Agrobacterium tumefaciens*, *Escherichia coli*, *Legionella pneumophila*

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