

DprE1 protein as a non-canonical substrate for the mycobacterial Tat secretion system?

Tuberculosis, caused by *Mycobacterium tuberculosis*, remains the leading cause of death from a single infectious agent and claims more than 1 million lives annually. A thorough understanding of mycobacterial physiology is essential to identify novel drug targets and develop more effective drugs and treatment regimens. The mycobacterial DprE1 protein is a highly vulnerable target of several potent antituberculosis drug candidates – including benzothiazinones BTZ43 and PBTZ-169 (macozinone). DprE1, together with the DprE2 subunit, forms an epimerase complex responsible for the final step in decaprenylphosphoryl arabinose (DPA) biosynthesis in mycobacteria. The resulting DPA then serves as the sole arabinose donor, which is required for the buildup of crucial cell-wall arabinan polymers. In our laboratory, we have demonstrated that the FAD-dependent epimerase subunit DprE1 is unexpectedly localized in the periplasm of mycobacteria, which likely increases its vulnerability to drugs. However, its export mechanism remains unclear.

In this talk, I will present our preliminary data suggesting that the DprE1 protein might be transported to the periplasm of mycobacterial cells via the Tat secretion system, even though DprE1 lacks the canonical twin-arginine motif.