Structural and functional insights into BAM- chaperone interactions in E. coli

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Abstract:

Over the last few years, the increase in antimicrobial resistance has become a severe concern to public health worldwide, especially in Gram-negative bacteria, which have been classified as an urgent threat due to their multidrug resistance. Gram-negative bacteria's outer membrane (OM) is a protective barrier, making them more resistant to antibiotics and detergents than Gram-positive bacteria. The OM contains unique β-barrel outer membrane proteins (OMPs). OMP's biogenesis is mediated by a multi-component protein complex: the β-barrel assembly machinery (BAM) complex. This protein complex is conserved across all Gram-negative bacteria, and BamA is required for viability, making it a potentially powerful drug target. In E. coli, this ~203 kDa heteropentameric complex comprises the major conserved subunit BamA (a OMP), and four accessory lipoproteins BamB –E. OMPs are transported across the periplasm by chaperone proteins like SurA and are delivered to the BAM complex, which folds the OMPs into the OM. To gain insight into how EcBAM interacts with SurA, we determined the structure of the BAM complex bound to SurA in the presence and absence of OMPs using cryo-EM. Our structures revealed different conformations in SurA when substrates are bound than when they are not bound. In addition, the structural characterization of the BAM complex bound to SurA has revealed their interaction sites. Current work focuses on determining the importance of specific residues in these interaction sites through mutagenesis and growth assays.