MS37.O05

The role of BamA in the biogenesis of beta-barrel membrane proteins

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Beta-barrel membrane proteins are essential for nutrient import, signaling, motility, and survival. In Gram-negative bacteria, the beta-barrel assembly machinery (BAM) complex is responsible for the biogenesis of beta-barrel outer membrane proteins (OMPs), with homologous complexes found in mitochondria and chloroplasts. Despite their essential roles, exactly how these OMPs are formed remains unknown. The BAM complex consists of a central and essential component called BamA (an OMP itself) and four lipoproteins called BamB-E. While the structure of the lipoproteins have been reported, the structure of full length BamA has been elusive. Recently though, we described the structure of BamA from two species of bacteria: Neisseria gonorrhoeae and Haemophilus ducreyi. BamA consists of a large periplasmic domain attached to a 16-strand transmembrane beta-barrel domain. Together, our crystal structures and molecule dynamics (MD) simulations revealed several structural features which gave clues to the mechanism by which BamA catalyzes beta-barrel assembly. The first is that the interior cavity is accessible in one BamA structure and conformationally closed in the other. Second, an exterior rim of the beta-barrel has a distinctly narrowed hydrophobic surface, locally destabilizing the outer membrane. Third, the beta-barrel can undergo lateral opening, suggesting a route from the interior cavity in BamA into the outer membrane. And fourth, a surface exposed exit pore positioned above the lateral opening site which may play a role in the biogenesis of extracellular loops. In this presentation, the crystal structures and MD simulations of BamA will be presented along with our work looking at the role of these four structural features in the role of BamA within the BAM complex.

[1] *Noinaj N, Kuszak AJ, Gumbart JC, et al., Structural insight into the biogenesis of β-barrel membrane proteins. Nature. 2013 Sep 19;501(7467):385-90.*

Keywords: beta-barrel membrane proteins, BAM complex, outer membrane