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Structure and function of the BAM complex in outer membrane protein insertion

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Transmembrane proteins in the bacterial outer membrane display a characteristic beta- barrel architecture. Folding and insertion of these Outer Membrane Proteins (OMPs) is essential for Gram-Negative bacteria and requires the action of both periplasmic chaperones and the outer membrane complex known as beta-Barrel Assembly Machine (BAM). BAM is a five protein complex consisting of the beta-barrel OMP BamA, and lipoproteins BamB, C, D, and E. High resolution structures of all the individual BAM subunits have been determined by us and other laboratories. However, the overall complex architecture remains elusive. BamA is the central component of BAM and consists of a membrane embedded beta-barrel and a periplasmic domain with five Polypeptide Translocation Associated (POTRA) motifs thought to interact with the accessory lipoproteins. Here we report the crystal structure of a fusion between BamB and a POTRA3-5 fragment of BamA. Extended loops L13 and L17 protruding from one end of the BamB beta-propeller contact the face of the POTRA3 beta-sheet in BamA. The interface is stabilized by several hydrophobic contacts, a network of hydrogen bonds and a cation-pi interaction. BamB residues R195, L192 and L194 are central to the interface and their mutation to alanine was previously shown to disrupt BamA:BamB binding. Similarly, mutations in the beta2-strand of BamA involved in the interface were also shown to weaken or abrogate BamB binding validating the observed interface. We demonstrated that the periplasmic five-POTRA domain of BamA is flexible in solution due to hinge motions in the POTRA2-3 linker. Here we report in vivo data showing that this flexibility is important for BamA function. Modeling BamB in complex with full- length BamA shows BamB binding at the POTRA2-3 hinge suggesting a role in modulation of BamA flexibility and the conformational changes associated with OMP folding and insertion. We will also present mass-spectrometry-based analysis of the effect of BAM subunit deletion in the outer membrane proteome.

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