

The β -barrel Assembly Machinery in Motion

Nicholas Noinaj¹, Jeremy W. Bakelar¹, Runrun Wu¹, Chen Sun¹, Karl Lundquist², Tommi White³, Thomas Klose¹, Wen Jiang¹, and James C. Gumbart²

¹Department of Biological Sciences, Purdue University, 240 S. Martin Jischke Dr., West Lafayette, IN, 47907, USA; nnoinaj@purdue.edu; jeremy.bakelar@dixie.edu; wu1250@purdue.edu; sun647@purdue.edu; tklose@purdue.edu; jiang12@purdue.edu

²School of Physics, Georgia Institute of Technology, 837 State Street, Atlanta, Georgia 30332; klundquist@gmail.com; jcgumbart@gatech.edu

³Department of Biochemistry and the Electron Microscopy Core Facility, University of Missouri, W117 Veterinary Medicine Building, 1600 East Rollins Street, Columbia, MO 65211; whiteto@missouri.edu

Beta-barrel outer membrane proteins (OMPs) are found within the outer membranes (OM) of Gram-negative bacteria and are essential for nutrient import, signaling, and adhesion. While the exact mechanism for the biogenesis of these OMPs is unknown, it is known that a 200 kDa five component complex called the beta-barrel assembly machinery (BAM) complex is responsible for this task. We have previously used X-ray crystallography and MD simulations to establish that BamA, the central and essential component, may serve as a catalyst on the membrane to reduce the energy required for insertion of new OMPs. Further, we have shown that lateral opening of the barrel domain of BamA is required for function, suggesting a route for the insertion of new OMPs directly into the membrane. Despite these studies, it is known that the BAM complex functions most efficiently when fully assembled. To gain insight into this intriguing mechanism, recently, we reported the structure of the BAM complex from *E. coli*, revealing unprecedented conformational changes in the barrel domain of BamA, which may be regulated by the accessory proteins BamB, C, D, and E. The periplasmic domain of BamA was found in a closed state that prevents access to the barrel lumen from the periplasm, indicating substrate OMPs likely do not enter the barrel during biogenesis, but rather may be inserted directly at the lateral gate. In this talk, I will review the previous studies with BamA, present the recent structural studies of the fully assembled BAM complex, and provide an update on our structural studies of BAM in nanodiscs using cryoEM.