

Architectures of Lipid Transport Systems for the Bacterial Outer Membrane

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The bacterial outer membrane is a lipid bilayer that plays a key role in resistance to antibiotics, detergents, and other external stresses. Despite decades of research on the bacterial envelope, it is unknown how phospholipids are trafficked between the bacterial inner and outer membranes, through the intervening hydrophilic space of the periplasm. We recently discovered that members of the mammalian cell entry (MCE) protein family form structurally diverse hexameric rings and barrels, and that some of these proteins may form “bridges” or “pipes” between the inner and outer membrane to facilitate lipid transport (Ekiert, et al. Cell 2017). We are now working to understand how MCE proteins help to create a periplasm-spanning transport system that links the inner and outer membranes. Using cryo-EM and X-ray crystallography, along with complementary genetic and biochemical approaches, we are unraveling how the components of the *E. coli* Mla, Pqi, and Yeb systems assemble into larger inner membrane, outer membrane, and even transenvelope complexes. This work will advance our understanding of a fundamental yet poorly understood aspect of bacterial cell biology, and may open up avenues to the development of new antibiotics that target the essential process of outer membrane biogenesis. In addition, the presence of MCE proteins in some double-membraned organelles, such as chloroplasts, suggests that understanding *E. coli* MCE systems will also have direct implications for lipid trafficking in other bacterial-derived organelles.