A complex machine for lipid transport across the cell envelope of Mycobacterium tuberculosis

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The complex cell envelope of Mycobacterium tuberculosis forms an impenetrable barrier around the cell, protecting it from host immune responses and the entry of harmful agents such as antibiotics. However, this barrier is a double-edged sword, as it limits the passive entry of nutrients that the bacterium requires to grow. Despite its importance, we have very little information on how small molecules are transported across the cell envelope, and how it is built and maintained. MCE transporters (originally thought to mediate Mammalian Cell Entry in M. tuberculosis) play a role in these processes and have been implicated in virulence, but their structures and functions remain poorly characterized. Here we show that MCE transporters in M. tuberculosis form large transenvelope complexes, consisting of 10+ subunits that may be inserted in both the inner and outer membranes, simultaneously. Coupled to an ABC transporter in the inner membrane that drives transport, a ~200 Å long "needle" formed by a 6-helix coiled-coil extends across the bacterial periplasm to the outer membrane. The needle creates a hydrophobic tunnel capable of mediating lipid transport directly between the two membranes. This remarkable machine is architecturally quite different from other transporters studied to date, and sheds light on the role of MCE proteins in cell envelope biogenesis, transport, and virulence in an important human pathogen.