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A lateral gate for autotransporter and outer membrane protein assembly

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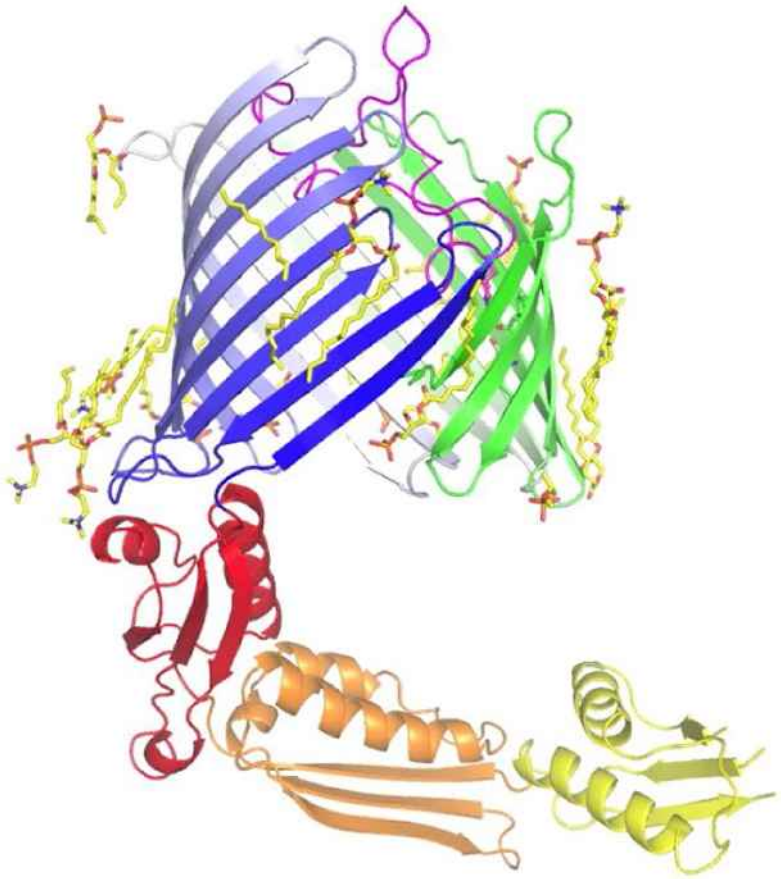
β-barrel proteins are key functional components of the outer membranes of gram-negative bacteria, mitochondria and plastids. They mediate transport across the membrane, act as receptors and are involved in bacterial pathogenicity. Despite their crucial roles, assembly and membrane insertion of β-barrel outer membrane proteins, which are mediated by β-barrel membrane proteins of the OMP85 family, have remained elusive. The crystal structure of the Escherichia coli OMP85 protein TamA [1], which is involved in autotransporter biogenesis, now provides a novel perspective on β-barrel membrane protein assembly. The protein was crystallized in lipidic phase and microseeding was employed to obtain high-quality 2.3 Å diffraction data. TamA comprises a 16-stranded transmembrane β-barrel and three N-terminal POTRA domains. The barrel is closed at the extracellular face by a conserved lid loop tightly interacting with a conserved lock region on the inner barrel wall. The C-terminal β-strand of the barrel forms an unusual inward kink, which creates a gate for substrate access to the lipid bilayer and weakens lateral inter-strand connection. These structural features immediately suggest a mechanism of autotransporter insertion based on barrel expansion and lateral release. Based on structural conservation of all core elements [2], this mechanism might well be relevant for the entire OMP85 family.

[1] *Gruss F, Zähringer F, Jakob RP, et al., The structural basis of autotransporter translocation by TamA. Nat Struct Mol Biol. (2013) 20:1318-20,* ***[2]*** *Noinaj N, Kuszak AJ, Gumbart JC, et al., Structural insight into the biogenesis of β-barrel membrane proteins. Nature. (2013) 501:385-90.*



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