Regulation of type III secretion needle formation in Pseudomonas aeruginosa

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Type III secretion systems (T3SS), found in several Gram-negative pathogens, are nanomachines involved in the transport of virulence effectors directly into the cytoplasm of target cells. T3SS are essentially composed of basal, membrane imbedded ring-like structures and a hollow needle formed by a single, polymerized protein. Within the bacterial cytoplasm, the T3SS needle protein requires two distinct chaperones for stabilization prior to its secretion, without which the entire T3SS is nonfunctional. The 2.0 Å X-ray crystal structure of the PscE-PscF$^{55-85}$-PscG heterotrimeric complex from *Pseudomonas aeruginosa* reveals that the C-terminus of the needle protein PscF is engulfed within the hydrophobic groove of the TPR-like molecule PscG, indicating that the macromolecular scaffold necessary to stabilize the T3SS needle is totally distinct from chaperoned complexes between pilus-forming or flagellum-forming molecules. Disruption of specific PscG-PscF interactions leads to impairment of bacterial cytotoxicity towards macrophages, indicating that this essential heterotrimer, which possesses homologs in a wide variety of pathogens, is a unique, attractive target for the development of novel antibacterials.