TssA: The cap protein of the Type VI secretion system tail

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The Type VI secretion system (T6SS) is a multiprotein and mosaic apparatus that delivers protein effectors into prokaryotic or eukaryotic cells. Recent data on the enteroaggregative *Escherichia coli* (EAEC) T6SS have provided evidence that the TssA protein is a key component during T6SS biogenesis. The T6SS comprises a trans-envelope complex that docks the baseplate, a cytoplasmic complex that represents the assembly platform for the tail. The T6SS tail is structurally, evolutionarily and functionally similar to the contractile tails of bacteriophages. We have shown that TssA docks to the membrane complex, recruits the baseplate complex and initiates and coordinates the polymerization of the inner tube with that of the sheath. Here, we review these recent findings, discuss the variations within TssA-like proteins, speculate on the role of EAEC TssA in T6SS biogenesis and propose future research perspectives.

Keywords:
bacteriophage; chaperone; contractile machine; protein transport; tail; TssA; type VI secretion

DOI 10.1002/bies.201600262

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Abbreviations:
EAEC, enteroaggregative *E. coli*; **T6SS,** Type VI secretion system.

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Introduction

The Type VI secretion system (T6SS) is a multiprotein machine widespread in Proteobacteria and Bacteroidetes and responsible for the transport and delivery of toxins into recipient cells (Fig. 1) [1–3]. The T6SS targets both eukaryotic and prokaryotic cells and therefore participates to pathogenesis toward plant, animal, or human cells, as well as to inter-bacterial competition [4–10]. Indeed, the T6SS antibacterial activity is responsible for re-shaping bacterial communities providing growth and colonization advantages [6, 11–18]. The effectors are deleterious enzymes (peptidoglycan hydrolases, phospholipases, DNases, etc) that are delivered into recipient cells as cargo by binding to components of the tail tube/spike complex, which is propelled by a contractile mechanism [6–8, 19–21]. This tail structure is evolutionarily, structurally, and functionally related to tails of contractile bacteriophages or of R-pyocins [22–28]. It is composed of an inner tube made by stacked Hcp hexamers and tipped by the VgrG trimeric spike complex (Fig. 1B) [29, 30]. The tail is surrounded by a sheath, made of TssB and TssC subunits, that is assembled in an extended conformation that stores mechanical energy necessary for its contraction (Fig. 1B) [31–33]. The assembly of the T6SS tail is controlled by the baseplate, a structure composed of the VgrG spike and the TssE, TssF, TssG, and TssK proteins [34–36]. The baseplate is anchored to the TssJLM trans-envelope complex, the first T6SS element to be assembled (Fig. 1B) [35, 37–42]. The TssJLM membrane complex therefore constitutes the docking station for the tail and has been proposed to serve as channel for the passage of the tail tube/spike complex that is propelled during sheath contraction [38].

T6SS biogenesis: A complex biological puzzle

Recent data using fluorescence microscopy approaches have provided insights onto the biogenesis pathway of the T6SS. The assembly proceeds inward, from the outer membrane to the cytoplasm: the membrane complex is assembled first, prior to the recruitment of the baseplate and polymerization of the cytoplasmic tail [35, 38, 43] (Fig. 2).