A Death-Dealing Nanomachine: Examining the physical stimuli response mechanisms of the bacterial Type 6 Secretion System

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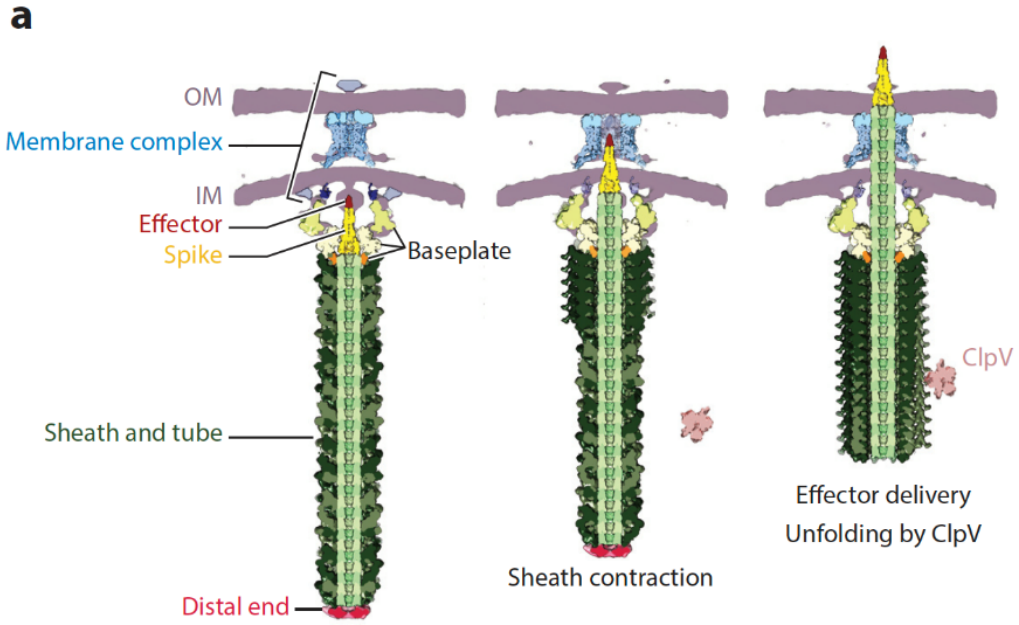
A wide variety of toxin delivery systems are used in interbacterial warfare and bacterial virulence. Gram-negative bacterial cells employ Type 6 secretion systems (T6SS) to kill other bacterial and eukaryotic cells[1] (Fig. 1). T6SS is a harpoon-like nanomachine that consists of a membrane complex[2] which spans both the inner and outer membrane of the bacterial cell. The triggering of a firing event leads to the polymerization and contraction of a sheath-tube complex, which rapidly ejects a central spike that pierces through a neighbouring cell membrane to deliver toxins and other effectors[3].
Despite insights into the structural and functional mechanisms behind the firing itself[3,4], many questions remain unresolved. These include:

(i) What triggers the firing of T6SS?
(ii) What are the nanomechanical properties of the central spike?
(ii) How fast, and what forces are required for the central spike to penetrate a membrane?
(iii) Does pore formation follow membrane rupture?



Here, we will use high-speed atomic force microscope (HS-AFM) imaging[5], as well as AFM indentation-type force spectroscopy[6] and confocal microscopy (CM) to study how the T6SS spike punctures bacterial and eukaryotic cell membranes. This includes T6SS of (1) P.aerigunosa that is capable of sensing attacks of neighbouring cells[7], and (2) B.thailandensis that causes disease by inducing membrane fusion between neighbouring mammalian cells to form multinucleated giant cells[8].

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