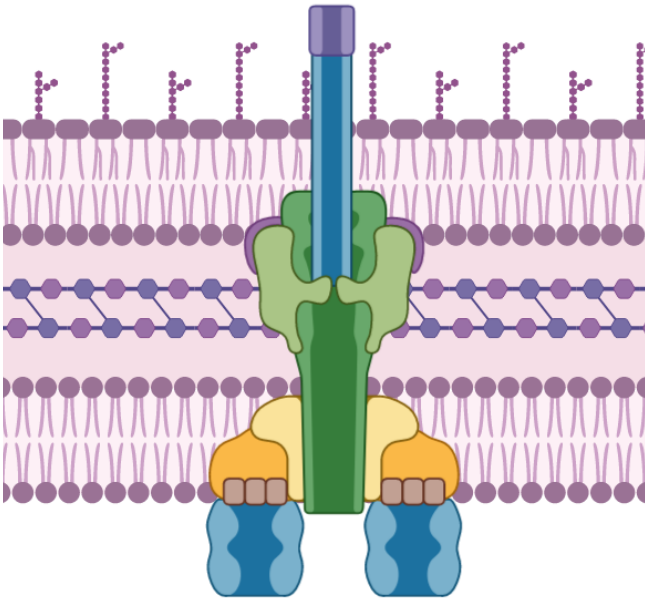
Type IV Secretion System (T4SS)

(Francisco Pérez-Montaño)



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Claim to fame: transferring genetic elements between bacteria and injecting virulence factors into target cells

What is T4SS? The T4SS is a biological "molecular syringe", a bacterial micromachine designed to transfer materials from the donor cell into a recipient cell. It serves two primary functions. Some T4SSs are employed by pathogenic bacteria to translocate a wide array of protein virulence factors, including DNA-protein complexes, into eukaryotic cells of infected hosts, while others facilitate horizontal gene transfer among bacterial populations, in a process termed conjugation.

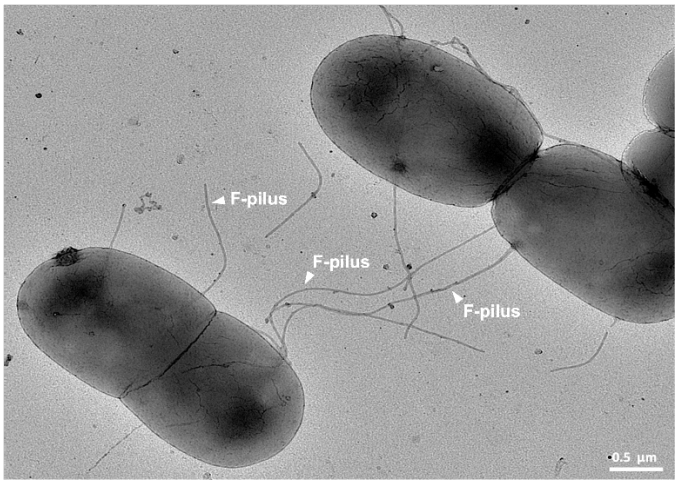
What does it look like? How big is it? The T4SS is a tunnel-shaped structure that traverses the cell envelope of many bacteria and terminates in a long, rigid, needle-like pilus protruding from the bacterial surface. The size of the structure can vary, but on average, it has an outer diameter of 8-10 nanometres, a length ranging from 2-20 micrometres, and an internal channel diameter of 2 nanometres.

How does the cell make it? The bacterium follows its genetic instructions to produce the necessary components, including the inner membrane complex, the core complex, and the extracellular pilus. Additionally, the bacterium produces the DNA and/or proteins that will be transferred across the machine directly into the target cell. Once all the components are produced, the bacterium assembles the T4SS pieces and translocates virulence factors into eukaryotic cells or facilitates the distribution of genetic material between bacteria.

How does it work? Upon receiving a set of signals that enable bacteria to recognize the presence of appropriate hosts or other compatible bacteria for gene transfer, proteins or genetic material are translocated inside the target cell. When virulence factors are transferred, eukaryotic cells are manipulated to promote bacterial infection. Conversely, when the purpose is to share DNA among bacteria, the surrounding population acquires specific abilities through horizontal gene transfer.

Where is it found? Which organisms? T4SSs are produced by many gram-negative and gram-positive bacteria, as well as by some archaea. Consequently, this micromachine can be found in nearly all environments colonized by microorganisms, including soil, freshwater, and marine ecosystems, either in symbiosis with plants or animals or associated with them as part of their microbiota, or as pathogens causing infections. They can even be found in extreme environments such as hot springs, volcanic fumaroles, acidic, or high-salt environments.

Some numbers? The number of different T4SS machines encoded in the genome of a bacterium can vary from 1 to 3 or 4, depending on whether these micromachines are used to promote infection in eukaryotic hosts or for conjugation with other bacteria. In other words, a bacterium could assemble up to 4 different molecular syringes that enhance the infective process by promoting the colonization of the host or by manipulating eukaryotic cells for its own purposes. However, when the aim is genetic transfer, only one of these protein secretion systems is enough to ensure the spread of resistance, virulence, and social traits among prokaryotes.



The T4SSs utilized in genetic transfer are marked with white arrows (F-pilus), from the free media repository Wikimedia Commons.

What is its importance to the microbe? The T4SS is the most sophisticated mechanism for gene transfer in bacteria. Its function is to spread the genetic information for properties of utility in a particular environment. Benefits may include antibiotic resistance, xenobiotic tolerance or the ability to use new metabolites, among others. Moreover, this micromachine is critical for the pathogenicity of many plant and animal-infecting bacteria. In other words, the ability to infect and cause diseases in many bacteria depends in most instances on the presence of this protein secretion system.

Its importance to us? The T4SS serves as a gene transmission mechanism, playing a crucial role not just in microbial evolution but also in human health. It serves as a platform for the dissemination and perpetuation of antibiotic resistance genes; antimicrobial resistance – AMR –

is considered by the World Health Organisation to be one of the most significant current health challenges. Infections by AMR pathogens, especially in hospitals, are difficult to manage, prolong illness durations, escalate healthcare expenditures, and amplifying mortality rates.

T4SS-mediated spread of AMR among microbes, especially pathogens, is promoted by the selection pressure of antibiotics in the environment. Therefore, massive reductions of antibiotics in the environment are needed, to be achieved by restricting clinical use of antibiotics to cases where they are effective, promoting the responsible utilization of antibiotics in food production, and preventing antibiotics from entering wastewaters from hospitals and industrial production facilities.

In addition, since this micromachine is responsible for the pathogenicity of many human- and animal-infecting bacteria, it is very important to study the T4SS system to uncover how it works and to characterize the different proteins that can manipulate host cells to promote diseases. In this way, this information can be used to develop drugs against pathogenic bacteria that target against protein effectors.