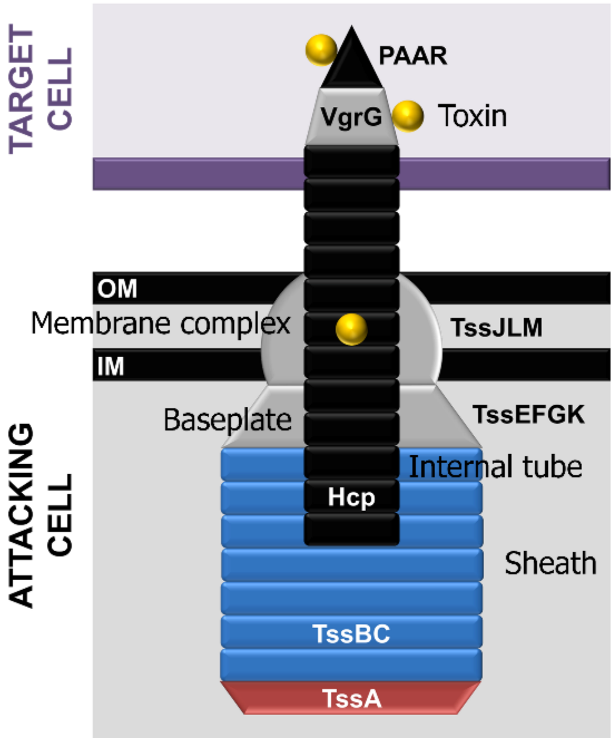
Type VI Secretion System (T6SS)

(Patricia Bernal)



Schematic representation of a T6SS machine at the moment of firing. The Hcp tube (black), the VgrG/PAAR tip complex (grey/black), and their associated effectors (yellow) are propelled from the attacking cell into a neighboring target cell (purple). The membrane complex and baseplate structures are shown in grey, whilst the sheath and the cap protein TssA are illustrated in blue and red, respectively. Image from Bernal et al., 2021 PNAS

Microbial competition and the weaponry involved

Microbes are the great transformers: they recycle everything possible to obtain food and energy from available resources. They do this as complex communities of different microbes. When new resources appear, microbes fiercely compete to take the most of them. However, once the winners have succeeded and the competition is over, a stable microbial community may be formed with its members tending to be transactional, that is, sharing resources among themselves, to achieve maximal efficiency of resource utilization. They live together more or less peacefully, except when they need to fend off newcomers.

Microbes have several strategies, weapons, and defense systems, which they can use to compete against others, including antibiotics, secretion systems, various immunity systems, and means of starving others of essential nutrients, like iron. Here, I explain one of these, the Type VI Secretion System, T6SS.

What is T6SS and what function does it serve?

The T6SS is a tiny bacterial machine that injects toxins into target cells. It is only found in certain types of bacteria (Gram-negative bacteria) and often targets other bacteria. It can be thought of as a powerful weapon that bacteria use to fight against other microbes. Phylogenetically speaking, there are different types of T6SS named 1 to 5 that have different characteristics that will be described below.

What does it look like? How big is it?

The T6SS structure looks a bit like a bacteriophage or a syringe. It has a tube surrounded by a contracting sheath, and it is capped with a puncturing tip to break through bacterial cell walls. The size of the structure can vary but on average is approximately 1 micron (1 µm, which is a thousandth of a millimeter; a human hair has a diameter of about 50 µm),. This is because the T6SS structure extends from one side of the bacterium to the other, and bacteria have an average diameter of about 1 micron.

How does the cell make it?

The bacterium follows its genetic instructions to produce the necessary parts, including the membrane complex, the baseplate and the tail composed of the internal tube and the surrounding sheath. The bacterium also produces the toxins that will be uploaded into the machine to be fired. Once all the parts are produced, the bacterium assembles the pieces including the toxins into the T6SS that will be ready to be fired when needed.

How does it work?

Once the machine is assembled, it is ready to be fired. Upon a signal that allows bacteria to recognise the presence of the enemy, like membrane disturbance after being attacked, the sheath contracts and the internal tube with the spike loaded with the toxins is ejected out of the cell and into the prey cell. In this way, the toxins are delivered to the target cell that, as a consequence, will get intoxicated and will stop growing or die.

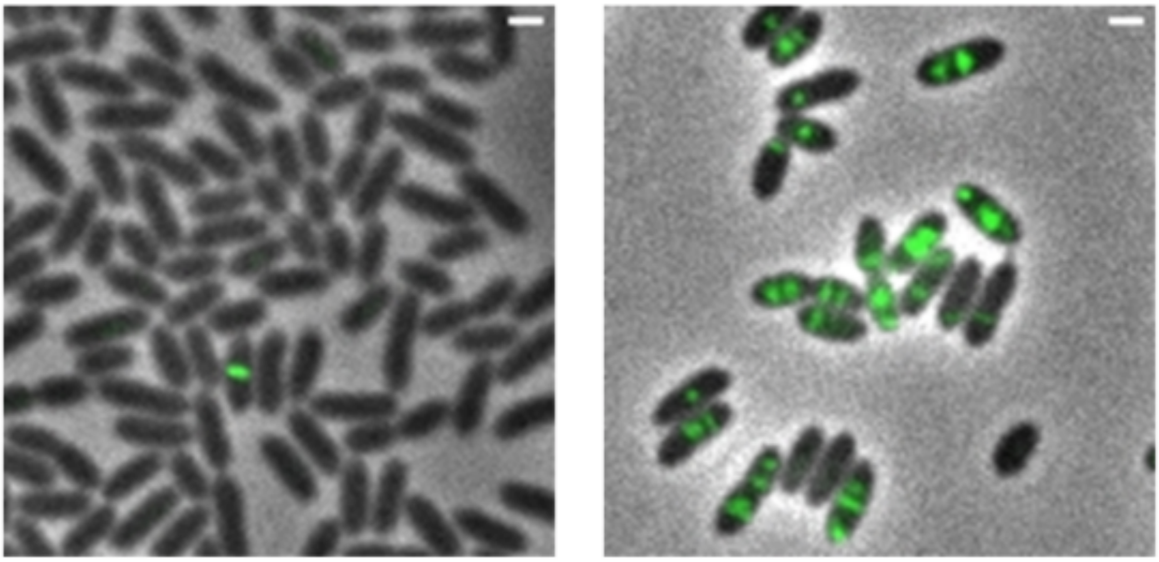
Where is it found (which organisms)?

The T6SS is found in certain types of bacteria known as Gram-negative bacteria, mostly within the Proteobacterium Phylum (a phylum is a group of evolutionarily-related organisms that share some behavioural characteristics). This Phylum is very diverse, and bacteria belonging to this Phylum can be found in many different environments, including soil, freshwater and marine ecosystems, in symbiosis with plants or animals, or associated with them as part of their microbiota, or as pathogens causing infections, and even in extreme environments such as hot springs, acidic environments or high-salt environments (salt pans).

Some numbers (e.g. rpm, how many per cell, etc.)

The number of different T6SS machines encoded in the genome of a bacterium can vary from 1 to 5. That is, a bacterium could assemble 5 different killing machines that will be activated differently according to needs and that will secrete different toxins. Moreover, the bacterium could assemble a variable number per cell of each type of T6SS machine.

Some T6SS machines (known as the speedy ones) are only assembled one at a time, and they are fired immediately after being assembled. They are part of an offensive strategy to attack competitors. Other T6SS machines are slower and once they are assembled can stay in the cells up to 10 minutes before they are fired. The bacterium can accumulate up to 6 machines of the slow type assembled at the same time and they will be fired upon a signal of being attacked. This is a defensive strategy.



Fluorescence microscopy images from a time-lapse recording of *Pseudomonas aeruginosa* expressing the sheath of one of the 3 T6SSs present in this bacterium (H1-T6SS) and fused to a green fluorescent protein (left). On the right, fluorescence microscopy images of the same strain expressing the sheath of a second T6SS (H2-T6SS) (right) fused to the same green fluorescent protein. The number of T6SS apparatuses per cell is lower for H1-T6SS (speedy system) than for H2-T6SS (slow system). Scale bars represent 1 μm. Image from Bernal et al., 2021 PNAS

Importance of T6SS to the microbe producing it?

The T6SS is extremely important for microbes because it allows them to fight off competitors. By killing competitors, bacteria increase their chances of survival in the niche, and being able to acquire and exploit some of its resources themselves.

Its importance to us (e.g. as a target for development of new antimicrobials to treat infections)?

The T6SS is a potent killing machine to kill bacteria, thus, like antibiotics, we can use it to kill bacteria that cause infections in animals (including humans) and plants (including crops). For scientists to be able to do so, it is very important to study the system to uncover how it works and to characterize the different toxins that can be fired. Toxins kill by impairing important vital functions in bacteria (DNA, RNA, protein, membrane, cell wall, etc.). Understanding better how they do this can help us develop new drugs that mimic them and that can be used to inhibit pathogenic bacteria.

The use of microorganisms such as bacteria to kill pathogenic microbes is known as biological control or biocontrol. Biocontrol can be used for example as a green alternative to the use of chemical pesticides used to reduce infections of crop plants, chemicals that are hazardous and contaminate the environment, especially soil and groundwater.