Researchers reveal SBP8a configurations

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A new study has shown previously unseen details of an anthrax bacteriophage — a virus that infects anthrax bacteria — revealing for the first time how it infects its host, and providing an initial blueprint for how the phage might someday be modified into a tool for the detection and destruction of anthrax and other potential bioterror agents.

The bacteriophage, known as Bacillus anthracis spore-binding phage 8a (or SBP8a, for short), is too small to be seen with a conventional light microscope. To create a portrait of the virus, researchers employed cryo-electron tomography, using an electron microscope to image a flash-frozen sample from many different viewing angles. With the help of computers, the scientists then recombined these views to produce three-dimensional renderings of the phage.

One of the surprising initial results was that the samples imaged contained SBP8a in four distinctly different configurations. While all four states are generally similar, with globular "heads" and linear "tails," significant differences can be seen that the researchers believe correspond to different steps in the viral infection process.

"The images we made from these four major populations clearly show in three dimensions exactly how these remarkable nanodevices are able to penetrate the anthrax cell, release their DNA from the bacteriophage's head and ultimately control its flow through the phage tail and into the cell," said University of Texas Medical Branch at Galveston assistant professor Marc Morais, senior author of a paper on the study now online in *Virology*.

Each of SBP8a's different states is marked by four key substructures: a hockey-puck-shaped "baseplate" at the opposite end of the tail from the head; a hollow tube running from the head to the baseplate; a sheath formed by six strands that wind around the hollow tube; and SBP8a's neck, which lies at the intersection of the bacteriophage's tail and its DNA-containing head and which is connected to the baseplate by the six-stranded helical sheath.

The process begins when the baseplate recognizes and binds to a suitable receptor on an anthrax bacterium. This binding causes the baseplate to immediately change its shape to a more open, clawlike structure, which in turn signals the sheath to contract to nearly half its length.

"When it contracts the tube has no choice but to be driven into the cell, much like a syringe," Morais said. "And in addition to contracting, the tail sheath is rotating, and that rotation exerts a torque on the neck protein, which opens the neck protein up so that DNA can now flow from the head into the tail, and then through the tail into the host cell's cytoplasm."

Morais' interest in SBP8a goes beyond the mechanics of its replication. He and his colleagues would like to take advantage of the fact that unlike other anthrax bacteriophages, SBP8a bonds to anthrax spores, not just anthrax bacteria. That gives it the potential to serve as the basis of a highly efficient detection system for the deadly agent.

"We want to push to high enough resolution where we can see secondary structure and make reliable models, and really rationally engineer these type of things," Morais said. "The genome has been sequenced now, and we're figuring out which parts can be removed and replaced with green fluorescent protein — the first step to endowing these bacteriophages with a reporter capacity and making them a detection tool.

"The great thing about our approach is that it is completely flexible. Every pathogenic bacterium has a phage associated with it. Thus, one could imagine tagging each pathogen-specific phage with a different colored signaling molecule such that you could make a cocktail of modified phages that glows a different color depending on which bacteria is present. Such a kit could be used to quickly identify a pathogen present in a bioterror attack."

Provided by University of Texas Medical Branch at Galveston