Shape-shifting volcano virus points to new ways to deliver drugs, vaccines

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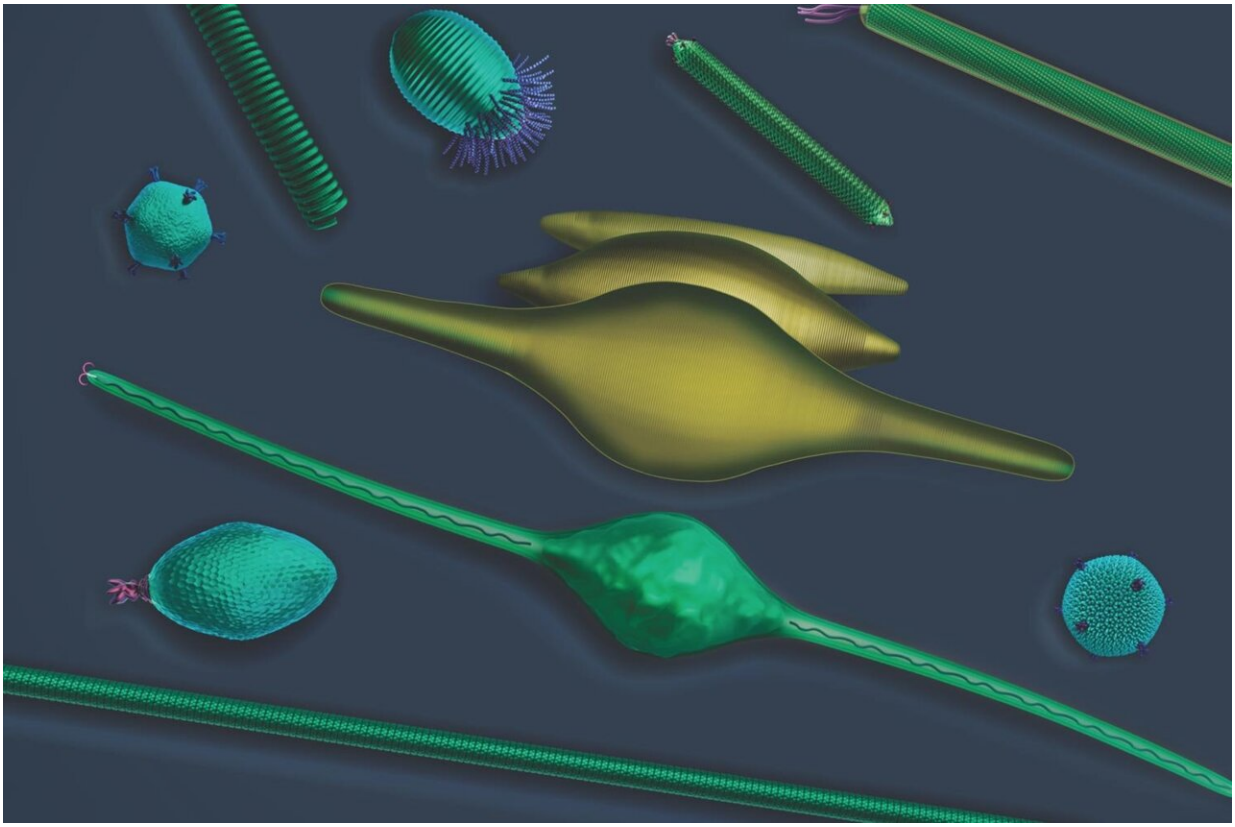

The lemon-shaped SMV1 virus is a formidable threat to the single-celled organisms it infects. Credit: The Egelman Lab, UVA

From hot volcanic springs where the water is nearly boiling acid, a University of Virginia researcher and his colleagues have discovered

how lemon-shaped viruses got their form. And that discovery could lead to new and better ways to deliver drugs and vaccines.

While the vast majority of viruses are either rod-like or spherical (such as the coronavirus responsible for COVID-19), scientists have been puzzled by the unusual forms of viruses found in some of the harshest environments on Earth.

The researchers were studying one such virus when they discovered it has strange properties that allow it to alter its shape. While it normally resembles a lemon or spindle, the virus can grow tails. The structure that lets it do that, the scientists realized, likely explains how ancient rod-like viruses gave rise to all the spindle-shaped viruses seen today.

"We can now understand a new principle in how proteins can form the shell that packages the DNA in a virus," said lead researcher Edward H. Egelman of the UVA School of Medicine. "This has implications for not only understanding how certain viruses evolved, but potentially can be used for new ways to deliver everything from drugs to vaccines."

The shape of viruses

The virus Egelman and his colleagues were studying, Sulfolobus monocaudavirus 1, or SMV1, has a protein shell surrounding the DNA that is spindle- or lemon-shaped. But it has been a puzzle for almost 20 years exactly how that many copies of the same protein can come together to form such a shape.

Egelman and his team were able to reveal the strange properties of SMV1 using high-tech cryo-electron microscopy and advanced image processing.

SMV1, the researchers found, contains strands of proteins that that slip

and slide past each other, due to the fact that they are "greasy." These seven strands of proteins were found in both the body and tail of the virus, and they give the virus a remarkable ability to shapeshift. Rather than having a fixed shape, it can balloon up like a pufferfish to accommodate genetic material. At the same time, these strands form an impenetrable barrier to prevent the acid that surrounds the strands from destroying the DNA inside the virus.

The virus is a formidable threat to the single-celled organisms it infects. Once infected, the host organisms turn into relatively giant factories churning out more virus. These host cells grow up to 20 times larger before a new army of viruses bursts forth.

Based on their findings, Egelman and his collaborators conclude that today's viruses shaped like spindles or lemons likely evolved from ancient rod-shaped ancestors. The rod-shaped viruses could only contain a limited amount of DNA, and the "greasy" properties that let SMV1 shapeshift would have let the ancestral viruses package more genetic material—a useful trait for viruses, from an evolutionary perspective.

"Viruses can pose great threats to human health, as we see from the COVID-19 pandemic," said Egelman, of UVA's Department of Biochemistry and Molecular Genetics. "It is thus crucial that we understand more about how viruses have evolved. But we can also learn from viruses, and create new technologies based upon the principles found in these very simple structures."

The researchers have published their findings in the scientific journal *Cell*.

More information: Fengbin Wang et al, Spindle-shaped archaeal viruses evolved from rod-shaped ancestors to package a larger genome, *Cell* (2022). DOI: 10.1016/j.cell.2022.02.019