Researchers reveal findings about virus that lives in Yellowstone hot springs

March 1 2018

Rebecca Hochstein, who earned her doctorate in MSU's Department of Microbiology and Immunology in 2015, is shown collecting samples in a hot spring in Yellowstone National Park. Hochstein is lead author of a study that explains how a lemon-shaped virus assembles itself and how the virus ejects the DNA it carries into host cells. Credit: Derek Loudermilk

For seven years as a graduate student at Montana State University, Rebecca Hochstein hiked into the backcountry of Yellowstone National Park.

Careful to avoid the bears whose tracks she saw on the trail, she collected samples from a 176-degree hot spring at the south edge of Hayden Valley. Then she returned to MSU, where she processed the samples, analyzed her findings and eventually focused her doctoral research on a lemon-shaped virus whose secrets she continues to reveal.

Rebecca Hochstein, who earned her doctorate in MSU's Department of Microbiology and Immunology in 2015, is lead author of a study that explains how a lemon-shaped virus assembles itself and how the virus ejects the DNA it carries into host cells. Contributed photo by Tina Loesekann.

Her most recent paper—this one published in *PNAS*, the official journal of theNational Academy of Sciences—explains a totally new way that viruses operate in building particles and how viruses can change shapes to interact with their host cells. With potential applications in medicine and biotechnology, the paper specifically focuses on the Acidianus tailed spindle virus, or Acidianus virus for short. The paper explains how nature assembles the virus and how the virus ejects DNA.

"There are really only three common shapes for viruses (spherical, cylindrical and lemon-shaped)," said co-author Martin Lawrence, a professor in MSU's Department of Chemistry and Biochemistry in the College of Letters and Science. "We have understood for many years the principles for the construction of cylindrical and spherical viruses, but this is the first time we have really understood how the third class of viruses is put together.

"We now understand how this third kind of virus shell is assembled and the dynamic process it uses to carry and then eventually eject the DNA that it is carrying," Lawrence said. "This understanding could potentially be adapted for technological uses.

"If we could load these virus shells with a different cargo, say a drug, and target it to a particular place in the body, such as a tumor, it could then deliver the drug to just that specific location, making the drug more effective, or reducing side effects," Lawrence said.

Hochstein's collaborators said her research is significant because it contributes to basic understanding and has the potential for broad applications. It also shows what can happen when scientists have access to one of the world's most sophisticated microscopes. Such microscopes have sparked a revolution in cryo-electron microscopy, for which the developers of the technology won the 2017 Nobel Prize in chemistry.

Hochstein and her collaborators from MSU, the University of California, Los Angeles, and the Max Planck Institute of Biochemistry in Germany learned more about the structure of the Acidianus virus by using a combination of cryo-electron microscopy and X-ray crystallography.

X-ray crystallography shoots X-rays at crystallized proteins to determine biomolecular structures. Cryo-electron microscopy fires electrons at proteins that have been frozen in solution, providing images of such high resolution that scientists can create models down to the atomic level. The cryo-electron microscope in Hochstein's project was the most sophisticated one in the world just five years ago, Lawrence said. The instrument worth approximately $7 million is located at the Max Planck Institute where Lawrence was on sabbatical from 2013-14.

Co-author Mark Young, a professor in MSU's Department of Plant Sciences and Plant Pathology in the College of Agriculture, said virologists and scientists interested in nanotechnology were excited to learn about a new way that nature has evolved viruses to build a virus particle.

Young added that he is a big proponent of discovery-based fundamental science and said Hochstein's research is a great example of that. He said her findings could someday have important applications.

"The detailed understanding of this virus isolated from a boiling acid hot spring in Yellowstone provides a potentially new virus-based nano-container that can operate at high temperature and acidic conditions which is of interest to biotech companies," Young said. "This is because it extends the conditions under which virus-based nano-cages can operate. Already, these types of nano-cages have been shown to be stable in the animal GI track, opening the possibility for their development as smart drug delivery systems."

Lawrence said the research team, among other things, was able to discover how the Acidianus virus makes a "remarkable transition" from a lemon-shaped virus into long, thin cylinders. Explaining how, he compared its structure to bricks connected by ropes.

"The bricks are actually connected to each other in long spirals, almost like a spiraling rope, and four to six of these spiraling ropes then wrap around each other to make the lemon-shaped container," Lawrence said.

To turn the lemon-shaped viruses into cylinders, the ropes have to slide against each other, Lawrence said.

"We think this transition is used to squirt the DNA from the virus into the cell that the virus is infecting," Lawrence said. "This answers the question of how the DNA leaves the virus. By analogy, how does one get juice out of a lemon? You squeeze it. In this case, the ropes in the shell squeeze the DNA inside, forcing it out."

Lawrence praised Hochstein for her years working in Yellowstone National Park and her involvement in every other phase of the research. Acidianus doesn't grow in the lab, so Alice Springs in Yellowstone Park's Crater Hills became her laboratory, Lawrence said.

Hochstein, first author of the *PNAS* paper, earned her doctorate in MSU's Department of Microbiology and Immunology in 2015. She is now a postdoctoral researcher at the University of Minnesota Twin Cities where she investigates the microbiome of the marine worm Capitella teleta.

Hochstein has switched her focus away from the lemon-shaped virus, but she said she is excited about her first publication in *PNAS*. Her previous findings about the Acidianus virus were published in 2015 and 2016 in the *Journal of Virology*.

"It was exciting to see all this come together as such a big story in a big journal," Hochstein said. "I put a lot of time and effort into this virus. It's nice to see that other people besides me think it's interesting and important."

More information: Rebecca Hochstein et al, Structural studies of Acidianustailed spindle virus reveal a structural paradigm used in the assembly of spindle-shaped viruses, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1719180115

Provided by Montana State University