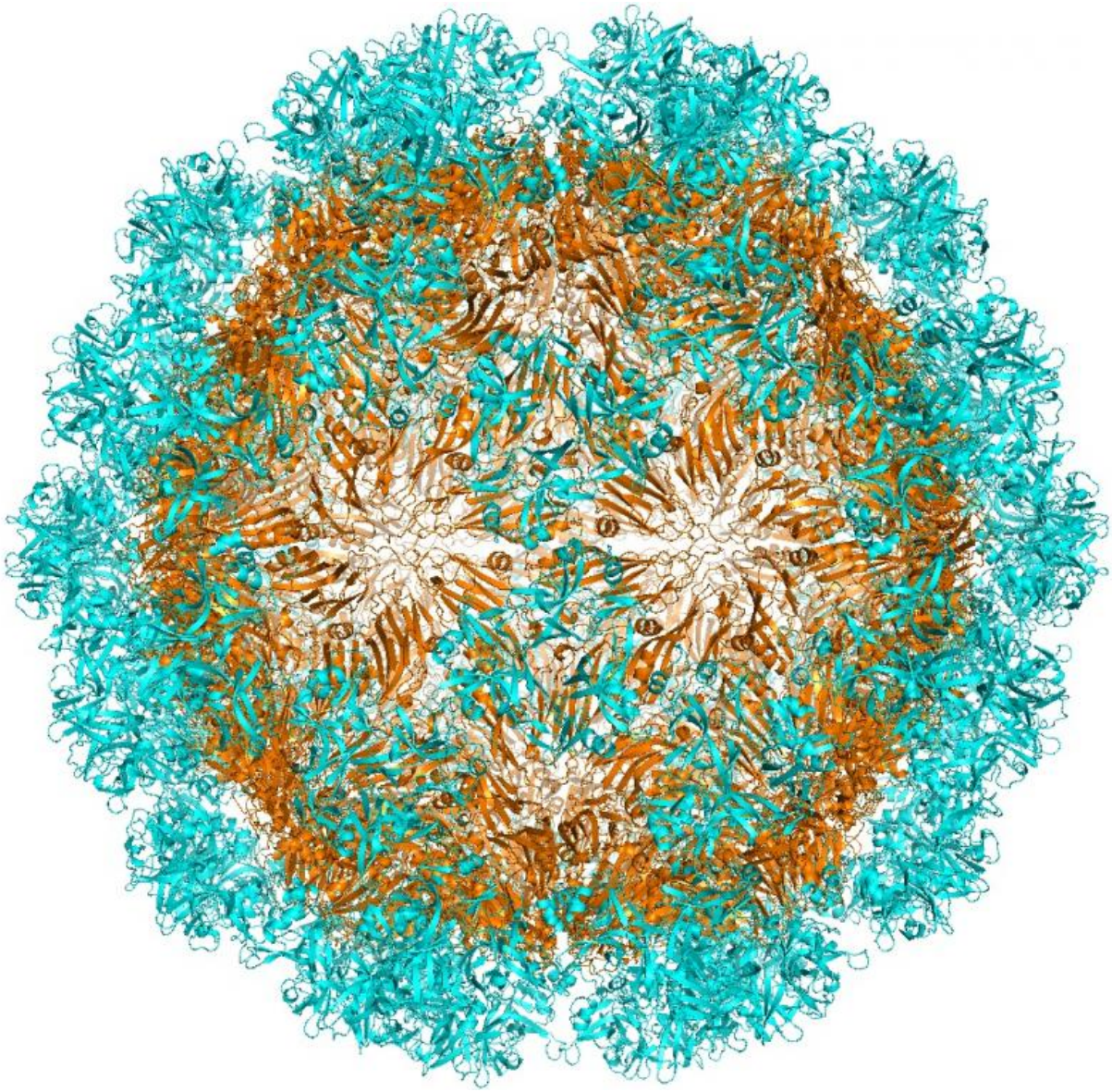
Worms point way toward viral strategies

August 25 2016, by David Ruth



The crystal structure of the Orsay virus shell known as a capsid, seen in a computer model created at Rice University. Rice researchers have received a

National Institutes of Health grant to study the mechanism of how the virus infects a nematode known as C. elegans, and by extension, how viruses infect organisms in general. Credit: Tao Laboratory/Rice University

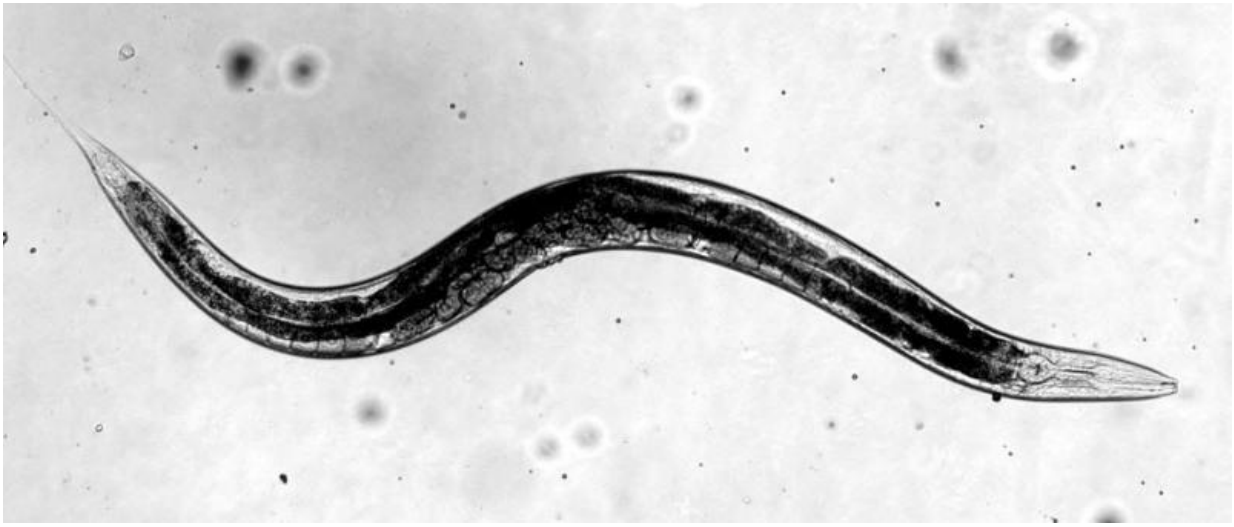
Rice University structural biologist Yizhi Jane Tao and geneticist Weiwei Zhong have won a prestigious National Institutes of Health R01 grant to study how the Orsay virus infects a specific worm.

They hope to reveal universal details about how viruses infect the intestine of animals, including humans, and how to fight them.

The five-year award for $1.25 million will help the researchers continue their study of the Orsay virus, the only one known to infect Caenorhabditis elegans, a species of nematode that is ideal for biological study because of its simplicity and transparency.

The worm and its virus brought Tao and Zhong together several years ago when they became the first to define the crystal structure of the Orsay virus through X-ray crystallography, a specialty of Tao's lab. The work revealed details of the viral capsid, the hard shell that protects Orsay's infectious contents until it can be delivered to a cell.

The virus infects the nematode's digestive tract. "We can't see the virus, but we can see the intestine cells," said Zhong, an assistant professor of biochemistry and cell biology. "The worm's natural lifespan is only two weeks, so we can watch what happens every day as the infection progresses."



A nematode from the Rice lab of biochemist Weiwei Zhong. Nematodes are favorite models of biological systems for their relative simplicity, their transparency and the ease with which scientists can manipulate their genetic sequences. Credit: Zhong Lab/Rice University

"This study will help us to understand how gastrointestinal viruses impact humans," said Tao, an associate professor of biochemistry and cell biology. "Intestinal cells are very hard to culture because they lose their polarity once you grow them in a petri dish.

"C. elegans' intestinal cells have a similar structure to humans', and we can use them as a model to understand how the virus is directed toward the apical membrane of the intestinal cell and gets released without disrupting the cell, causing it to lyse (break down)," she said.

"The bigger picture is to try to understand how the virus interacts with the host at different stages of the infection," Tao said. "For example, we want to know how viruses interact with a receptor and get into the cell, how it interacts with the host cell to ensure replication of the genome

and, during the later stage, how it modifies the host system to ensure the release of the viral particle."

Tao and Zhong also plan to map C. elegans' antiviral pathways through computer models and experiments. They expect to shed light on the mechanisms used by such gastrointestinal viruses as rotavirus, astrovirus and norovirus.

"Worms are different; humans have innate immunity and acquired immunity," Zhong said. "We have antigens that help build up antibodies, but worms do not. They only have innate immunity, but not the specialized immune cells."

"One of the things we study is how to use host immunity to fight the virus," she said. "For example, worms can be used to find what genes are involved in antiviral immunity. We can then check whether these genes are homologues of genes that humans also have. It's likely the mechanism of how these worms fight viruses will give us some insight into human-virus interactions."

More information: Read the project description at https://projectreporter.nih.gov/project_info_description.cfm?aid=9196930&icde=29989905&ddparam=&ddvalue=&ddsub=&cr=2&csb=FY&cs=DESC

Provided by Rice University