Antiviral used to treat cat coronavirus could hold key to COVID-19

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Biochemist Joanne Lemieux is working with U of A colleagues to find out whether a compound known to cure a deadly coronavirus-caused disease in cats might also work against COVID-19 in humans. Credit: University of Alberta

University of Alberta researchers are racing against the clock to test an antiviral drug that has been proven to cure a cat coronavirus and is hoped to have the same effect on people with COVID-19.

"Our lab has been working as fast as we can to get our results out," said biochemist Joanne Lemieux. "We have not taken weekends, the days of the week have blurred. We're all working non-stop to get results as fast as we can."

The project is one of 11 at the U of A to receive funding from the federal government's $52.6 million investment in COVID-19 research.

"There is a possibility that combination therapy can be used, so there are multiple lines of attack," Lemieux said.

Following the worldwide outbreak of severe acute respiratory syndrome (SARS) in 2003, chemist John Vederas, biochemist Michael James (now a professor emeritus) and other U of A scientists studied a mechanism that stopped the virus from replicating in the laboratory. The compounds, known as protease inhibitors, have since been further developed in the United States, tested and shown to also stop a fatal virus in cats.

Now Vederas, Lemieux and virologist Lorne Tyrrell are combining their labs' efforts to test the inhibitor against the new coronavirus that is causing the worldwide COVID-19 pandemic.

"I'm very excited about this research project," Lemieux said. "It's nice to think that we can make a difference."

How protease inhibitors work

It is estimated that five to 10 percent of all new drugs in development worldwide are protease inhibitors. They have been used successfully to target diseases including high blood pressure, congestive heart failure, HIV, Type 2 diabetes and even cancer.

COVID-19 is a ribonucleic acid (RNA) virus, as are many other infectious viruses such as Ebola, hepatitis C, West Nile and polio. Proteases are enzymes that allow the virus to replicate inside a human host.

"When the virus enters a cell, the RNA is translated into a polypeptide—a long single protein chain—and the protease chops that long chain into many different parts, which then cause the damage," explained Lemieux.

"If the protease does not work, the virus cannot replicate in the cell, so it's a pretty clear antiviral target," she said.

Vederas' lab in the Faculty of Science will produce the inhibitor drug, and Lemieux's lab will determine the crystal structure of the COVID-19 protease after it is blocked by the drug to observe how it works.

Tyrrell will test its effect against the viral load in a cell culture at his lab, which is federally approved to work with deadly pathogens such as COVID-19.

Connection to a cat virus

There are several promising things about this protease inhibitor that make the U of A researchers hopeful it will be a fit for COVID-19.

Genome sequencing of the novel coronavirus indicates that its protease is nearly identical (96 percent) to the protease in the original SARS virus.

"Of the 306 amino acid residues in the chain that makes the 3CL protease of the "Wuhan' virus, only 12 are different and they are highly similar in properties," the researchers stated in their research proposal.

Another good sign is that a derivative of the same protease inhibitor was recently shown by American veterinary investigators to cure cats of feline infectious peritonitis, a coronavirus-caused condition that is almost always fatal to the animals.

"The key compound affected cures or significant remissions in all the cats," the researchers stated.

"It is very exciting that the drug was effective and tolerated in cats," said Lemieux, while cautioning that it still must be proven and tested in humans.

Translating discovery into life-saving products

Lemieux, who is director of the Membrane Protein Diseases Research Group within the U of A's Faculty of Medicine & Dentistry, usually focuses her research on proteases associated with other diseases such as Parkinson's and urinary tract infections, but all work in her lab has shut down except for the COVID-19 project.

"When I teach my classes at the university I try to impart that fundamental research can really assist us in drug development," she said. "I try to get the students excited about protein structures and protein chemistry, and especially how proteases can be inhibited for drug development."

Tyrrell, who is the founding director of the Li Ka Shing Institute of Virology, said another advantage for the U of A project is that the institute has a commercialization hub designed to take promising bench research to patients as soon as possible through licensing or partnerships with pharmaceutical companies. It is led by Michael Houghton, who identified the hepatitis C virus and has more than 70 patents in development.

Tyrrell said pharmaceutical companies can sometimes be reluctant to develop drugs against viruses that may be fleeting if they can be contained through public health measures, such as the SARS and MERS outbreaks. He said that may be different this time.

"With the crisis right now, it is critical that virologists translate some of the things we are discovering into products," said Tyrrell.

Lemieux said the U of A researchers hope to know within the next two months whether the protease inhibitor they are developing is effective against the COVID-19 virus.

"Obviously cats and humans are different," said Lemieux. "We're far away from developing something to treat people, but I would call these promising first steps towards development of a protease inhibitor drug to treat either this outbreak or future ones."

Provided by University of Alberta