Researchers unlock new potential porcine virus treatment

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UConn researchers have identified a novel small molecule for the development of a preventative treatment for a serious and costly disease in pigs.

Porcine reproductive and respiratory syndrome virus (PRRSV) costs an estimated $1.2 billion annually in the U.S. In Europe, the estimated yearly loss is €1.5 billion. The virus causes respiratory disease in piglets, and miscarriages or stillbirths in sows.

There is currently no effective vaccine or treatment for PRRSV. Some scientists are working on genetically modified pigs to block viral infection, but this strategy will take decades to have a measurable impact.

Researchers from the College of Agriculture, Health and Natural Resources (CAHNR) have identified a small molecule that can successfully disable the virus' mechanisms for reproducing and evading the host organism's immune system.

They published these findings in the *Journal of Virology*. Jiaqi Zhu (CAHNR), is the first author of this paper.

UConn collaborators include Xiuchun "Cindy" Tian, professor of animal science; Antonio Garmendia, professor of pathobiology and veterinary science; Neha Mishra, associate professor of pathobiology and veterinary science, and Kyle Hadden, professor of pharmaceutical science.

This work is a collaboration between UConn and Northwest A&F University in China, where Young Tang, former UConn associate professor, is currently faculty.

The researchers began this work by using artificial intelligence to screen a bank of small molecules to identify which ones might be good candidates. The algorithm compared the structure of the viral protein the researchers wanted to target against those of the small molecules.

They then narrowed their results down to a single chemical that could

inhibit the virus without producing toxic effects.

The researchers targeted a protein called NendoU. This protein is highly conserved, meaning that when the virus mutates, this protein will likely stay the same because it plays such an essential role in the virus' ability to reproduce.

The researchers found that the number of viral particles in cells treated with the small molecule was more than 1,000 times fewer than the untreated control group.

"Basically, the virus comes into the untreated cell and uses the cell's machinery to amplify and create more viruses," Tian says. "So, if you treat the cells with this particular chemical, compared to untreated cells, it's going to reduce it by 1,000 times in terms of viral number."

NendoU is also common across other closely related viruses.

"We were thinking this [chemical] could also work on other viruses in this order," Zhu says. "So, we tested it on another virus called chicken infectious bronchitis virus and it also worked very well."

COVID-19 belongs to the same viral family as PRRSV. This means that even though PRRSV is not a risk to human health, this research could have applications for human anti-viral drug development.

These findings build on previous work from this group in which, in collaboration with technology-enabled pharmaceutical company, Atomwise Inc., they identified a different chemical that disrupts the virus' ability to enter the host cell.

"By shutting the door for viral entry and inhibiting those that are already in the cells, we could combine these two small molecules in the future,

and potentially have a stronger and synergistic effect on disease control," says Tian.

The researchers are working with UConn's Technology Commercialization Services (TCS) to advance the development and commercialization of this technology. Engaging with TCS early on, they protected their intellectual property and developed a strategic commercialization plan.

As part of these efforts, TCS facilitated one-on-one meetings with five of the world's 10 largest animal health care companies, along with multiple other organizations interested in the technology.

"We have received amazing interest from industry, and the feedback has been extremely helpful, setting up the development path of the technology," says Ana Fidantsef, industry liaison with TCS.

"We hope these interactions will lead to collaborations that will immensely help the swine market and industry."

More information: Jiaqi Zhu et al, Discovery of small molecules against porcine reproductive and respiratory syndrome virus replication by targeting NendoU activity, *Journal of Virology* (2024). DOI: 10.1128/jvi.02034-24

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