Researchers produce virus-resistant pigs, could vastly improve global animal health

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Researchers at the University of Missouri have successfully produced a litter of pigs that are genetically resistant to a deadly porcine virus.

Coronaviruses, highly contagious and widespread viruses known for their distinctive microscopic halos, are responsible for a variety of deadly intestinal diseases in livestock. One such virus, Transmissible Gastroenteritis Virus (TGEV), commonly infects the intestines of pigs, causing almost 100 percent mortality in young pigs. Now, a team of researchers from MU, Kansas State University and Genus plc—a global leader in animal genetics— has succeeded in breeding pigs that are resistant to the virus by means of gene editing.

"Previous research had identified an enzyme called ANPEP as a potential receptor for the virus, meaning it could be an important factor in allowing the virus to take hold in pigs," said Randall Prather, distinguished professor of animal sciences in the College of Agriculture, Food and Natural Resources. "We were able to breed a litter of pigs that did not produce this enzyme, and as a result, they did not get sick when we exposed them to the virus."

Prather and his colleagues edited the gene responsible for making the ANPEP enzyme, resulting in a litter of seven pigs with a "null" gene that did not produce the enzyme. When exposed to the TGEV virus, these pigs did not become infected, showing that the presence of the ANPEP enzyme is necessary for an infection and gene editing can create pigs that are resistant.

"It's a tremendous financial burden for farmers to put time, money and labor into animals that will get sick," said Kristin Whitworth, co-author on the study and a research scientist in MU's Division of Animal Sciences. "Breeding pigs with genetic resistance will help to ease that burden. In terms of animal welfare, if we can prevent these pigs from getting sick, we have a responsibility to do so."

In comparison to the scores of gene mutations that occur naturally during the reproductive process, researchers only altered the expression of a single gene. Those pigs lacking the enzyme were healthy and experienced no changes in development.

"The collaboration with Randy and his team has established some of the most rewarding milestones of my career," said Raymond "Bob" Rowland, a professor of diagnostic medicine and pathobiology at Kansas State University and co-author on the study. "Porcine coronaviruses are a global threat to the pig industry. One of the greatest concerns for U.S. producers are outbreaks of new coronaviral diseases. Once again, this work demonstrates the importance of this technology in solving complex disease problems. Genetic modification to protect pigs from endemic and emerging diseases is the future of the pork industry."

This study follows a similar success achieved in 2015, when MU's genetic engineering team made pigs resistant to the deadly and costly Porcine Reproductive and Respiratory Syndrome (PRRS) virus by using gene editing. The University of Missouri has partnered with Genus plc to commercialize this method of producing virus-resistant pigs, which will improve animal health and wellbeing and greatly reduce losses in livestock production worldwide due to viral infections, making global pig farmers more sustainable. Genus plc is currently seeking FDA approval for the use of gene editing technology for use in eradicating the PRRS virus.

"Successful studies like these are critical to our continued quest at Genus to nourish the world by pioneering improved genetics and new innovations," said Jonathan Lightner, Global head of Research and Development at Genus plc. "The opportunity to advance technologies like gene editing—which have the potential to eradicate deadly animal diseases—is incredibly exciting and strong partnerships like ours with the University of Missouri are critical to this prospect, and the future of food and agriculture."

The study also sought to determine whether editing out ANPEP would produce resistance to Porcine Epidemic Diarrhea Virus, which killed nearly 7 million pigs in a 2013 outbreak. While pigs lacking the enzyme still contracted the virus, researchers are optimistic that the study bodes well for future research.

"With ANPEP eliminated, we can focus on a smaller field of potential culprits," said co-author Kevin Wells, associate professor of animal sciences at MU. "In this area of research, every step helps."

The study, "Resistance to coronavirus infection in amino peptidase N-deficient pigs," was published in *Transgenic Research*.

More information: Kristin M. Whitworth et al, Resistance to coronavirus infection in amino peptidase N-deficient pigs, *Transgenic Research* (2018). DOI: 10.1007/s11248-018-0100-3

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