Clearing a xenotransplantation hurdle—detecting infectious agents in pigs

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A shortage of organs for transplantation—including kidneys and hearts—means that many patients die while still on waiting lists. So, research at the University of Alabama at Birmingham and other sites has turned to pig organs as an alternative.

Using gene-editing, researchers have modified such organs to prevent rejection, and research with primates shows the modified pig organs are well-tolerated.

An added step is needed to ensure the safety of these inter-species transplants—sensitive, quantitative assays for viruses and other infectious microorganisms in donor pigs that potentially could gain access to humans during transplantation.

The U.S. Food and Drug Administration requires such testing, prior to implantation, of tissues used for xenotransplantation from animals to humans. It is possible—though very unlikely—that an infectious agent in transplanted tissues could become an emerging infectious disease in humans.

In a paper published in *Xenotransplantation*, Mark Prichard, Ph.D., and colleagues at the University of Alabama at Birmingham have described the development and testing of 30 quantitative assays for pig infectious agents. These assays had sensitivities similar to clinical lab assays for viral loads in human patients. After validation, the UAB team also used the assays on nine sows and 22 piglets delivered from the sows through

caesarian section.

"Going forward, ensuring the safety of these organs is of paramount importance," Prichard said. "The use of highly sensitive techniques to detect potential pathogens will help to minimize adverse events in xenotransplantation."

"The assays hold promise as part of the screening program to identify suitable donor animals, validate and release transplantable organs for research purposes, and monitor transplant recipients," said Prichard, a professor in the UAB Department of Pediatrics and director of the Department of Pediatrics Molecular Diagnostics Laboratory.

The UAB researchers developed quantitative polymerase chain reaction, or qPCR, assays for 28 viruses sometimes found in pigs and two groups of mycoplasmas. They established reproducibility, sensitivity, specificity and lower limit of detection for each assay. All but three showed features of good quantitative assays, and the lower limit of detection values ranged between one and 16 copies of the viral or bacterial genetic material.

Also, the pig virus assays did not give false positives for some closely related human viruses.

As a start to understanding the infectious disease load in normal healthy animals and ensuring the safety of pig tissues used in xenotransplantation research, the researchers then screened blood, nasal swab and stool specimens from nine adult sows and 22 of their piglets delivered by caesarian section.

Mycoplasma species and two distinct herpesviruses were the most commonly detected microorganisms. Yet 14 piglets that were delivered from three sows infected with either or both herpesviruses were not

infected with the herpesviruses, showing that transmission of these viruses from sow to the caesarian-delivery piglet was inefficient.

Prichard says the assays promise to enhance the safety of pig tissues for xenotransplantation, and they will also aid evaluation of human specimens after xenotransplantation.

The UAB researchers say they subsequently have evaluated more than 300 additional specimens, and that resulted in the detection of most of the targets. "The detection of these targets in pig specimens provides reassurance that the analytical methods are functioning as designed," said Prichard, "and there is no a priori reason some targets might be more difficult to detect than others with the methods described here."

More information: Caroll B. Hartline et al, Xenotransplantation panel for the detection of infectious agents in pigs, *Xenotransplantation* (2018). DOI: 10.1111/xen.12427

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