

PORK SAFETY

Title: Adaptation of a human seasonal H3 influenza A virus to efficiently infect and replicate in the swine host, **NPB #16-129**

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Scientific Abstract

The current diversity of influenza A viruses (IAV) circulating in swine is largely a consequence of human-to-swine transmission events and subsequent evolution in pigs. However, little is known about the requirements for human IAVs to transmit to and subsequently adapt in pigs. Novel human-like H3 viruses were detected in swine herds in the USA in 2012 and have continued to circulate and evolve in swine. Reverse genetics (rg)-generated reassortants between a human-like H3N1 isolated from swine and a seasonal human H3N2 virus with common HA ancestry were evaluated by *in vitro* models to understand the contributions of individual gene segments on the ability of these viruses to infect pigs. Swine-adapted human-like H3 (hu-H3) demonstrated abundant attachment to epithelial cells from upper-, mid- and lower- swine respiratory tract tissues by virus histochemistry, while the seasonal human virus bound to fewer cells. Kinetics of virus growth in porcine intestinal epithelial cells (SD-PJEC) and in *ex-vivo* porcine trachea explants was significantly reduced by replacing the swine hu-H3 with the human seasonal H3, indicating the swine-adapted hu-like H3 was important for binding and entry in swine cells. The swine-adapted H3 with human seasonal internal genes grew efficiently at 33°C, but had decreased growth at 40°C, the temperature representing the lower respiratory tract of growing pigs. Although the swine adapted H3 was crucial for the infectivity in pigs and swine tissue, these results suggest that the adaptation of these novel H3 viruses to swine was multigenic since the swine-adapted HA alone was not sufficient to confer the full phenotype of the wild-type H3N1 parental swine virus onto the putative ancestral human H3N2 virus.

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