Heterologous prime-boost vaccination protocols using whole inactivated influenza A virus vaccines to drive improved heterologous cross-protection, NPB# 16-111.

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Scientific Abstract
Influenza A virus (IAV) is a highly diverse and contagious swine pathogen, which causes financial losses to the US swine industry through decreased production, increased vaccine and treatment costs and in many cases elevated mortality due to an increase in secondary bacterial pneumonia. Additionally, IAV-S is a zoonotic pathogen with public health concerns for swine workers, attendees at swine exhibitions or fairs and the emergence of IAV with pandemic potential. Whole inactivated virus vaccines (WIV) played an important role in the prevention and control of IAV-S in previous years. However, repeated failures of current WIV products and the overall lack of efficacious IAV vaccines have become extremely frustrating for producers in the swine industry, and the choices are limited in the types of vaccines currently licensed for use in swine, even though custom made WIV vaccines are available. A major cause of vaccine failure on farms is presumed to be the diversity of strains that co-circulate in North American swine. Although protection against homologous infection is adequate under ideal conditions, WIV vaccines do not prevent infection with heterologous or antigenically diverse strains of IAV. We evaluated different vaccination protocols by alternating the administration of relevant IAV antigens from the H1 subtype, in comparison to giving antigens as multivalent vaccines. A similar strategy was reported to be effective against H3 subtype viruses in Europe. We tested 6 different vaccination scenarios, with vaccines containing either one or two viruses, and selected 3 commonly identified H1 IAV, Viruses 1, 2, and 3. The heterologous prime-boost strategy was not successful for the H1 viruses selected for our study. In fact, all groups that received only WIV exhibited greater respiratory disease than the unvaccinated challenge control pigs and were not protected from infection. The only group included in our study that demonstrated protection from disease and infection were pigs that were infected with live mismatched strain 1, allowed to recover, vaccinated with a WIV with mismatched strain 2, followed by challenge with Virus 3. This vaccination group was also the only group that had a robust immune response to the strains contained in the vaccine before challenge. These results demonstrate the extreme difficulty in controlling H1 viruses from the U.S. with WIV and a potential advantage for modified live virus vaccines against IAV in swine.