Recent Results from Studies with the new 2009 A/H1N1 Influenza A Virus

Project 1: Serologic cross-reactivity of serum samples from U.S pigs against the new 2009 H1N1 influenza virus

Purpose of study: An important concern is to address whether U.S commercial swine herds are susceptible to the 2009 A/H1N1 influenza viruses isolated from persons in California, New York, and Mexico.

Experiment:

- Three 2009 A/H1N1 influenza A viruses isolated from persons in 2009 in California (A/CA/04/2009), New York (A/NY/18/2009), and Mexico (A/Mexico/4108/2009) were obtained from the Centers for Disease Control and Prevention (CDC) and grown in vitro (i.e., in a permissive cell line).
- A standard hemagglutination inhibition (HI) test was used to investigate antigenic relatedness between these three 2009 A/H1N1 influenza A viruses and 19 H1 Swine Influenza Virus (SIV) strains known to be circulating in U.S. swine herds or with SIV strains used for five licensed U.S H1N1 SIV vaccines. Antigenic relatedness would be predicted on the basis of how well these antisera could inhibit the three 2009 A/H1N1 influenza A viruses from agglutinating (clumping) red blood cells. This test indicates the presence of antibodies that prevent the influenza virus from attaching to red blood cells and is therefore indicative that the animal may have protective antibodies. The CDC and USDA-APHIS-Center for Veterinary Biologics report an 8-fold or greater reduction in HI titer a significant reduction in cross reactivity between virus hemagglutinin variants.
- Thirty-eight serum samples from pigs vaccinated with 19 H1 SIV isolated from U.S commercial swine operations between 1999-2008 (NADC H1 serum reference panel) were tested in the standard HI test. The 19 H1 SIV in the NADC H1 serum reference panel used in this study represent all four phylogenetic (genetically characterized) clusters (α, β, γ, and δ) of all the endemic H1 swine influenza viruses known to circulate in the U.S.
- An additional 14 serum samples from pigs vaccinated with five different commercial products used to vaccinate pigs against H1 swine influenza viruses in the U.S were tested by the standard HI test.

Results:

- Eleven of the thirty-eight serum samples from pigs inoculated with U.S H1N1 SIV had a measurable HI titer against the A/CA/04/2009 H1N1 influenza virus. The same experiment with the A/NY/18/2009 H1N1 influenza virus had similar results. In contrast, twenty two of the thirty-eight serum samples from pigs inoculated with U.S H1 SIV had a measurable HI titer against the (A/Mexico/4108/2009) H1N1 influenza virus.
- Serologic cross-reactivity with anti-sera from 5 commercially-available SIV H1 vaccines was additionally assessed by HI with the three 2009 A/H1N1 strains. Cross reactivity was consistently low between the vaccine antisera and all 2009 A/H1N1 novel strains tested, although titers were slightly higher with the isolate from Mexico. This suggests that currently available vaccines may provide only limited protection against challenge with the novel H1N1.

Conclusion: Results of this experiment suggest that pre-existing immunity induced by swine influenza viruses circulating in the U.S swine herd may not protect pigs against the new 2009 A/H1N1 influenza viruses presently circulating in people. Importantly, vaccines currently used

to protect pigs in U.S swine operations against swine influenza virus may not be effective against the new 2009 H1N1 influenza viruses.

Limited cross-reactivity of serum samples from the NADC H1 SIV antiserum reference panel or sera from pigs vaccinated with commercial vaccines was demonstrated against the 2009 A/H1N1 influenza virus (A/CA/04/2009) isolated in California as measured by a standard HI test. A second 2009 A/H1N1 strain from New York, A/NY/18/2009, was also used with the NADC H1 antiserum reference panel with very similar results to A/CA/04/2009. However, a third strain, A/Mexico/4108/2009, demonstrated broader cross-reactivity with the NADC H1 antiserum reference panel. This was especially apparent in the H1γ phylogenetic cluster. The cross-reactivity with the H1γ phylogenetic cluster is important since this is the genetic group in which the HA from the 2009 A/H1N1 originated. This would suggest that pre-existing immunity to certain currently circulating H1N1 SIV strains may protect against the outbreak virus. However, the differences between the novel H1N1 isolates suggest that there may be biologic variation in host and/or virus properties responsible for the variation in serologic cross-reactivity. It remains unknown whether this variation would have any effect on protection from live challenge in pigs from circulating strains of the novel 2009 A/H1N1 from the human population.

Serologic cross-reactivity with anti-sera from 5 vaccines was also assessed by HI with the three 2009 A/H1N1 strains. Cross reactivity was consistently low between the vaccine antisera and all 2009 A/H1N1 novel strains, although titers were slightly higher with the isolate from Mexico. This suggests that currently available vaccines may provide only limited protection against challenge with the novel H1N1.

Next Steps: ARS scientists will test the efficacy of a select subset of SIV vaccines from this in vitro study in a pig vaccination challenge model to determine whether the measurable HI titers detected in vaccinated pigs correlate with protection.