Title: Toward Animal Challenge-Free Prediction of Vaccine Efficacy

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The problem:
Memory B cells circulate throughout the body after a pathogen has been cleared, and continue to monitor for pathogen re-appearance long after infection. This sentinel activity is the basis for why vaccinations are able to prevent disease from reoccurring. Vaccine development requires clinical trials to ensure safety and efficacy which necessitates that animals be challenged with the pathogen after vaccination. Despite memory B cells playing this large role in memory immunity, little research has been performed to evaluate antigen-specific B cells for their molecular variability.

Objective: Here, we evaluated a B cell tetramer reagent specific to PRRSV as a candidate predictor of vaccination efficacy. Secondly, scientific research training and experience was provided to a DVM graduate student and a DVM student.

What was done:
A B cell tetramer was assembled with biotinylated PRRSV nonstructural protein 7 (NSP7), streptavidin, and phycoerythrin (PE, a highly fluorescent marker). The tetramer was shown by ELISA to specifically bind antibodies from PRRSV-immune serum, but not from naïve serum. The PRRSV immune serum produced an average OD_{450} 10-times that of the PRRSV naïve serum on indirect ELISA, indicating an increased presence of anti-NSP7 IgG antibodies.

Next, PRRSV-specific memory B cells were isolated from PRRSV-immune and PRRSV-naïve pig spleen and inguinal lymph node by incubation with B cell tetramer, followed by magnetic selection. Isolated cells were then tested to determine the strength of the memory response, as determined by relative proportion of PRRSV-specific B cells. The results showed that the NSP7 B cell tetramer was able to bind memory B cells at a higher frequency than PRRSV naïve splenocytes. ELISPOT assay of the enriched NSP7 specific B-cells showed that approximately 0.2% of all memory B-cells from the lymph node were NSP7 specific, and 0.1% of memory B-cells from the spleen were NSP7-specific.

Significant findings and recommendations:
These research results showed that a biochemical reagent differentiated pigs that were immune to PRRSV from non-immune pigs. The finding provides proof-of-concept that a blood test can predict vaccine efficacy, thus justifying further studies to clarify the relationship between binding characteristics, and magnitude of response that has the potential to replace live animal testing and infectious disease challenge for evaluating vaccine efficacy.

How the findings will assist the practicing veterinarian:
The scientific aspects of the project have the potential for long-term benefit by providing veterinarians in the field with superior vaccine products that were enable by invention of a better method of evaluation. A successful outcome of the research will enable veterinarians to explain how their profession is dedicated to animal welfare and the development of methods that reduce the use of animals in swine veterinary research. Providing access to swine veterinary students gives them a better life-long ability to assimilate research presentations and literature, improving their abilities to provide outstanding veterinary service to clients.

What we can learn about the methods used:
The B cell tetramer is a general tool that, in principle, can be designed for any antigen and disease agent, making it applicable to vaccine testing and immunity investigations broadly in the service of improving swine health.

Take home messages:
Immunology research leads to practical tools and solutions that advance swine health
Scientific research opportunities for veterinarians and students advances the profession