Vaccine Research at VIDO
By Dr. Volker Gerdts, DVM

Take-home message: The need for vaccines
At the Vaccine and Infectious Disease Organization (VIDO), several projects are aimed at developing novel and more effective vaccines for pigs. Infectious diseases remain the major cause of morbidity and mortality in swine production. Recent outbreaks of porcine circovirus (PCV), porcine reproductive respiratory syncytial virus (PRRSV) or swine influenza virus (SIV) have demonstrated that infectious diseases can have devastating effects on Canada’s swine industry, and that vaccination remains a cost-effective strategy to control these diseases. The importance of modern vaccine research is highlighted by the need for better food safety and the threat of importing devastating diseases such as foot-and-mouth disease or hog cholera.

Vaccines: An evolving family of tools
Vaccines traditionally consist of either attenuated (weakened) live, or inactivated (killed) pathogens. In general, live vaccines are more effective as they tend to stimulate stronger immune responses, similar to natural infection. However, live vaccines have the risk of potentially causing disease, especially in animals that are compromised by stress or other diseases. Killed vaccines are very safe but often induce weaker immune responses and require the addition of vaccine adjuvants. Live vectored vaccines or DNA vaccines are recently-developed vaccine technologies that are very safe and capable of inducing immune responses that are similar to natural infection. However, neither DNA vaccines nor vectored vaccines are licensed for pigs in Canada, though promising experimental vaccines are already in the final stages of development.

Adjuvants: Often required to improve vaccine efficacy
Adjuvants are added to a vaccine formulation to enhance its ability to stimulate the immune system. Adjuvants represent a variety of substances, each of which can enhance the immune response. The innate, or natural, immune response represents the first line of defence and is strongest within hours of infection. Stimulation of the innate immune response also sets the stage for the adaptive immune response (the antibody response), which is active for days to weeks post-infection.

Ideally, the addition of adjuvants results in stimulation of both arms of the immune response. Novel adjuvants or immunostimulators consist of substances that do this by providing a “danger signal” to the immune system. Immunomodulators of interest to us include a large family of molecules called cationic host defense peptides (HDPs). These molecules are essential components of the innate immune response and have a wide spectrum of functions against bacteria, viruses and parasites. Figure 1 shows the antimicrobial activity of porcine HDPs against porcine bacterial pathogens. Current projects at VIDO are investigating the potential of HDPs as vaccine adjuvants.

Vaccine delivery: More than just an injection
Proper vaccine delivery is an important factor for effectiveness. Modern vaccines are being designed to be more economical (smaller and fewer doses required), and are aimed at reducing side effects at the injection site. Delivery via the mucosal surfaces, of the respiratory tract for example, is key because more than 90 per cent of all pathogens—regardless of species—enter the body and initiate infection at mucosal surfaces. Immunization via muscle or skin rarely induces mucosal responses.

We recently developed a gut-loop model in young pigs that enables the testing of oral (mucosal) vaccines against intestinal infections such as E. coli. This model consists of surgically created intestinal loops that allow the measurement of mucosal

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immune responses following local vaccination. We found, for example, that the effectiveness of vaccines against post-weaning colibacillosis depends on the presence in the pig of specific complementary molecules (called F4-receptors). Since pigs display the F4 receptor in varying amounts depending on their genetic background, alternative delivery systems are required that can deliver the vaccines across the mucosal lining of all pigs whether or not they have the receptor. Viral vectors represent such an alternative and current research is focused on the development of such vectored vaccines against E. coli.

**Vectored vaccines: The future for swine vaccines?**

One of the most effective ways to deliver vaccines to mucosal surfaces is with live but weakened viruses or bacteria used as vectors that actually infect the mucosal surfaces. Such vectors have been developed for vaccine delivery in humans and animals. These vectors do not cause disease, are relatively easy and cost-effective to produce, and induce both types of immune responses when delivered orally or intranasally. Viral vectors such as poxvirus, herpesvirus and adenovirus have been developed for veterinary vaccines, and several vectored vaccines are already licensed for use in animals.

Efficacy of these vaccines is mainly determined by the ability of the vector to infect and replicate within the target animal and thus produce large amounts of vaccine antigen. At VIDO, porcine adenoviruses are being developed as vectors for swine vaccines. Bacterial vectors also have great potential as mucosal vaccines, with attractive advantages over present-day injectable vaccines. For example, live attenuated bacteria such as Lactobacillus can target mucosal tissues and deliver the vaccine antigen across the mucosal surface.

**Particulate delivery systems: Alternative delivery strategies**

Particulate delivery systems in the form of small microspheres represent novel alternatives for vaccine delivery. They protect the antigen from degradation in the gastrointestinal tract and ideally could be administered with feed, requiring very little labor. Microparticles have been developed to incorporate the vaccine and release it after uptake across the mucosal tissues. However, the major obstacle is poor uptake, requiring the use of large amounts of vaccine. Current research is focused on finding ways to increase uptake in the intestine, making these vaccines more cost-effective for use in modern swine production.

**Conclusion**

Vaccination represents a very cost-effective strategy to reduce animal suffering, improve the economics of livestock production, and reduce the spread of many infectious diseases from animals to humans. Especially in the face of today’s economic challenges for swine production, modern vaccine research must lead to novel vaccines that can meet these goals while being cost-effective and easy to administer.

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**Contact Information:**

Dr. Volker Gerdts, DVM, Associate Director (Research) & Chief Science Officer, Vaccine and Infectious Disease Organization (VIDO), University of Saskatchewan, 120 Veterinary Road, Saskatoon, SK S7N 5E3, Phone: 306-966-1513, Fax: 306-966-7478, Email: volker.gerdts@usask.ca

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**Figure 1:** Antimicrobial activity of the host defence peptide (HDP) porcine beta defensin 1 (PBD-1) against Streptococcus suis and Actinobacillus pleuropneumoniae. Bacteria were co-cultured for 24 hours in the presence of 20 μg/ml PBD-1 (striped bars) or media alone (black bars) after which the number of viable bacteria was assessed.