Are intrauterine vaccines the future for swine immunisation?

Vaccines stimulate the body’s immune response against specific infectious agents. Designed to induce active-acquired immunity, vaccines prepare the immune system to fight the disease-causing microorganism by mimicking an infection. This approach leads to the creation of a ‘memory’ of that microorganism such that when the immune system encounters the real microorganism, it is then ready to fight it. As a result, the vaccinated individual is less likely to become ill. Vaccines contain biomolecules that resemble the microorganism and are often made from weakened or killed forms of microorganisms, its toxins, or its surface proteins as well as adjuvants that direct the immune response.

Very young animals are more susceptible to infections than adults because their immune system is not yet sufficiently developed to defend their bodies from infections. During this vulnerable period, newborn animals are protected by antibodies acquired through their mother’s colostrum and milk (passive immunity). Even then, they are not completely immune to infection and they can still get sick. At the time of weaning, passive immunity begins to wane and the piglets can become susceptible to infections. Since the swine industry heavily relies on the reproductive success of sows as well as piglet survival and growth, sows and weanling pigs are routinely vaccinated against diseases.

The most common route of vaccination is through intramuscular (IM) injection. However, using this route can be a challenging task for animal workers and stressful for the pigs, especially since they usually require two doses of the vaccine for it to be effective. Dr Heather Wilson and her team at VIDO at the University of Saskatchewan are exploring alternative vaccination routes. Notably, they looked for opportunities for vaccination that could work well within current animal husbandry practices. They must optimise vaccine formulations to provide an effective and robust immune response, often by including adjuvants.

**MUCOSAL VACCINES**

Besides the IM route, some vaccines can be administered to the mucosa, which is the living tissue that lines the inner surface of organs in the digestive, urinary and genital tracts. The benefits of mucosal vaccines are that they are less invasive than IM injections, and they induce a potentially stronger mucosal and systemic (generalised) immune response. Wilson explains that the antibodies in a systemic immune response in the muscle, and a mucosal vaccine. She explains that the antibodies in a systemic vaccine act like soldiers protecting a building after an invasion has occurred. A mucosal vaccine similarly has soldiers patrolling the building but also the ‘grounds’ - the mucosa, such as the gut, respiratory tract, urogenital tract - where most infection occurs. Thus mucosal vaccines can stop pathogens before they actually invade the body.

Specifically for swine, it is important to help protect young animals and prevent illness from pathogens such as porcine endemic diarrhoea virus (PEDV), which causes severe diarrhoea and dehydration, and results in a high level of mortality. Wilson and her team are investigating the effects of giving a PEDV vaccine during artificial insemination in the uterus. Wilson explains, ‘Artificial insemination (AI) is a normal part of the husbandry of pigs in over 90% of the industry, which means that the uterus is readily accessible for vaccination when the AI dose is administered.’ By adding the vaccine to the semen prior to insemination, their method takes advantage of current routine husbandry practice of breeding, which takes place several times a year.

**THE UTERUS AS A VACCINE INDUCTION SITE**

There has been a lot of research on mucosal vaccines to establish them as potent enough to protect animals via both a mucosal and systemic immune response. Mucosal vaccines are challenging to produce because most foreign molecules encountered at the mucosa (such as food, dust, indigenous flora) do not trigger a robust, active immune response. Instead, the immune system has evolved to respond to them with the phenomenon of mucosal immune tolerance. Especially in the gut where there is such a huge amount of commensal flora present, it can be challenging to administer a vaccine and trigger a robust but targeted immune response. The researchers decided to tackle the uterus as a site of induction because it does not have a large commensal flora and therefore may be more inclined to respond to foreign bodies with mucosal immunity rather than mucosal tolerance.

To determine whether an appropriately formulated vaccine delivered to the uterus would effectively induce immunity, Wilson’s team conducted studies on female rabbits. They delivered a single dose of a vaccine against two types of antigens: a herpes virus protein and the porcine parvovirus and it included a triple adjuvant (TriAdj) cocktail to promote a robust immune response. The vaccine was administered either via the IM route or the intrauterine (IU) route in female rabbits. The researchers then examined the immune response, both locally – on mucosal sites – and systemically – in the bloodstream.

Wilson’s team found a significant immune response in the uterus and at distal mucosal sites including the vagina and the lungs, as well as a systemic immune response, with the detection of large numbers of antigen-specific antibodies in the bloodstream. The IU vaccination had a dose-dependent effect on the concentration of antigen-specific antibodies in the blood: the more vaccine administered the higher the number of antibodies were produced. These findings confirm that the uterus can be used as a site for vaccination and that vaccine formulation with appropriate adjuvants can trigger both generalised and mucosal immunity.

**A NEW APPROACH FOR ANIMAL HUSBANDRY**

The Wilson lab then carried out an experiment involving breeder pigs. Sows were immunised with a commercial porcine parvovirus (PPV) vaccine by the IM route at prior pregnancy cycles. The Wilson lab then administered an IU vaccine of PPV formulated with the TriAdj at oestrus along with semen. They observed induction of PPV antibodies in serum that was higher than titre observed in sows administered the IM vaccine alone. However, when the PPV vaccine was administered into the uterus at breeding alone, a strong antibody
Porcine epidemic diarrhoea virus (PEDV) most severely affects young piglets that have not been able to build up immunity.

The Wilson Lab develops intrauterine vaccines to protect breeding pigs against reproductive diseases as well as protection for newborn and weaning piglets against infectious disease.

The adjuvants may further enhance the local immune response and, therefore, may be suitable for formulation in an intrauterine vaccine.

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Research Objectives

The Wilson Lab develops intrauterine vaccines to protect breeding pigs against reproductive diseases as well as protection for newborn and weaning piglets against infectious disease.

Dr Heather Wilson

Wilson and her team show that intrauterine vaccination induces a promising vaccination method for swine and could also be developed for other livestock. They demonstrate that IU vaccination is not only safe, effective, and animal-friendly, it works well within current husbandry practices. In combination with their optimised vaccine formulations, this method or coupling vaccination with breeding could help change future vaccination practice for the animal husbandry industry.

References


What are the next steps for your research?

We have optimised the PEDV spike protein antigen to improve the immune response acquired by IU immunisation. We continue to test new polymeric nanoparticle adjuvant formulations to find a single dose IU vaccine that protects the sow and the suckling piglets. Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) continues to be an important disease impacting pregnancy in pigs. We are investigating whether an IU vaccine formulated with PRRSV antigens can protect against this important disease. Once established and marketed in pigs, the next step will be to test IU vaccination in other livestock.