

Viral Particle-Based Display of Multiple Antigens for Companion Animal Immunosterilization – *Coonrod*

Surgical sterilization represents the current state of the art for companion animal fertility control because it is 100% effective and permanent, and, by removing the hormone-producing gonadal tissue, also prevents undesirable secondary sexual behaviors. However, given that the procedure is labor-intensive, expensive, and requires trained veterinary professionals, there is currently considerable worldwide interest in developing new non-surgical alternatives. For these new approaches to gain wide acceptance, they will need to be as effective as surgical sterilization and, ideally, also reduce the overall time, effort and cost per treatment.

A single-dose permanent immunosterilant for female dogs and cats represents one promising alternative to surgical sterilization. This type of strategy first identifies essential components of the reproductive axis and then generates recombinant versions of these factors using prokaryotic or eukaryotic expression systems. The synthetic reproductive antigens are then combined with carrier molecules and injected into the host animal. The formulation then essentially tricks the immune system into generating a potent and specific immune response against the target reproductive antigens, thus suppressing fertility. Two types of immune responses, humoral (circulating antibody-based) and cellular (T-cell-based), are usually generated following immunization. Humoral responses primarily block fertility by binding to and blocking the function of reproductive antigens while T-cell-based responses can directly target and destroy the antigen-producing cells, thus resulting in permanent sterility.

The immunocontraceptive approach represents an attractive alternative to surgery because the components of the vaccine can be inexpensively produced using large-scale bioreactors. Further, once optimized, the vaccine could also be given as a single injection or oral administration. Finally, if the formulation can be engineered to generate a potent T-cell mediated autoimmune response that targets female germ cells, a localized transient inflammatory response could potentially be generated within the ovary that is sufficient to ablate the entire germ cell population, thus resulting in permanent sterility. Additionally, given that hormone-producing follicular cells require oocytes for growth and function, immune-induced germ-cell depletion would also prevent hormone synthesis and, therefore, prevent unwanted reproductive behaviors.

The feasibility of the immunocontraceptive approach has been demonstrated in previous studies, which showed that the fertility of both male and female dogs and cats can be suppressed following immunization with reproductive antigens such as Gonadotropin Releasing Hormone or proteins of the Zona Pellucida. However, in most cases, the observed contraceptive effects were transient in nature, likely due to either the host's immune response becoming tolerant of the vaccine or to decreasing titers of the antibody. Therefore, in order to take immunocontraception from an experimental to a practical level, vaccine formulations need to be developed that induce more potent germ-cell-depleting immune responses in the host animal. Virus-like particles (VLPs) from the parvovirus capsid have been successfully utilized in dog and cat vaccine formulations to incite potent and long-lived immune responses against a range of associated infectious-disease-based antigens. Therefore, we are currently testing the hypothesis that permanent sterility can be achieved in dogs and cats by using vaccine formulations that contain hormonal and oocyte-restricted antigens that have been conjugated with these VLPs.