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Utilizing vaccine vectors and other novel tools for feline contraception
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Surgical sterilization is considered the gold standard for permanent sterilization of domestic cats in terms of both safety and efficacy. However, in many circumstances it is not logistically practical or economically possible to sterilize large numbers of feral cats. An alternative permanent sterilization method that was safe, affordable, practical and economical would therefore have the potential to greatly reduce the need for euthanasia of these companion animals. In the past few decades, many contraceptive vaccines have been tested in various species with varying levels of success. Subunit vaccines contain reproductive peptides or proteins, such as gonadotropin releasing hormone (GnRH), mixed with an immunological adjuvant. One such vaccine, GonaCon, was generally safe and effective in female cats, but more than half of vaccinated cats conceived by the end of the five-year study\(^1\). An alternative approach for contraceptive vaccination is to use live-attenuated viral vaccine vectors. In this setting, an attenuated virus is engineered to express reproductive peptides and/or proteins so that an immune response is induced that inactivates the reproductive system. We chose feline herpesvirus-1 (FHV-1), a species-restricted virus that persistently infects domestic cats, as a contraceptive vaccine vector. FHV-1 infection in cats typically results in mild clinical disease but induces strong, durable immunity. Previous studies showed that genetic deletion of FHV-1 thymidine kinase (TK), which encodes an enzyme involved in nucleotide metabolism, or deletion of FHV-1 glycoprotein E (gE) and glycoprotein I (gI), which facilitate cell-to-cell spread, resulted in an attenuated FHV-1 that replicates well \textit{in vitro} but poorly \textit{in vivo} and causes few clinical signs of disease. We therefore deleted TK, gE and gI from FHV-1. We then demonstrated that cats vaccinated with the attenuated FHV-1 vector displayed no clinical disease or evidence of virus shedding. To develop the attenuated FHV-1 strain into a recombinant contraceptive vaccine, we decided to redirect the immune response from FHV-1 to recombinant GnRH by genetically attaching GnRH to those FHV-1 proteins that are the most immunogenic. To determine which FHV-1 proteins stimulate the strongest immune response, eight FHV-1 proteins were purified and tested in an ELISA with serum from FHV-1-infected cats. Three of the FHV-1 proteins, gC, gB and gD, were found to elicit exceptionally strong antibody responses in cats. GnRH was then genetically attached to these proteins, with the goal of inducing high levels of anti-GnRH antibodies. Other proteins that are essential for reproduction but otherwise dispensable for normal feline physiology, such as GnRH receptor (GnRH-R), luteinizing hormone receptor (LH-R) and zona pellucida 3 (ZP3), are also being inserted into the FHV-1 genome. In a future study, the ability of the attenuated, recombinant FHV-1 contraceptive vaccine to cause long-term or permanent sterilization of cats will be evaluated.