

Landscape Phage-Peptide Constructs for Low-Cost Immunocontraception of Dogs

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Dog overpopulation remains a serious welfare concern and is a worldwide problem. Our goal is to develop effective, low-cost contraceptive vaccines based on phage-peptide constructs where the peptides mimic sperm that bind to zona pellucida (ZP) proteins at fertilization. Administration of the vaccine would result in an anti-sperm antibody response that would interfere with sperm delivery or function in the male or female genital tract, leading to a contraceptive effect. Due to the natural ability of phage to stimulate B and T cell responses (without adjuvants), the vaccine may also inhibit spermatogenesis and steroidogenesis via induction of cytokine reactions in males.

In this study, contraceptive vaccines are composed of landscape phage particles carrying ZP-binding peptides, where phage body plays the role of carrier protein/adjuvant and multiple (4000/phage particle) copies of a ZP-binding peptide stimulate production of anti-peptide antibodies. Multiple candidate phage-peptide constructs were selected from a 9-mer landscape phage display library using our novel selection procedure on intact dog oocytes surrounded by ZP proteins. Four of the candidates were injected intramuscularly into one-year-old male dogs. Booster immunizations were given at 3 weeks and again at 7 weeks following initial immunization. Sera collected from immunized dogs were characterized as to the presence of anti-peptide/anti-sperm antibodies as well as testosterone levels and size of testicles.

All phage preparations were shown to induce production of high levels of serum IgG antibodies that persisted for at least 5-6 months. Testosterone levels varied during the study, showing some decrease (with the lowest testosterone amount of 0.3 ng/ml) in two dogs after booster immunizations. Interestingly, testicular widths in all dogs were decreased when measured 2-3 months after the second booster immunizations.

To conclude, the identified phage-peptide constructs may be useful in the design of immunocontraceptive agents for dogs. Importantly, the cost of phage-based vaccines should be much lower than the cost of peptides vectored in mammalian viruses or the cost of production of synthetic peptides fused to a carrier protein because phages are bacterial viruses that can be easily and economically obtained in large quantities from bacterial cultures. Additionally, recombinant phage preparations based on landscape phage are very thermostable, making them very robust during shipping, storage, and operation.