FILAMENTOUS PHAGE AS A PLATFORM FOR DEVELOPMENT OF CONTRACEPTIVE VACCINES FOR ANIMALS

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Filamentous bacteriophages (phages) are long (~1 μm) and thin (~7 nm) particles that consist of an outer protein capsid enclosing genetic material. Such particles can be re-engineered and utilized as carriers for antigenic peptides displayed on phage surfaces as fusion molecules to phage coat proteins. Exogenous peptides exposed on filamentous phages were demonstrated to induce humoral as well as cell-mediated immune responses, making phage particles an attractive antigen delivery system for development of new vaccines. Our research group is focused on construction of phage-based vaccines for contraception of wild and feral animals, including cats and dogs. The vaccines are whole phage particles displaying antigenic peptides with contraceptive properties. Antigens explored in the vaccine design include zona pellucida (ZP)-binding peptides as well as gonadotrophin releasing hormone (GnRH) peptide or its derivatives. Phage-peptide constructs are created using different approaches, including selection of target-binding peptides from phage display libraries, molecular cloning of antigenic peptides into phage vectors, and chemical conjugation of synthetic peptides to phage coat proteins. Multiple phage-peptide constructs with contraceptive potentials were obtained and characterized for their ability to interact with target molecules *in vitro* and stimulate immune responses in animals. High titers of anti-peptide antibodies were detected in serum samples collected from mice and dogs after administration of ZP-binding phage as well as phage-GnRH-based preparations. Several phage-peptide constructs were tested for reduction of pup numbers in preliminary fertility trials in mice. Phage-peptide treated groups had a significantly lower mean number of pups/mouse than PBS or phage vector-injected controls. It was shown that phage-peptide preparations administered parenterally (at high doses of 500 μg/injection) do not cause any side effects in dogs, either local or systemic, even after repeated administrations. Additional advantages of filamentous phages over other vaccine platforms include low production costs because phages can be obtained in large quantities in bacterial cultures and ease of shipping, storage, and delivery in non-refrigerated field conditions since phages are very thermostable. The data obtained by our group and reported by others provide firm support that filamentous phages hold great promise as carrier delivery vehicles for contraceptive vaccines.