

# Immunocontraception: Filamentous Bacteriophage as a Vaccine Platform for Wildlife Fertility Control

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Population control of wild and invasive animal species is a global issue of importance to public health, animal welfare and the economy. Although many methods for regulation of animal reproduction are available, the need for effective, safe, and inexpensive contraceptives remains. Immunocontraceptives (contraceptive vaccines) are designed to stimulate the immune system in order to block critical events in the reproductive process and suppress fertility. Platforms used for vaccine development play a central role in vaccine efficacy, safety, and practicality. One nontraditional platform used for development of contraceptive vaccines is based on filamentous bacteriophages (shortened phages). Filamentous phages comprise a group of rod-shaped bacterial viruses. The core of the virion is a DNA molecule, which is surrounded by phage coat proteins. Phages can be engineered to display fusion (non-phage) peptides as a part of their coat proteins. Phage fusions with antigenic determinants induce humoral as well as cell-mediated immune responses in animals, making them attractive vaccine carriers. Here, ongoing work is focused on development of phage-based vaccines for advancement of contraception in wild pigs. Phages displaying peptides for potential contraceptive uses were isolated from phage display libraries selected against intact pig oocytes surrounded by zona pellucida (ZP). Theoretically, this approach enables identification of peptides that mimic sperm surface molecules binding ZP at fertilization. When administered to pigs, these phages stimulated production of anti-sperm antibodies. Anti-sperm antibodies have potential to reduce fertility by disrupting events associated with fertilization, including sperm motility, the acrosome reaction, and/or aspects of sperm-egg interaction. Indeed, incubation of porcine oocytes with sera collected from pigs immunized with phage-peptide fusions developed to bind porcine ZP decreased sperm binding to oocytes, percent embryo cleavage, and percent cleaved embryos that developed to blastocysts in vitro. Phage-peptide constructs used in these studies were selected following a protocol designed to favor species specificity. Species-specificity is a valuable characteristic of contraceptive vaccines for oral administration to be used in control of wild animal populations to limit negative effect on non-target species. Advantages of the phage platform include environmental stability, low cost, and safety of phage-based preparations for immunized animals and those administering the vaccines. (Funded by Alabama Farmers Federation, the Animal Health and Disease Research program and the Scott-Ritchey Research Center, College of Veterinary Medicine, Auburn University).