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IMMUNOCONTRACEPTION RESEARCH UPDATE

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Abstract:

IMMUNOCONTRACEPTION OF WILDLIFE PEST SPECIES

There is growing interest and support for developing the technology needed to effectively implement nonlethal methods for resolving problems caused by wildlife pest species. As part of its alternative methods research development program, the Denver Wildlife Research Center initiated research in 1991 to develop immunocontraceptive vaccine technology to inhibit reproduction in deer and other problem species. Recent advancements in immunology and molecular biology have made it possible to produce and administer genetically engineered contraceptive vaccines. It is theoretically possible that these vaccines can be made species-specific through genetic engineering or through selective administration by injection, oral baiting or possibly inhalation.

Vaccine Development Concepts

Immunocontraceptive vaccines work to control fertility by causing the production of antibodies against a reproductive tract protein (eggs or sperm) or hormone associated with reproduction in an animal. Several approaches have been considered in developing a strategy for vaccine development, including production of antibodies against: (1) a layer around the egg (zona pellucida or ZP), (2) sperm head proteins, (3) chorionic gonadotropin hormone, (4) follicle stimulating hormone (FSH), (5) luteinizing hormone (LH), and (6) gonadotropin releasing hormone (GnRH). Based on current technology, ZP of porcine origin (PZP) and GnRH vaccines appear to be the most effective and developmentally feasible for wide dissemination in target animals on a cost effective basis. Therefore, the DWRC is focusing its research on development of these vaccines.

The ZP is a noncellular glycoprotein layer between the egg and granulosa cells surrounding it. The ZP functions in the process of sperm/egg recognition, providing species specificity and ensuring that only a single sperm penetrates the egg at fertilization. Antibodies produced in the female to the ZP proteins will bind to the ZP of its own eggs, thereby blocking conception by preventing sperm penetration.

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GnRH is a hormone, from the hypothalamus at the base of the brain, that controls the release of pituitary reproductive hormones FSH and LH. GnRH is a "self" hormone, and to be made "foreign" and immunogenic, GnRH must be coupled to an antigenic foreign protein carrier. In the GnRH immunocontraceptive approach, antibodies produced to GnRH/carrier proteins will interfere with the biological activity of circulating GnRH, thereby preventing release of FSH and LH which, in turn, will affect the ovaries and testes and cause temporary (one to two years) sterility in both sexes.

Research Plan and Progress to Date

Current research is focused on developing genetically engineered vaccines and oral vaccine delivery systems for control of reproduction in white-tailed deer and several other pest species. Studies have been conducted in three major areas in cooperation with Baylor College of Medicine (BCM), Pennsylvania State University (PSU) and the Colorado Division of Wildlife (CDOW):

ZP Vaccines--Studies have been conducted to determine efficacy of natural and genetically engineered recombinant ZP vaccines in controlling reproduction. The genetically engineered ZP has had some limited success and will be a major focus of future research. Three years of deer PZP immunocontraceptive research at PSU have yielded important information defining critical antibody titer levels (and their duration) needed to prevent conception. The PZP vaccine has been quite successful in contracepting female deer for 3 years; of 9 of the PZP deer treated in 1992 and 1993 (of which only 4 received vaccine boosts in 1994), 8 were infertile through the summer of 1995 and one deer delivered one fawn. These same PZP deer will continue in the study through the spring of 1996 to determine the duration of the PZP immunocontraceptive effect. In 1994, a study was initiated at BCM to determine which of the many peptides in the large PZP protein produced antibodies resulting in contraception. A new mimotope technology was used for this study, in which antibodies from previously sterilized deer were used to identify the active peptides that produced contraception. This peptide selection may allow the DWRC to synthesize and produce an economical vaccine rather than using the PZP isolated from pig ovaries.

A study titled "Development of immunocontraception technology to control reproduction in the coyote" is in the final stages of planning and is scheduled to begin this fall at the field station in Logan, Utah.

GnRH Vaccines--Three new GnRH immunocontraceptive peptides were designed at DWRC and synthesized under contract at Colorado State University. These new designs assure consistent alignment of the peptide and increased density when coupling them to the carrier protein. These peptides are coupled to a large immunogenic protein, keyhole limpet hemocyanin (KLH), and are being tested in deer. One peptide was tested in 1994 on 4 female and 4 male deer. This technique has application for sterilization of deer at certain locations. This contraceptive vaccine was effective in both sexes. It has also has been successful in preventing conception in Norway rats at DWRC.

GnRH is also being tested with avian species. In 1994, male cowbirds vaccinated with avian GnRH demonstrated a reduction in spring testosterone levels that correlated with their immune response to the GnRH vaccine. In addition, the second year of a starling avian GnRH immunocontraceptive study

has begun. In 1994 these birds demonstrated an excellent immune response to the vaccine, indicating that starlings can be successfully vaccinated. These birds were boosted this year to determine the immune response a year later and to determine the effect on testosterone inhibition. Initial analysis of results shows that the vaccine looks promising.

Oral Vaccine Delivery--Traditional delivery of vaccines by darts is expensive, difficult to administer, and does not reach a large segment of the target population. Therefore, the DWRC is investigating oral delivery systems. A white-tailed deer study has been conducted to assess the effectiveness of a genetically engineered and attenuated bacterium (BCG) as a model delivery vehicle for oral immunization. Immune response data demonstrated that BCG can be effectively used as a live carrier vector to orally vaccinate deer. In a second test to improve the efficiency of oral vaccine delivery, an "adhesive liposome" was designed and synthesized at DWRC. The liposome, a spherical micro container for a vaccine, increases the percentage of uptake as the vaccine moves through the digestive tract. This liposome has been used to orally immunize and contracept rats at DWRC. A study was initiated in 1994, in cooperation with CDOW at their Fort Collins, Colorado ungulate facility, to determine the feasibility of using liposomes to orally vaccinate white-tailed deer with GnRH. Hormone concentrations and antibody levels are being tested to assess the efficacy of the current vaccine, with preliminary results indicating that the deer can be orally vaccinated.

This year we began a study to determine the best design for encapsulating a harmless live bacterial vaccine vector in an alfalfa feed cube designed for ruminants. This study is designed to determine the limits of vaccine bait viability at various storage conditions and field applications and will include temperature and humidity as variables.

An immuno-marker assay is in the process of development which will allow a researcher to determine if an animal has taken an immunocontraceptive bait. The assay is designed to be used in the lab or field and will require as little as a single drop of blood on an assay stick.