RESEARCH ABSTRACT

SWINE HEALTH

Title: Induction Of Cross-Protective Immunity Without Exposure To Live PRRSV - **NPB #08-197**

Investigator: Luis Enjuanes

Institution: Centro Nacional de Biotecnología (CNB), CSIC

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Scientific abstract

Porcine reproductive and respiratory syndrome (PRRS) is the main infectious disease affecting swine. Nevertheless, limited information is available on the immune response against the virus causing the disease (PRRSV), and current vaccines against PRRSV have a limited efficacy. Best results have been obtained using modified live vaccines, although they have several problems such as incomplete protection, virus shedding and possible reversion to virulence. Vector- based vaccines could represent and advantage to stimulate both humoral and cell immune responses against PRRSV. Nevertheless, the results reported to date using viral vectors do not provide the expected protection and new vectors must be explored. The main novelty of the project proposed comes from the use of the transmissible gastroenteritis virus (TGEV)-based vector to express different PRRSV antigenic combinations. These vectors stably express high levels of heterologous genes, are potent interferon-α inducers, essential for antiviral defense, and present antigens in mucosal surfaces, providing both secretory and systemic immunity. A TGEV derived vector (rTGEV) was generated, expressing PRRSV GP5 and M proteins, described as the main inducers of neutralizing antibodies and cellular immune response, respectively. Protection experiments showed that vaccinated animals developed a faster and stronger humoral immune response than the non-vaccinated ones. Nevertheless, low levels of neutralizing antibodies were elicited after rTGEV inoculation, similarly to what occurs with PRRSV infection. This could be due to a steric hindrance caused by the glycosylation sites mapping close to the neutralizing epitope in GP5 protein. Therefore, a set of rTGEV vectors expressing M protein and GP5 mutants, with a modified glycosylation pattern, were generated. These vectors expressed GP5 and M proteins, presumably forming a heterodimer, in at least a 75% of the infected cells. To increase rTGEV stability and improve expression levels, serial passages and virus cloning were performed. Immunization with a killed vaccine based on this rTGEV vector has provided data indicating that vaccinated animals elicited a higher and faster PRRSV specific humoral immune response, including the induction of both neutralizing and non-neutralizing antibodies. Moreover, in vaccinated animals lung damage was decreased when compared with the non-vaccinated ones. The efficacy of this live vaccine in protection was also analyzed. A faster and stronger PRRSV specific humoral response was developed in the vaccinated animals compared to that of the non-vaccinated ones. Moreover, lung damage was significantly lower in vaccinated animals compared with non-vaccinated ones. Nevertheless, a weak neutralizing antibody response was elicited in both cases. This modest results, when compared with those obtained using the killed-vaccine, suggest that rTGEV vector stability may be the handicap to achieve more promising results. Therefore, a new strategy has been developed to improve rTGEV vectors stability. All together, data obtained indicate that TGEV represents a new and promising strategy to achieve protection against PRRSV.

These research results were submitted in fulfillment of checkoff-funded research projects. This report is published directly as submitted by the project's principal investigator. This report has not been peer-reviewed.

For more information contact:

National Pork Board • PO Box 9114 • Des Moines, IA 50306 USA • 800-456-7675 • Fax: 515-223-2646 • pork.org