Title: Induction of Cross-Protective Immunity Without Exposure to Live PRRSV - NPB #07-112

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 an 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. This vector stably expressed PRRSV antigens in more than 80% of the TGEV infected cells. Moreover, the expression levels were maintained after inoculation of piglets. Protection experiments showed that vaccinated animals developed a faster and stronger humoral immune response than non-vaccinated animals. The rTGEV vector also reduced viremia and the replication of PRRSV in the lung of vaccinated pigs. Low levels of neutralizing antibodies were produced after rTGEV inoculation, similarly to what occurs with PRRSV infection. This could be due to a steric hindrance caused by the glycosylation sites present close to the neutralizing epitope in GP5. Therefore, a set of rTGEV vectors expressing M protein and GP5 mutants with a modified glycosylation pattern were generated. One of these vectors stably expressed GP5 and M proteins in at least a 75% of the TGEV infected cells. Preliminary data from in vivo experiments have shown that vaccinated animals elicit a higher and faster PRRSV specific humoral immune response, including neutralizing and total antibodies. The efficacy of this rTGEV vector in protection experiments will be analyzed. Alternatively, the presence of an immunodominant (decoy) epitope close to the neutralizing epitope in GP5 could be deleterious for a strong neutralizing immune response. Therefore, an rTGEV expressing M protein and a GP5 mutant with a modified glycosylation pattern and lacking the decoy epitope was generated. The quality and stability of this vector is being analyzed. All together, data obtained indicate that TGEV represents a new and promising strategy to achieve protection against PRRSV.