RESEARCH ABSTRACT

SWINE HEALTH

Title: Evaluation of adjuvants at the mucosal area for the development of innovative mucosal vaccine against PRRS - **NPB # 08-187**

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Scientific Abstract:

PRRS is an economically important chronic endemic viral disease of pigs. Currently practiced control and prevention strategies have been inadequate to reduce economic losses to the pork industry. Stimulating the immune system systemically (i.e. via injection) results mainly in systemic protection, but low mucosal immune responses are generated. On the other hand, adequate stimulation of the mucosal immune system results in production of both mucosal and systemic protection, so that infectious agents are blocked from entry into the body. But practically, it is difficult to elicit protective mucosal immunity to vaccine antigens due to high alert immune regulatory mechanisms at mucosal surfaces. However, it is possible to overcome that regulatory barrier with the help of potent adjuvants administered along with the vaccine antigens. Based on the immune responses elicited to PRRSV-MLV by the adjuvanticity of nine different bacterial preparations belongs to *Mycobacterium, Streptoccocus,* and *Vibrio* species, three of the preparations: *Mycobacterium tuberculosis* whole cell lysate (*M. tb* WCL); Cholera toxin B subunit; and *Streptoccocus pyogenes* product (Picibanil/OK432) were found to potentiate the PRRSV-MLV (RespPRRS®) specific adaptive immunity. These adjuvants overcame the immune suppression induced by the PRRSV antigens and favored the generation of anti-PRRSV specific adaptive immunity. Subsequently, detailed analysis of on one of the three adjuvants (*M. tb* WCL) with PRRSV-MLV administered IN resulted in upregulated anti-PRRSV specific immune responses. Such as increased PRRSV specific cytotoxic T lymphocytes, NK cells (also rescued its cytotoxicity), and myeloid cells. Also increased the levels of Th1 cytokines (IL-12 and IFNγ), PRRSV specific neutralizing antibody titers, and importantly downregulated the immunosuppressive cytokines (IL-10 and TGFβ) compared to pigs received PRRSV-MLV with no adjuvant. Finally, following virulent heterologous PRRSV challenge in mucosally immunized pigs (PRRSV-MLV with *M. tb* WCL), we found significant rescue in body weight loss, reduced lung inflammation, and significantly less PRRSV load. In addition, favorable anti-PRRSV mucosal and systemic immune responses were detected in mucosally immunized and homologous or heterologous PRRSV challenged pigs. Thus, we conclude that protective anti-PRRSV mucosal immunity is critical to control PRRSV outbreaks, and that could be achieved by intranasal administration of conventional PRRSV-MLV along with a potent adjuvant.