Title: The effect of PRRSv infection on the thymus – a source of immune dysregulation? – NPB #13-175

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Scientific Abstract: PRRSv infection has been shown to cause an acute lymphopenia (loss of cells in the blood), lymphadenopathy (increased size of lymph nodes due to increased cell numbers) and thymic atrophy (decreased thymus size due to decreased number of cells) in conjunction with PRRSv antigen staining in the thymus; however, the relationship between these features and subsequent immune dysregulation has not been evaluated. Lymphopenia coincidental with impaired thymic output is likely to have a significant impact on the peripheral pool of functional T cells. Ultimately, this would impair the ability of the pig to mount a protective immune response and clear the virus, a characteristic feature of PRRSv pathogenesis. The thymus was significantly impacted by PRRSV infection, but severity was related to the challenge strain. Infection with the moderately pathogenic strain (SDSU73) resulted in a decrease in thymic size and cellularity, and changes in gene expression, but these changes were limited within the first few weeks post-infection, with near resolution to normal by day 21 following challenge. In stark contrast, the effect on the thymus was more pronounced following infection with JXwn06 highly-pathogenic PRRSV and there is no indication of resolution to normal. The number of differentially expressed genes in the thymus of JXwn06-infected pigs was nearly twice as many as observed in the thymus of SDSU-73 infected pigs. Apoptotic cells were found primarily in the thymic cortex, but PRRSV antigen staining was found primarily in the medulla. Thus, the induction of apoptosis following challenge was likely an indirect affect of PRRSV infection, though the cells positive for PRRSV antigen have not been thoroughly characterized. Overall, the changes in gene transcription will provide useful data for further characterizing the mechanism of cell death and cellularity changes associated with PRRSV infection, and ideally lead to identifying interventions to lesson the negative impact of infection on this important lymphoid organ.