

# The Effect of PRRSV Vaccination and WUR Genotype on the Gene Expression Profile in Blood of Nursery Pigs Following Co-infection with PRRSV and PCV2b

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### Summary and Implications

Previous results have shown that pigs that were vaccinated (Vac) with a porcine reproductive and respiratory syndrome (PRRS) modified live virus (MLV) had lower PRRS viral load (VL) but higher porcine circovirus 2b (PCV2b) VL following co-infection with PRRSV and PCV2b than non-vaccinated (nonVac) pigs. In this study, we identified differentially expressed genes (DEGs) at 4 and 7 days post infection (dpi) between Vac and nonVac (VacStatus) pigs. Five DEGs were predicted to decrease replication of PRRSV at 7 dpi in Vac pigs, which may relate to the partial protective effect of the vaccine against PRRS. Other DEG at 4 and 7 dpi were predicted to decrease innate immune response in Vac pigs, which may contribute to the higher PCV2b VL in Vac pigs. These DEGs in blood, and their biological functions, can help us understand PRRS vaccination effects on host-response mechanisms to coinfection with PRRSV and PCV2b in nursery pigs.

### Introduction

Co-infection with PRRSV and PCV2 is a useful model for co-infection in the field, with PRRSV enhancing replication of PCV2. Both PRRSV and PCV2 can suppress host immune defenses. PCV2 infection can reduce the efficacy of PRRS MLV vaccines. In previous work, genetic marker WUR10000125 (WUR) on chromosome 4 was found to be strongly associated with weight gain and viremia after infection with PRRSV. Allele B at WUR is favorable and dominant to allele A. Previous analyses of the co-infection experiments studied here, also showed that PRRS vaccinated pigs had lower PRRS VL but higher PCV2b VL than non-vaccinated pigs after co-infection with PRRSV and PCV2b. This indicates that PRRS vaccination has a partial protective effect against PRRSV infection but enhances PCV2 infection. The goal of this research was to explore the host-mechanisms responsible for these differences. Data on host gene expression profiles in blood

were used to assess the effect of PRRS MLV vaccination and WUR on co-infection with PRRSV and PCV2b.

### Materials and Methods

Three-week-old Large White\*Landrace barrows (n=199) were preselected based on WUR genotype (50% AA and 50% AB) and randomly assigned to one of two rooms. Pigs in one room were vaccinated with a PRRS MLV vaccine. After 28 day post vaccination, all pigs in both rooms were co-infected with field strains of PRRSV (KS62, heterologous to the PRRS MVL strain) and PCV2b, and were followed for 28 dpi.

In total, RNA was prepared from 151 blood samples collected from 28 pigs from 7 litters that had one piglet for each VacStatus x WUR genotype combination: Vac-AA, Vac-AB, nonVac-AA, nonVac-AB, at 0, 4, 7, 11, 14, and 28 dpi for gene expression analysis in blood using 3'RNAseq (QuantSeq). Differential expression (DE) analysis was done separately for each dpi using a generalized linear model that included the effects of WUR genotype, RNA RIN score, sequencing lane, VacStatus, and the interaction between VacStatus and WUR genotype. Ingenuity Pathway Analysis (IPA) software was used for pathway enrichment analysis of significant DEGs ( $q \leq 0.2$ ).

### Results and Discussion

No DEGs were identified ( $q \leq 0.2$ ) for the effect of WUR or for the interaction between VacStatus and WUR at any time point, which indicates that these may not have a large effect on the gene expression in blood following vaccination and co-infection. For VacStatus, DEGs ( $q \leq 0.2$ ) were identified at 4 dpi (40 DEGs) and at 7 dpi (63 DEGs). Based on IPA, PRRS vaccination led to differences in gene expression levels compared to non-vaccinated pigs at 4 dpi, that may result in increasing viral infection and decreasing immune response of cells. At 7 dpi, IPA analyses indicated that PRRS vaccination led to differences in gene expression that may result in decreasing inflammation, viral replication, immune response of phagocytes, and leukocyte migration. These differences in gene expression may, however, also result from differences in the number and types of blood cells such as monocytes between Vac and nonVac pigs.

Taken together, this study indicates that PRRS vaccination may modulate blood gene expression levels which were predicted to trigger lower innate immune responses following co-infection with PRRSV and PCV2, resulting in less inhibition of PCV2b viral infection.

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