# Quantitative Trait Locus on *Sus scrofa* Chromosome 4 Associated with Host Response to Experimental Infection with Porcine Reproductive and Respiratory Syndrome Virus

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## Summary and Implications

The objective of this study was to conduct a genome-wide association study to discover the genetic basis of host response to PRRS virus using data from the PRRS Host Genetics Consortium NPB and PRRS-CAP project. Approximately 1,600 commercial crossbred piglets were experimentally infected with the Porcine Reproductive and Respiratory Syndrome (PRRS) virus. Blood samples and body weights were collected up to 42 days post infection (dpi). Experimental pigs and their parents were genotyped with Illumina's Porcine 60k BeadChip. Phenotypes analyzed were viral load (VL = area under the curve for log-transformed qRT-PCR based serum virus from 0-21 dpi) and weight gain from 0-42 dpi (WG). Heritabilities estimated using pedigree information were moderate at 0.41 for VL and 0.29 for WG. A 1 Mb region on *Sus scrofa* chromosome (SSC) 4 was found to be associated with VL and WG and explained a substantial amount of genetic variation. The frequency of the favorable allele for the most significant single nucleotide polymorphism (SNP) was 0.15. These results show that there is a host genetic component to PRRS virus infection and that there is room for genetic improvement.

## Introduction

Porcine Reproductive and Respiratory Syndrome is one of the most economically important diseases in the swine industry. Many diseases are effectively treated with drug administration or prevented by vaccination. However, effectiveness of vaccination has been limited for PRRS; therefore, additional methods to control the virus must be explored. The objective of this study was to conduct a genome-wide association study to discover the genetic basis of host response to PRRS virus using data from the PRRS Host Genetics Consortium NPB and PRRS-CAP project.

## Materials and Methods

Eight groups of 200 commercial crossbred piglets from PRRS-free farms were infected with PRRS virus isolate NVSL 97-7985 between 25 and 35 days of age at experimental facilities at Kansas State University. Blood samples and body weights were collected up to 42 dpi. Whole genome analyses focused on serum VL up to 21 dpi and WG from 0 to 42 dpi. Serum VL was quantified using area under the curve for log-transformed qRT-PCR based serum virus at 0, 4, 7, 11, 14, and 21 dpi. Experimental piglets and their parents were genotyped with the Illumina 60k BeadChip. Parental breeds included Large White, Landrace, Yorkshire, Duroc, and Pietrain.

Heritabilities, genetic correlations, and SNP effects were estimated from pedigree information with an animal model using ASREML. Associations of SNP genotypes with traits were analyzed using the software GenSel. Haplotypes of the experimental piglets and their parents were determined using PHASE software. Parental haplotypes were used to determine which allele for a particular SNP came from the sire or dam.

## Results and Discussion

Pedigree-based heritability estimates across all trials were moderate at 0.41 for VL and 0.29 for WG. The estimated genetic correlation between VL and WG was -0.47. The phenotypic standard deviation was 7.5 units for VL and 4.1 kg for WG.

A 1 Mb region on SSC4 that included 36 polymorphic SNPs on the 60k BeadChip panel was associated with both VL and WG. The 1 Mb region explained 14.6% of the genetic variance for VL and 9.1% for WG. The effect of this region on VL and WG was present in all 8 trials. A single SNP in the 1 Mb region, SNP WUR10000125 (WUR), accounted for over 99% of the variance in VL and WG that was captured by the region. The effect of the WUR SNP acted in a dominant manner, with the B allele estimated to decrease VL by 4 units (0.53 phenotypic sd, Table 1) and increase WG by 2 kg (0.49 phenotypic sd, Table 1). The effect of the WUR SNP was highly significant for both traits ($p < 10^{-16}$). The frequency of the B allele was low across all trials at 0.15.

The WUR SNP was segregating in all parental breeds involved in the crosses. Irrespective of whether the favorable B allele came from the sire or dam, the effect was present, i.e. decreased VL and increased WG. The difference between AB and BA genotypes was not significant ($p > 0.89$).

### Implications

The swine industry has been fighting PRRS for more than 20 years, with little to no success. Genetic improvement of host resistance is an additional tool that can be used to reduce the devastating effects of the virus, ultimately reducing the economic impact. These results demonstrate that there is a substantial host genetic component in response to infection with PRRS virus and that selection for resistance is possible. The 1 Mb region on SSC4 harbors a QTL that reduces the effects that PRRS has on performance. A single SNP from the 60k BeadChip could be used for selection. With a low frequency of the favorable allele, there is plenty of room for genetic improvement. Furthermore, the effect of SNP WUR was present in all the breeds commonly used in the U.S. swine industry, allowing for faster genetic progress

compared to the effect being present in only 1 breed. Further work is, however, needed to confirm that this same region also confers reduced susceptibility to other strains of PRRS virus.

| SNP WUR Genotype | VL | WG (kg) | N VL | N WG |
|---|---|---|---|---|
| AA | 108.1 ± 0.6 | 14.1 ± 0.3 | 862 | 983 |
| AB | 103.2 ± 0.7 | 16.1 ± 0.4 | 320 | 345 |
| BB | 105.3 ± 1.2 | 15.9 ± 0.7 | 44 | 43 |

**Table 1.** LS Means (±SE) of the effect of SNP WUR1000125 on viral load (VL) and weight gain (WG), along with the number (N) of animals for each genotype by trait. Viral load was calculated as area under the curve for log-transformed qRT-PCR based serum virus from 0-21 days post infection. Weight gain was calculated as gain from 0 to 42 days post infection.