Blood Transcriptome in Healthy Piglets as a Potential Biomarker to Improve Disease Resilience

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Summary and Implications

Disease resilience is a concept that combines resistance and tolerance. Depending on individual resilience, the performance of pigs can be different in commercial herds, where they are exposed to various pathogens, compared to nucleus breeding herds. Here, we designed a natural disease challenge model in pigs to measure resilience traits and to generate population-level gene expression data. Our results suggested that gene expression patterns in young healthy pigs showed significant associations with mortality following exposure to disease and are, therefore, promising as early disease resilience predictors for use in nucleus breeding programs.

Introduction

Improving disease resilience is an issue of considerable importance in swine breeding programs. However, evaluation of resilience after exposure to disease conflicts with the high-health conditions required in pig nucleus breeding herds. Hence, developing blood biomarkers of resilience that can be obtained at the nucleus herd level can help to overcome this limitation. In this study, we investigated blood gene expression profiles of young healthy pigs prior to exposure to a natural polymicrobial disease challenge by applying quantitative genetic analysis to population-level transcriptome data.

Materials and Methods

Seven batches of weaned barrows (n = 441 Yorkshire x Landrace) from healthy multiplier farms were entered into the experimental facility in Québec, Canada. They were acclimated in a healthy quarantine nursery and blood samples were collected at ~27 days of age for quantifying gene expression levels using 3'mRNA sequencing with globin blocking. Two weeks after bleeding, the pigs were moved to a nearby natural disease challenged nursery-finisher, where several resilience phenotypes were measured, including average daily gain in the challenge nursery (NurADG, n=378) and finisher (FinADG, n=342), mortality (n=441), and the number of treatments per 180 days (Trt180, n=396). The expression data were adjusted by a linear mixed model with batch as a fixed effect, pen in the quarantine nursery as a random effect and two covariates, age that pigs entered quarantine nursery and RNA quality (RIN). Gene modules and their eigengene values were obtained by the WGCNA software. Association analysis of gene expression and modules with four resilience traits was conducted by the trait-specific mixed models. Associations with false discovery rate < 0.05 and < 0.01were considered statistically significant for gene expression and modules, respectively. Functional annotation analyses by the DAVID software were performed using genes which showed a significant association with mortality using both single genes and modules.

Results and Discussion

The expression of 3,523 genes in blood at a young age was significantly associated with subsequent mortality (FDR < 0.05). Most of these genes (n=3,441) showed lower expression in pigs that subsequently died during the natural disease challenge. The expression of only two genes was positively associated with NurADG (FDR < 0.05) and there were no significant associations with FinADG and Trt180. Hence, we investigated the associations of gene modules with mortality. In WGCNA results, 30 modules were identified initially, which were then grouped to 12 merged modules. Among the 42 modules, 6 initial modules were significant (FDR < 0.01), which were also included in two significant merged models (FDR < 0.01). In addition, the eigengene values of these 8 modules were lower for the pigs which died during the challenge. Genes in the top 3 WGCNA modules overlapped with single gene association results. The overlapping genes were related to RNA metabolic processes, organ morphogenesis and viral processes based on the DAVID gene ontology database.

In conclusion, our findings support the hypothesis that disease resilience of pigs in high-health herds could be predicted by gene expression profiles in blood collected on young healthy animals.

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