

Title: Re-defining growth efficiency accounting for the interaction between host genome and commensal gut bacteria - NPB project #16-020

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Date Submitted: 05-04-2019

Scientific Abstract:

The overall objective of this study was to assess the power of microbiome predictions based on fecal samples, to foresee growth and carcass composition in populations of healthy pigs. Specific objectives of the proposal were: 1- Quantify the impact of microbiome composition on lean growth in swine. 2- Quantify the heritability of relative taxa abundance in swine. 3- Explore the hypothesis that specific regions of the genome are related to the ability of the host to select relative taxa abundance. 4- Evaluate the effectiveness of the inclusion of microbiome taxa relative abundance as direct source of variation in predicting growth and carcass traits in pigs.

Fecal microbiome sequences were generated and organized in Operation Taxonomic Units (OTU) representing specific microbial species that were employed in subsequent analyses. Fecal samples, collected from a population of pigs at three time points, including weaning, week 15 post weaning (hereafter “week 15”), and end-of-feeding test (hereafter “off-test”), were used to evaluate changes in the composition of the fecal microbiome of each animal over time. Firmicutes and Bacteroidetes were the most abundant phyla at all three time points. The most abundant genera at all three time points

included *Clostridium*, *Escherichia*, *Bacteroides*, *Prevotella*, *Ruminococcus*, *Fusobacterium*, *Campylobacter*, *Eubacterium*, and *Lactobacillus*. Two enterotypes were identified at each time point. Enterotypes at week 15 and off-test were significantly associated with growth parameters. Alpha diversity and operational taxonomic unit (OTU) richness were moderately heritable at week 15, h^2 of 0.15 ± 0.06 to 0.16 ± 0.07 and 0.23 ± 0.09 to 0.26 ± 0.08 , respectively, as well as at off-test, h^2 of 0.20 ± 0.09 to 0.33 ± 0.10 and 0.17 ± 0.08 to 0.24 ± 0.08 , respectively, whereas very low heritability estimates for both measures were detected at weaning. Alpha diversity at week 15 had strong and negative genetic correlations with BF, -0.53 ± 0.23 to -0.45 ± 0.25 , as well as with ADG, -0.53 ± 0.32 to -0.53 ± 0.29 . These results are important for efforts to genetically improve the domesticated pig because they suggest fecal microbiota diversity can be used as an indicator trait to improve traits that are expensive to measure.

These research results were submitted in fulfillment of checkoff-funded research projects. This report is published directly as submitted by the project's principal investigator. This report has not been peer-reviewed.

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We evaluated the power of microbiome measures taken at three time points over the growth test period (to foretell growth and carcass traits of pigs). We measured prediction accuracy as the correlation between actual and predicted phenotypes in a five-fold cross-validation setting. Phenotypic traits measured included live weight measures and carcass composition obtained during the trial as well as at slaughter. We employed a null model excluding microbiome information as a baseline to assess the increase in prediction accuracy stemming from the inclusion of operational taxonomic units (OTU) as predictors. We further contrasted performance of models from the Bayesian alphabet as well machine learning and semi-parametric kernel models. In most cases, prediction accuracy increased significantly with the inclusion of microbiome data. Accuracy was more substantial with the inclusion of microbiome information taken at weeks 15 and 22, with values ranging from approximately 0.30 for loin traits to more than 0.50 for back fat. Conversely, microbiome composition at weaning resulted in most cases in marginal gains of prediction accuracy, suggesting that later measures might be more useful to include in predictive models. The inclusion of OTU predictors could potentially be used to promote fast growth of individuals while limiting fat accumulation. Early microbiome measures might not be good predictors of growth and OTU information might be best collected at later life stages.

We evaluated the potential interaction between the host genome and its gut microbiome in swine. Three thousand and one pigs, originating from 28 founding Duroc Sires, were used in the study. Half of the pigs were generated through purebred matings while half by matings with F1 Landrace x Large White dams. All pigs were genotyped with the Illumina PorcineSNP60 Beadchip while sires were sequenced at an average depth of 10x. Fecal microbiome samples were collected at weaning, week 15 and week 27 of the feeding trial, along with backfat thickness (BF), live weight (WT), and loin depth (LD) measures. We estimated heritability for taxa of the gut bacteria, identifying taxa that are important for the phenotypes, as well as scanning the host genome for single nucleotide polymorphisms (SNPs) potentially influencing the gut microbiome composition in both crossbred and purebreds. Forty-eight taxa from week 15 and 20 at week 27, were significantly associated with backfat, weight and loin depth at an FDR of 5%. Taxa with a substantial contribution to traits variation included *Succinivibrio dextrinosolvens*, *Lactobacillus reuteri*, *Prevotella copri*, *Peptococcus niger*, and *Oxalobacter formigenes*. Heritability estimates for the significant taxa at weaning, week 15, and week 27 ranged from low to moderate (0.01 to 0.34) and were heterogeneous between crossbred and purebreds. Several SNPs were found significantly associated with OTUs at week 15 and 27. These SNPs located in chromosome regions that contained a total of 378 genes, belonging among others, to pathways that protect epithelial cells in the host gut, transfer substances transmembranes, promote cell proliferation, differentiation, motility, and survival.

We estimated the microbiability and investigate its impact on heritability estimates of meat quality and carcass traits; we estimated the microbial correlation between the meat quality and carcass traits in swine populations. The study population consisted of 1,123 three-way cross individuals genotyped with 60K SNP chips and phenotyped for carcass and meat quality traits. Fecal 16S microbial sequences for all individuals were obtained at three different stages: off test (OT: 196.4 ± 7.80 days); week 15 (W₁₅: 118.2 ± 1.18 days); and weaning (WEAN: 18.64 ± 1.09 days)). Data were analyzed using the single and multi-trait model, which included the fixed effects of dam line, contemporary group, and sex as well as random effects of pen, animal additive genetic and microbiome. The last two were modeled with the use of relationship matrices among individuals obtained by genomic and microbial information. Analyses were conducted in ASREML v.4. The contribution of microbiome to all traits was significant although it varied over time with increase from WEAN to OT for most traits. Adding microbiome information did not affect the estimates of genomic heritability of meat quality traits but changed the estimates of carcass composition traits. Decrease in heritability was best observed for OT, where decrease in heritability ranged from 2% for carcass average daily gain (CADG) to 10% for fat depth. Microbial correlations ranged from -0.93 ± 0.11 between firmness and shearing force to 0.97 ± 0.02 between CADG and loin weight. Results suggested that gut microbial composition can contribute to the improvement of complex traits in swine. These results may lead to establish a newer approach of genetic evaluation process through the addition of gut microbial information.