

PUBLIC HEALTHWORKER SAFETY

Title: Effects of early-life antibiotic administration on porcine respiratory microbiota and piglet immunity – **NPB #18-050**

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Scientific Abstract:

The view on the use of antimicrobial in food animals has changed due to the increased knowledge on antibiotic resistances and their effect on the microbiota composition. Still, the impact of antibiotic treatments on the swine respiratory microbiota is poorly understood. To address this later and taking into account results from previous studies, it was hypothesized that antibiotic administration to piglets during the lactation period interferes with normal colonization patterns of the respiratory microbiota. It was also hypothesized that an impaired immune response play a role in antibiotic-mediated disturbances of the nasal microbiome. This study aimed, therefore, to characterize the impact of Tulathromycin administration, at either 4 or 19 days of age, on the diversity of the nasal microbiota over a 56-day period (lactation and post-weaning). Additionally, this study also sought to determine host genetic variations associated with the immune response in the context of a hypothetical antibiotic-associated dysbiosis.

To accomplish the abovementioned objectives, 85 piglets from litters of 10 different sows were randomly allocated to one of the following treatment groups. The control group 1 (n=29) consisted of piglets that did not receive antibiotics. Groups 2 (n=27) and 3 (n=29) received a single intramuscular injection of Tulathromycin, at either 4 or 19 days of age, respectively. Tulathromycin was administered at a dosage of 2.5 mg/kg, following manufacturer's recommendations. Nasal swabs were collected from sows post-farrowing and from piglets on days 4 (T1), 12 (T2), 19 (T3), 28 (T4) and 56 (T5) of age. In addition, a blood sample was obtained from peri-weaned piglets from all groups. NS collected through the study were used to assess nasal bacterial composition by amplifying the V3-V4 regions of 16S rRNA gene. Thus, sequences generated by Illumina MiSeq technology were processed using the Divisive Amplicon Denoising Algorithm 2 (DADA2) workflow and microbiome analyses were conducted by means of R software. Genomic host DNA was separated from total DNA extracted from blood to perform genome-wide association studies (GWAS) among the genotypes of the sampled pigs and their nasal microbiota composition. Genotyping was conducted using 50K GeneSeek® Genomic Profiler porcine beadchip (Neogen Genomics).

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Due to mortality across the study period, the number of sampled piglets within treatment groups differed between the assessed time points (T1 to T5). However, mortality was evenly distributed among groups. Overall, the nasal microbiota composition was dominated by Proteobacteria, Firmicutes and Actinobacteria whereas the predominant genera were *Moraxella*, *Actinobacillus* and *Rothia*. Based on diversity and composition analyses, the microbiome was not significantly different between treatment groups at any of the time points analyzed; nasal microbiota was stable regardless of antibiotic treatment. Remarkably, nasal microbiota diversity increased significantly with age, between pre-weaning (T1 to T3) and post-weaning (T4-T5) time points. Regardless to the treatment group, GWAS revealed a total of 4 single-nucleotide polymorphisms (SNPs) associated with the nasal microbiota diversity shortly after birth (T1). When considering the change in microbial composition over time, GWAS detected 2 associated SNPs. However, the candidate genes identified could not be related to piglet's immune response.

The obtained results could not validate the exposed hypothesis as the antibiotic administration to piglets during the lactation period did not interfere with normal colonization patterns of the nasal microbiota. Furthermore, the SNPs identified as possible genetic markers for nasal microbiota diversity did not show an apparent relationship with the host immune response. In conclusion, the present results point out that the age and the transition to nursery/finisher sites may exert a greater influence over the nasal microbiome of piglets than early-life antibiotic treatments.