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A Bayesian Approach to Investigating the Effects of Metaphylaxis on the Microbiome-Resistome of Commercial Feedlot Steers

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In beef feedlots, metaphylaxis is used to prevent respiratory disease in high-risk cattle. It is unknown whether or how this practice impacts the microbiome or resistome of treated cattle. The goal of this study was to apply Bayesian modeling to metagenomic data in order to identify the effects of metaphylaxis in commercial feedlot cattle.

Upon feedlot arrival, cattle were assigned to a treatment (N=193) or control (N=186) pen. Fecal samples were obtained from 15 cattle per pen ("Day 0"). All 193 cattle in the treatment group were injected with tulathromycin and cattle were then housed in separate pens. After 11 days, fecal samples were obtained from the 30 steers sampled previously ("Day 11" samples). Total DNA was subjected to shotgun sequencing. Reads were aligned to a database of antimicrobial, metal and biocide resistance determinants (ARDs, MRDs and BRDs), and NCBI RefSeq for taxonomic classification. Counts of features were compared between treated and control cattle.

Sequencing produced 5.89B reads; 3.8M (0.06%) aligned to 343 unique ARDs/BRDs/MRDs, the majority of which were tetracycline ARDs. Frequentist analytic approaches showed no difference in the microbiome-resistome of treated and control cattle on either Day 0 or 11, but both groups experienced a dramatic shift between Day 0 and 11. However, such methods do not optimally account for data hierarchy, overdispersion or zero-inflation. Therefore, we are applying hierarchical Bayesian models to validate results and provide robust measures of group differences; results indicate this is a more suitable approach for metagenomic data from complex study designs.

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