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The effect of breed and gender on drug depletion and differential gene expression associated with drug metabolism after flunixin and fenbendaolze administration

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Despite the critical role animal health plays in food production sustainability, drug metabolism knowledge is very limited. We are evaluating genetic variation in pharmacokinetic profiles and liver gene expression in pigs. In Phase 1, eight sires derived from four breeds were mated to a common sow population. A random crossover design was utilized and drugs were administered intravenously. The drugs examined were flunixin (FLU), enrofloxacin, fenbendazole (FBZ) and sulfamethazine. Blood was collected 10 times over 48 hours. Pharmacokinetics parameters derived from a non-compartmental analysis of drug and metabolite plasma concentration vs. time profiles were analyzed. Phase 1 revealed breed differences for FLU and FBZ and gender differences for FBZ (all P-value<0.05). FBZ and FLU were selected for phase 2 where liver gene expression is studied in 96 animals per drug. Blood samples and pharmacokinetic data were collected from all dosed pigs. After 48 hours, the pigs were given another dose of the same drug and slaughtered 1 hour after drug administration. Liver samples from all pigs were collected at slaughter and stored in RNA. Later the RNA was extracted. Six genes involved in drug metabolism were evaluated using qPCR to identify differential expression between gender and/or breeds. The genes were *cyp1a2, cyp2e, cyp3a22, cyp3a29, phenol sulfotransferase(ps)* and *p-glycoprotein*. Results to date show differential expression of cyp3a29 and 3a22 between breeds given FLU and breed differences in ps expression in pigs given FBZ.

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