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Host genetics affect the composition of the lower gut microbiota in dairy cows

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Symbiotic microorganisms are organized into specific ecosystems along the gastrointestinal tract of animals. In ruminants, studies showed a complex crosstalk between the ruminal microbiota and the host: beyond its role in the digestive process, the microbiota modulates the host phenotype but is also under the influence of the host genome. Concerning the intestinal microbiota, its role on numerous traits, in particular health maintenance, is increasingly described and could make it a key component of a sustainable breeding. However, its genetic control remains elusive. In this context, the present work will aim to perform a comprehensive genetic study of the lower gut microbiota. Faecal samples were collected between 2020 and 2022 from a population of 1930 Holstein cows, reared on 140 French commercial farms. Microbiota 16S rRNA analyses were performed on the samples and the data were processed to obtain amplicon sequence variant (ASV) tables. Genetic parameters were estimated using animal models for (1) the samples' diversity expressed as the Shannon index, and (2) the abundance of the most frequently observed ASVs and genera (with a prevalence threshold of 60%). The 152 ASVs and 87 genera analysed showed low to moderate heritability estimates. Indeed, 32% of ASVs had a heritability between 0.05 and 0.23 (s.e. from 0.04 to 0.10), with an ASV of the *Negativibacillus* genus being the most heritable taxon. Almost half of the genera had heritabilities ranging from 0.05 to 0.21 while the Shannon diversity index appeared to be poorly heritable ($h^2=0.04$, s.e.=0.05). Overall, our results demonstrate that the host genetics shapes the composition of the cow faecal microbiota. These first encouraging results will be complemented to assess the genetic correlations between the microbiota composition and production traits, and to identify genomic regions involved in the genetic determinism of the bovine gut microbiota through GWAS analyses.

Session 41

Theatre 10

A model including host genotype, gut microbiome, and fat deposition measures in swine

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We propose a systematic approach to elicit the host genome control over microbial composition and tissue deposition while accounting for these two components' effects on each other. We developed a mediation test in a Structural Equation Model (SEM) and applied it to measured and latent dependent variables describing fat deposition in swine (*Sus scrofa*). Host genotype (G) contribution was determined using a 60k SNP beadchip. Gut microbiome composition was assessed using 16S sequencing of faecal swabs at 18 and 26 weeks of age (M1 or M2, respectively). Back fat accumulation was measured with ultrasound scan at 18 weeks of age (P1). In addition, a latent variable was constructed (P2), compounding ultrasound and mechanical backfat measures at slaughter, together with the weight of the belly cut. We focused our analysis on this measure that we considered the relevant target endogenous variable. We implemented a SEM and a standard model used in Genome-Wide Association Studies (sGWAS). Both included common effects to account for environmental variation and family stratification. The SEM aimed at estimating the sign and magnitude of the following mediated paths: Path1: G->P1->P2; Path2: G->M2->P2; Path3: G->M1->P2; Path4: G->P1->M2->P2; Path5: G->M1->M2->P2; together with the direct path Path0: G->P2. The sGWAS model, without using microbial information, estimated the total effect of G on P2, such as Path00: G->P2. The two models were run for each 42,546 SNP included in the analysis. The significance of the estimates was assessed using bootstrapping, which allowed to obtain an empirical distribution of the estimates by sampling with replacement. Compared to the sGWAS model, the SEM identified additional SNPs with significant mediated effects. Notably, these did not overlap with those identified as having a significant effect with the standard GWAS model. While the loci showing stronger total effects were primarily located on SSC1 and SSC5, the loci with the strongest indirect effects were found on SSC9, SSC6, SSC7, and SSC13. Results suggest that gut microbial information can be successfully included in (more complex) models.