Genetic determinism of sperm DNA methylation in French Holstein cattle

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Session 69 Theatre 2

Transgenerational effects of heat stress in dairy sheep

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Previous studies on dairy cattle showed that the effect of cows' birth month, detected on the breeding values of granddaughters, is likely due to heat stress (HS) suffered during the pregnancy. In the framework of SCALA-MEDI project, the present study aims to investigate the transgenerational effect of HS in dairy sheep. In Sarda breed, births of ewes are concentrated in November and December. However, a differential exposure to HS, along gestation (summer-autumn) and across years or locations, can be observed. Pregnancies, lactation and climate data were recorded from 1980 to 2022 in 2 experimental farms located in the North and in the South of Sardinia. Milk yields of 4,931 genotyped ewes born from 1999 to 2022 were used to estimate GEBV by an animal model based on genomic relationships. GEBV of lactating ewes were analyzed with a linear model that included, as fixed covariates, the Temperature-Humidity Indexes (THI) recorded during pregnancies of dam (D), granddam (GD) and great-granddam (GGD) and GEBV of sires to adjust for non-maternal genetic effects. As a measure of HS, the average THI and the count of days where THI>23, were considered in the 1st, the 2nd and the 3rd thirds of the gestation. Both the HS measures led to the same results. No significant effects were detected in the 1st third of gestation. A significant negative effect of HS was observed in the 2nd third of GD pregnancy only. In the last third, significant negative effects of HS were estimated for D, GD and GGD. The most negative effect was observed for GGD and corresponded to -0.31 liter (-0.013 s.d.u.) per unit of average THI. These results suggest that epigenetic modifications in germ cells of embryo due to HS can be transmitted to further generations.

Session 69 Theatre 3

Genetic determinism of sperm DNA methylation in French Holstein cattle

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Methylation quantitative trait loci (meQTL) are genetic variants that influence DNA methylation. In cattle, little is known about the genetic determinism of DNA methylation, either at the level of individual methylation sites (CpGs) or on a global scale. In this study, we investigated the sperm methylome of 262 Holstein bulls obtained by reduced representation bisulfite sequencing. After filtering out CpGs without individual variability or co-localizing with SNPs, we performed sequence-based GWAS of three groups of methylation phenotypes: (1) principal component scores of the most variable CpG sites, (2) average DNA methylation rate for genomic regions (e.g. whole chromosome, gene, promoter), and (3) DNA methylation rates of individual CpG sites. We then examined the SNPs significantly associated with CpG methylation (-log10(P) > 7.3) and classified them according to their proximity to the CpG, i.e. cis (<1 Mb), cis long-range (>1Mb, on the same chromosome), and trans (on different chromosomes). We found meQTLs for all phenotypic categories, most of which had cis-regulatory effects. In addition, our study identified candidate genes involved in methylation pathways. Taken together, these results demonstrate a genetic determinism of DNA methylation in cattle and thus an interplay between genetic variation and epigenetic regulation. CF is recipient of a CIFRE PhD grant from ANRT and APIS-GENE. This work was part of the POLYPHEME project funded by ANR (ANR-21-CE20-0021) and APIS-GENE.