A large study to assess the magnitude of foetal programming in cattle

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Epigenetic biomarkers for environmental enrichment and parity in pregnant sows

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Changes in the blood cells' epigenome, such as variations in DNA methylation, have been proposed as markers of the long-term effects of various factors in humans and in livestock. Therefore, this study aimed to identify pan-genomic DNA methylation variations in association with the well-being of animals submitted to contrasted welfare states. Pregnant sows of mixed parities (low parity (LP) – 2nd and 3rd gestation and high parity (HP) – 4th gestation or higher) were housed in two contrasting conditions throughout gestation (0 to 105 days): in a conventional system on a slatted floor (C: LP, n=9 and HP, n=6) or in an enriched system on accumulated straw with additional space per sow (E: LP, n=6 and HP, n=7). At gestation day 98, pan-genomic DNA methylation from the sows' blood mononuclear cells was analysed by reduced representation bisulphite sequencing (RRBS), following the lab's protocol. Only CpGs sites covered by at least 10 uniquely mapped reads (CpG_{10}) were retained and filtered out using a list of 105,171 known Single Nucleotide Polymorphisms (SNPs). Methylation percentages at each CpG_{10} were calculated and cluster analyses were conducted. Differentially methylated cytosines (DMCs) were identified using methylKit v1.0. ($\Delta_{meth} \geq 25\%$ and adjusted *P*-value <1%) considering the following comparisons: $[LPvsHP]_C$ and $[LPvsHP]_E$ (parity effect); $[CvsE]_{LP}$ and $[CvsE]_{HP}$ (system effect). Cluster analyses revealed a clear separation corresponding to parity groups. [LPvsHP] displayed more DMC in C (5,391) than in E (3,886) with a similar loss of methylation (53 and 55% in C and E, respectively). Regarding the housing effect, the contrast [CvsE] displayed more DMCs in HP (2,769) than in LP sows (2,183), with an equal number of hypo and hyper DMCs. DMC-targeted genes were mostly associated with cell migration and adhesion, and other immune processes. Taken together, these results suggest that parity has a stronger effect on the immune cells' methylome than the housing system.

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Prenatal factors may influence the future performance of dairy cows. We therefore investigated the impact of a suboptimal prenatal environment of a cow on the performance of the resulting daughter in the Holstein breed. The factors investigated in this analysis were associated either with the use of assisted reproductive technologies (sexed semen, embryo transfer (ET) or ET combined with *in vitro* fertilization (IVF-ET)) or with different stress factors during dam's gestation (parity, milk fat-to-protein ratio as a proxy for the metabolic status of the dam). The effects on daughter's performance of these factors, occurring before or during different periods of the dam's gestation, were tested in a model including non-genetic effects commonly used in genetic evaluations and the own direct genomic value for the trait considered, as a covariate. Depending on the factor considered, from 10,000 to 200,000 genotyped cows were used. IVF-ET calves were found to have more difficult birth conditions, suggesting a heavier weight, although neither IVF-ET, nor ET had any effect on the stature in first parity and on the milk performance of the resulting cows. Cows born from heifers and derived from sexed semen produced slightly less milk (-0.3%) than their counterparts derived from conventional AI. Low and high fat/protein ratios of the dam's milk, which are indicators of metabolic disorders, were associated with slightly reduced offspring milk production (-1%) and fertility. The parity of the dam was positively associated with the milk performance of the offspring. For all the factors tested in our study the adverse effect was moderate (e.g. less than 1% for milk yield), suggesting that the negative impact of foetal programming appears to be limited. Further work will be carried out to investigate the effects of other situations, on a wider range of traits and breeds. CF is recipient of a CIFRE PhD grant from ANRT and APIS-GENE. This work was part of the POLYPHEME project funded by ANR and APIS-GENE.