Prenatal and Postnatal Dietary n-3 Fatty Acid Supplementation Alters Buffy Coat DNA Methylation Profile in Pigs

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Summary and Implications
The objective of this study was to determine the effect of maternal long chain n-3 fatty acid supplementation on the DNA methylation profile of offspring buffy coats. We demonstrated several methylated regions across the genome were influenced by maternal n-3 dietary treatment. Therefore, feeding n-3 fatty acids to sows during gestation and lactation may result in a DNA methylation imprint on offspring buffy coats that persists beyond the nursery phase and may alter the phenotype of the growing pig.

Introduction
Offspring from sows fed long chain n-3 fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), during gestation and lactation have been demonstrated to have attenuated febrile responses to the innate immunogen, lipopolysaccharides (LPS). However, the contribution of DNA methylation to differences observed in this phenotypic response is unknown. In order to further understand these epigenetic responses, we utilized massively parallel deep sequencing of methylated regions of the genome to determine the effect of prenatal and postnatal dietary enrichment of DHA and EPA on buffy coat DNA methylation profile.

Materials and Methods
Fifteen sows (n=5 per treatment) were randomly selected from within one of three dietary treatments one week post weaning: 1) control diet throughout gestation, lactation, and nursery phase (CCC); 2) n-3 fatty acid supplementation in the form of Gromega™, rich in DHA and EPA, fed throughout gestation, lactation and nursery phase (GGG); or 3) DHA and EPA supplementation only in the gestation and lactation stage, control diet devoid of DHA and EPA in the nursery (GGC). At 11 weeks of age and after 8 weeks of nursery feeding, buffy coats were collected and DNA isolated. The DNA was enriched for CpG methylation and subjected to next generation sequencing.

Results and Discussion
Approximately 77% of total reads were mapped to the pig genome, and 623,838 unique methylated regions were identified. In total, mapped base pairs covered approximately 25% of the genome. Preliminary analysis revealed distinct chromosome-specific patterns of methylation among the treatment groups. Across the genome, numerous highly methylated regions were detected that were treatment independent. Conversely, several treatment-specific methylation patterns were also detected on specific chromosomes. Figure 1 depicts a region on chromosome 13 with distinct DNA methylation patterns between the Gromega supplemented diets, GGC and GGG, and the control diet, CCC. Further understanding of the mechanisms contributing to maternal environmental influences on DNA methylation of offspring and association with specific phenotype is essential for improving animal agriculture.

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