REPETITIVE ELEMENT METHYLATION EXTENT IS ASSOCIATED WITH INFANT GROWTH AND DEVELOPMENTALLY RELATED GENE METHYLATION

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Background and Aims: Fetal programming describes the theory linking environmental conditions during embryonic and fetal development with risk of diseases later in life. Environmental insults in-utero may lead to changes in epigenetic mechanisms, resulting in deleterious changes to overall placental function. In this study, we aimed to examine the impact of birthweight percentile on repetitive element methylation in placental tissue, and to determine if repetitive element methylation could be an indicator for changes in methylation of specific CpG loci.
Methods: Placental tissues were obtained from patients delivering at Women and Infants Hospital in Providence, RI. Birthweight percentile and levels of LINE1 and AluYb8 methylation were determined for 380 subjects; methylation profiling was performed using the Illumina Infinium27 Methylation BeadArray on 184 subjects. We used multiple linear regression to investigate the association between birthweight percentile and repetitive element methylation, and used model-based methods, such as gene set enrichment analysis, to test the association between repetitive element methylation and individual CpG loci methylation levels.
Results: Birthweight percentile was a significant predictor of both LINE1 and AluYb8 methylation levels, with maternal smoking during pregnancy predicting only AluYb8 methylation levels. Increasing levels of AluYb8 were associated with increasing average class methylation of individual CpGs found in polycomb group target sites. Developmentally related transcription factor binding sites and important cellular processes pathways were over-represented for differentially methylated loci associated with both LINE1 and AluYb8.
Conclusions: AluYb8 methylation status may be a biomarker for individual CpG loci changes occurring in polycomb group target sites, and for specific changes occurring in developmental pathways. It may therefore be a potential biomarker for epigenetic changes occurring during development.