Epigenetic consequences to offspring of nutritional deficiency in pregnancy

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Epigenetic modifications of the genome are implicated in phenotypic differences in physiological fitness and disease susceptibility, and could account for the increasingly recognized links between the prenatal and early postnatal nutritional environment and adult health and disease. A mismatch between nutrient availability in early and later life appears to precipitate the emergence of major adult and increasingly childhood onset diseases: obesity, cardiovascular disease, and type 2 diabetes. Epigenetic silencing of imprinted genes through DNA methylation and histone modification is an important mechanism underlying fetal and postnatal growth and development. We have used a rat model to investigate whether methylation and allelic expression of the Igf2 and H19 genes are influenced by maternal nutrition during pregnancy. Female rats were maintained throughout pregnancy on a control *ad libitum* chow diet or on 30% of the control food intake (undernourished). Our studies demonstrate: 1) Developmentally regulated methylation at the Igf2 differentially methylated regions (DMRs) from fetal to juvenile and adult stages; 2) Tissue-specific effects of prenatal undernutrition on Igf2 DMR methylation; 3) Tissue-specific postnatal reactivation of the silenced maternal Igf2 allele, indicating loss-of-imprinting (LOI). These alterations in methylation are in some cases associated with altered levels of Igf2 expression at a tissue level. Our studies indicate that maternal nutrition does influence the epigenetic state of the offspring genome at specific chromosomal regions in a tissue-specific manner. Such epigenetic alterations in early life may contribute to epigenetic variability within the population that influences the risk of diseases in adulthood.