Excess of methyl donors in maternal diet affects post-natal down-regulation and DNA methylation of Igf2 and H19 in liver

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Maternal nutrition during preconceptual period, gestation and lactation can lead to epigenetic alterations and influences fetal growth, development and susceptibility to metabolic adult diseases. Proteins and some specific amino-acids play a major role in these effects. Methionine and folic acid are involved in the folate cycle that is central to fetal growth and development processes. Our objective was to identify the underlying epigenetic mechanism by which these nutrients influence early growth and may contribute to the establishment of a nutritional imprinting.

Female rats were fed diets containing either 8 or 20% protein and supplemented or not with high amounts of methyl donors (MD) and cofactors (methionine, choline, Vit-B12, zinc, betaine) during 3 weeks before mating, gestation and lactation.

The impact of maternal MD supplementation on the folate cycle was evidenced by an increase in maternal homocysteinemia. MD supplemented diets reduced fetal and postnatal growth, and this effect was emphasized when combined to protein restriction. Weight gain at adulthood and sensitivity to a hypercaloric diet was slightly impaired in the male-only offspring of MD supplemented dams. The normally occurring post-natal down-regulation of Igf2 and H19 was affected by MD supplementation, resulting in an up-to 20 times over-expression in liver at weaning. The methylation status of Igf2/H19 differentially methylated regions (DMRs) and imprinting control regions (ICRs) was influenced by maternal diet. Metabolic consequences were considered at early and late stages of development.