IMPACT OF GESTATIONAL WEIGHT GAIN ON METHYLATION OF IMPRINTED GENES IN UMBILICAL CORD AND ITS RELATIONSHIP WITH POSTNATAL GROWTH AND METABOLISM

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INTRODUCTION AND OBJECTIVES

Imprinted genes are critical for placental function and normal fetal growth and development. Very little is known about the impact of maternal obesity on imprinted genes and their role in postnatal growth and metabolism.
In this context, we aimed:

1) To identify umbilical cord DNA methylation sites (CpG) associated with gestational weight gain (GWG).
2) To identify which of these CpGs lie within imprinting control regions (ICRs).
3) To study the association of these CpGs with offspring's growth and metabolism.

MATERIALS AND METHODS

A pilot study was conducted in 16 pregnant women with different degrees of GWG. The newborns were followed up from birth to 6 years of age. Umbilical cord DNA methylation was assessed using microarray Infinium Methylation EPICBeadChip (Illumina). Beta regression models (false discovery rate (FDR) < 0.05 and odds ratio>1.5 or <0.67) were performed to identify the CpGs associated with GWG. The CpGs that lied within ICRs were selected and correlated with anthropometric and metabolic parameters of the offspring.

RESULTS

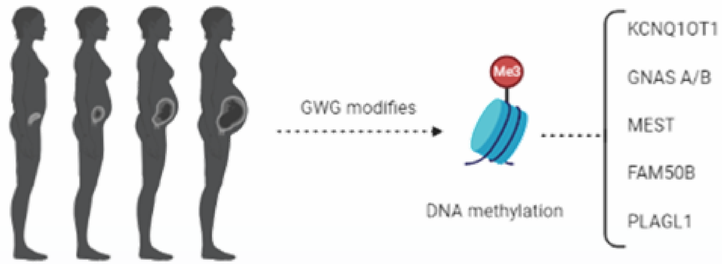

Figure 1. Genes present in ICRs whose DNA mehtylation is modified through GWG.

2773 differentially methylated CpG were identified, out of which 8 lied within ICRs. The top 5 CpGs, which annotated for *KCNQ1OT1*, *GNAS A/B*, *MEST*, *PLAGL1* and *FAM50B* (FDR<0.001 and odds ratio>1.03. Figure 1), were chosen for the study. The methylation of all these CpGs was positively correlated with GWG (r from 0.603 to 0.826; all p<0.02). The CpGs that annotated for *KCNQ1OT1* and *GNAS A/B* were negatively associated with the levels of glycated haemoglobin (HbA1C) and glucose in the offspring at 6 years of age (r=-0.610, p=0.016 and r=-0.705, p=0.003, respectively. Figure 2). The CpGs that annotated for *MEST* and *FAM5OB* were negatively associated with visceral (renal) fat at 6 years of age (r = -0.627, p = 0.012 and r = -0.634, p = 0.011, respectively. Figure 2). Finally, the CpG annotated for *PLAGL1* were associated with height and glucose at 6 years of age (r=-0.652 p=0.008; r = -0.806 p < 0.001; r = -0.806 p <0.001 respectively. Figure 2).

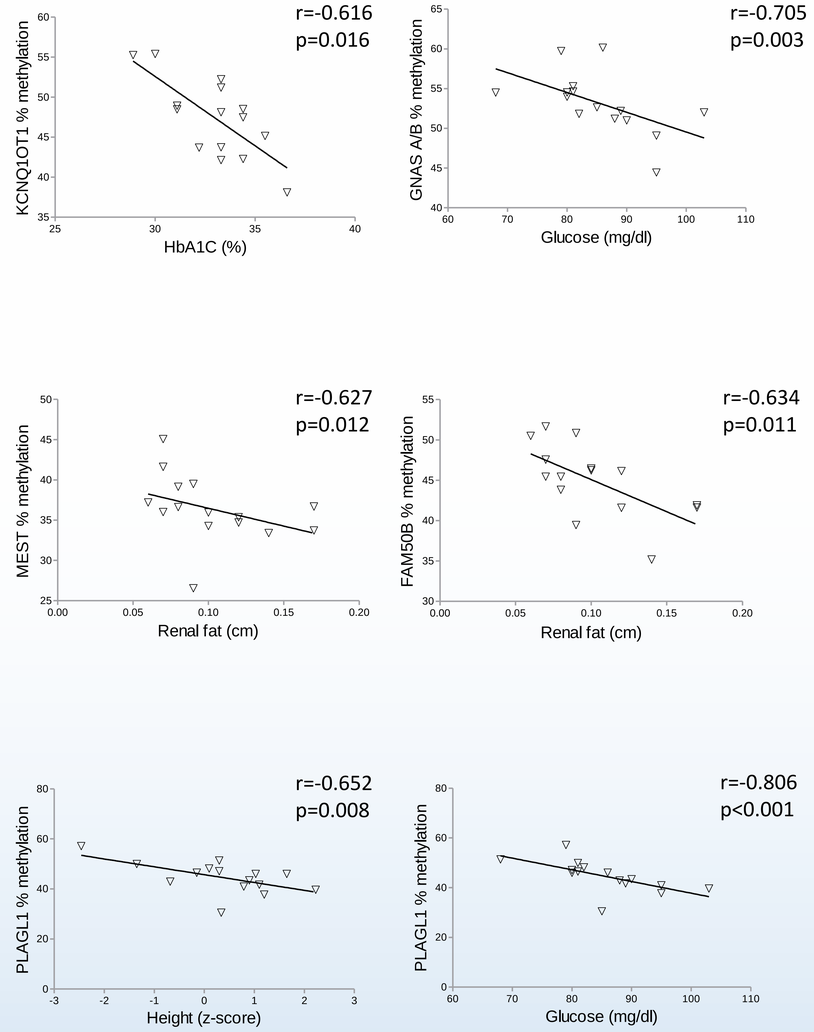

Figure 2. Gene correlations with cardiometabolic parameters of the offspring at 6 years of age.

CONCLUSIONS

This preliminary study suggests that excessive gestational weight gain can cause changes in DNA methylation of imprinted genes and thereby regulate postnatal growth and metabolism in the offspring.

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