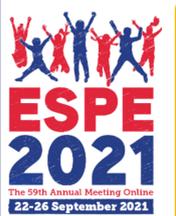


METHYLATION OF UMBILICAL CORD GENES ASSOCIATES WITH GESTATIONAL WEIGHT GAIN AND OFFSPRING'S CARDIOMETABOLIC PROFILE

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INTRODUCTION AND OBJECTIVES

Excessive gestational weight gain can cause an adverse intrauterine environment and increase the risk of cardiometabolic diseases in the offspring. Epigenetics could be one of the mechanisms involved in this regulation. We aimed to study the DNA methylation profile of umbilical cord tissue associated with gestational weight gain (GWG), and its relationship with cardiometabolic and anthropometric parameters in the offspring at 6 years old.

MATERIALS AND METHODS

A methylation array was done (Infinum®Methylation EPIC BeadChip) in umbilical cord tissue samples of 24 pregnant women with and without gestational obesity. The CG dinucleotides whose methylation was associated with GWG were validated in a cohort of 87 mothers and newborn pairs by pyrosequencing (Figure 1) and their gene expression was studied through RT-PCR. 61 newborns were followed up at 6 years old and their cardiometabolic and anthropometric parameters were assessed.

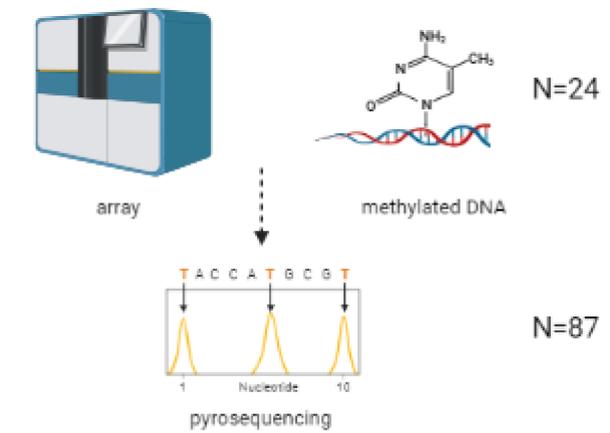


Figure 1. Methodology followed. Created in BioRender.com.

RESULTS

Methylation

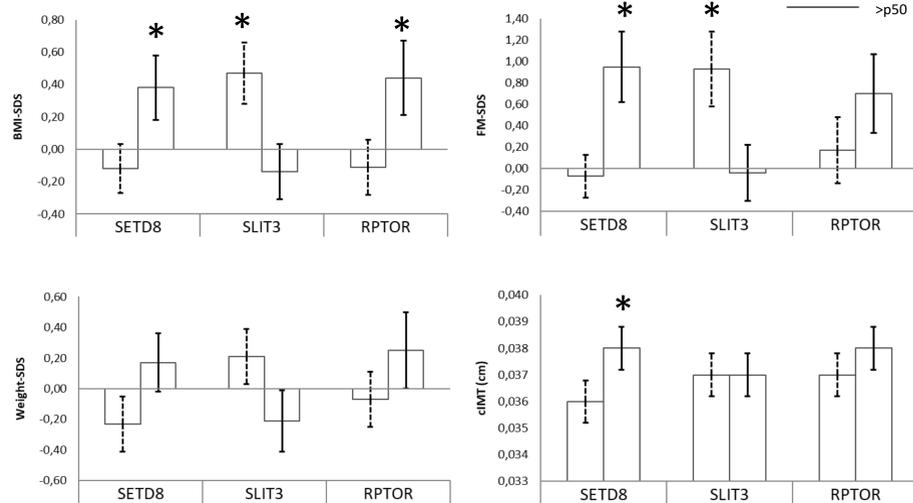


Figure 2. Differences between groups of methylation percentages.* indicates significant differences ($p < 0.05$).

Gene expression

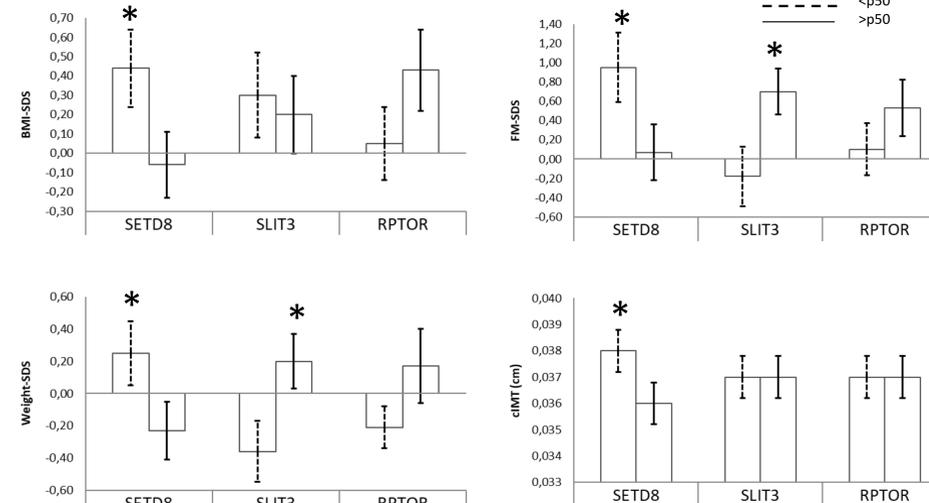


Figure 3. Differences between groups of gene expression levels.* indicates significant differences ($p < 0.05$).

CONCLUSIONS

The methylation and gene expression of umbilical cord genes associates with GWG and the cardiometabolic profile of the offspring at 6 years old. Epigenetic changes in the umbilical cord could explain the relationship between gestational obesity and cardiometabolic risk in later life.

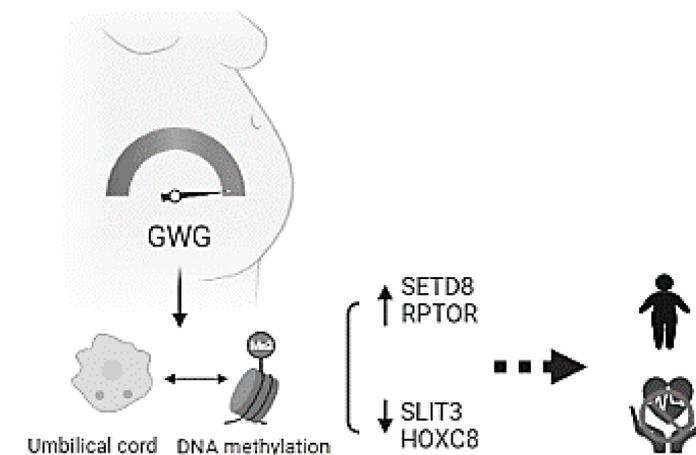


Figure 4. Graphical summary of the results obtained. Created in BioRender.com.

The array identified 2778 CG dinucleotides differentially methylated and associated with GWG (all $p < 0.05$) with gene annotation. Five genes were chosen for validation: SETD8, SLIT3, HOXC8, RPTOR and TMEM214. Children with higher methylation of SETD8 and lower methylation of SLIT3 showed a worse cardiometabolic profile at 6 years old (higher BMI, fat mass, waist circumference and cIMT; all $p < 0.05$. Figure 2). The gene expression levels of SETD8 and SLIT3 were opposite to their methylation levels and the children with lower and higher expression of SETD8 and SLIT3, respectively, presented differences in their cardiometabolic profile at 6 years old, in opposite way to methylation (Figure 3). The methylation levels of HOXC8 and RPTOR also showed significant associations with different cardiometabolic parameters, but no relation between methylation and gene expression was observed.



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