HYPERMETHYLATION AT THE IMPRINTED *C19MC* microRNA CLUSTER: A NEW LINK BETWEEN MATERNAL METABOLISM AND INFANT'S GROWTH.

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Introduction

Maternal obesity can have long-term consequences for the offspring's health, including increased risk of type-2 diabetes and cardiovascular disease. The *C19MC* imprinted locus on chromosome 19q13.4 comprises a cluster of 46 microRNAs, which are usually expressed only in the placenta and from the paternal allele exclusively. Besides its role favouring trophoblast migration, the *C19MC* locus is deregulated in several human cancers. It is unknown whether the degree of DNA methylation at the *C19MC* locus could be linked to maternal metabolism and infant's growth.

Objectives

Study the association between DNA methylation at *C19MC* and maternal weight, blood pressure and post-load glucose, and with the infant's weight and length.

Methods:

The degree of DNA methylation at 3 CpG dinucleotides in the *C19MC* promoter was studied by means of pyrosequencing in placentas from 79 healthy pregnancies. The studied chromosomal location within the cluster was chr19:54,151,133-54,151,183. A glucose-challenge test was performed between 24 and 28 weeks of gestation. Maternal weight and blood pressure data were also collected prior to birth. Women were grouped according to their pregestational BMI and their pregnancy weight gain into 3 weight groups. At delivery, placentas were collected and weighed, and the weight and length of the newborns were measured (gestational age 39 1 weeks; birth weight z-score 0.31 0.89).

Results

Increased placental methylation at the *C19MC* locus was associated with maternal obesity (p=0.016). Furthermore, higher levels of methylation were also associated with higher maternal systolic blood pressure (r=0.430; p=0.001) and post-load glucose levels (r=0.264; p=0.035). Higher placental methylation levels were also associated with increased infant's growth, showing positive associations with weight z-score (p=0.267; r=0.026) and height z-score (r=0.272; p=0.024) at birth. All these associations remained significant after adjusting for confounding variables.

Table 1: Correlations of C19MC methylation pecentages with maternal and newborn's growth variables (n= 79).

		C19MC methylation (%)
Systolic blood pressure	r	0.430
	p	0.001
Post load glucose levels	r	0.264
	p	0.035
Birth weight Z-score	r	0.267
	p	0.026
Birth height Z-score	r	0.272
	p	0.024

Conclusions

This study shows for the first time that aberrant hypermethylation at the *C19MC* locus provides a link between a poorer maternal metabolic phenotype and increased growth of the offspring.

Table 2: Multiple regression analyses of C19MC methylation pecentages with maternal and newborn's growth variables (n= 79).

	Beta	Sig.	R2
Systolic blood pressure	0.402	0.001	0.314
Post load glucose levels	0.265	0.031	0.198
Birth weight Z-score	0.253	0.037	0.101
Birth height Z-score	0.303	0.011	0.079

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