DYSREGULATION OF PLACENTAL miRNA IN MATERNAL OBESITY IS ASSOCIATED WITH PRE-AND POST-NATAL GROWTH

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Authors have nothing to declare.

Background:

Human placenta exhibits a specific miRNA expression pattern. Some of these miRNAs are dysregulated in pregnancy disorders like preeclampsia and intrauterine growth restriction (IUGR), and are potential biomarkers for these pathologies. No studies have been performed in maternal obesity

Objective and hypotheses:

(1) Define the placental miRNA profile in pregnant women with: a) pre-pregnancy (preOB) or gestational obesity (gestOB), b) gestational diabetes (GDM) and c) small for gestational age children (SGA).

(2) Explore the associations of circulating miRNAs dysregulated in maternal obesity with pre- and post-natal growth.

Methods:

TaqMan Low-Density Arrays (TLDAs) were used to profile the placental miRNAs in 30 pregnant women [6 preOB, 6 gestOB, 6 GDM, 6 SGA and 6 controls]. The miRNAs differentially expressed in maternal obesity were validated in 80 pregnant women (25 preOB, 25 gestOB and 30 control). Placentas and new-borns were weighed at delivery and at 1 year of life.

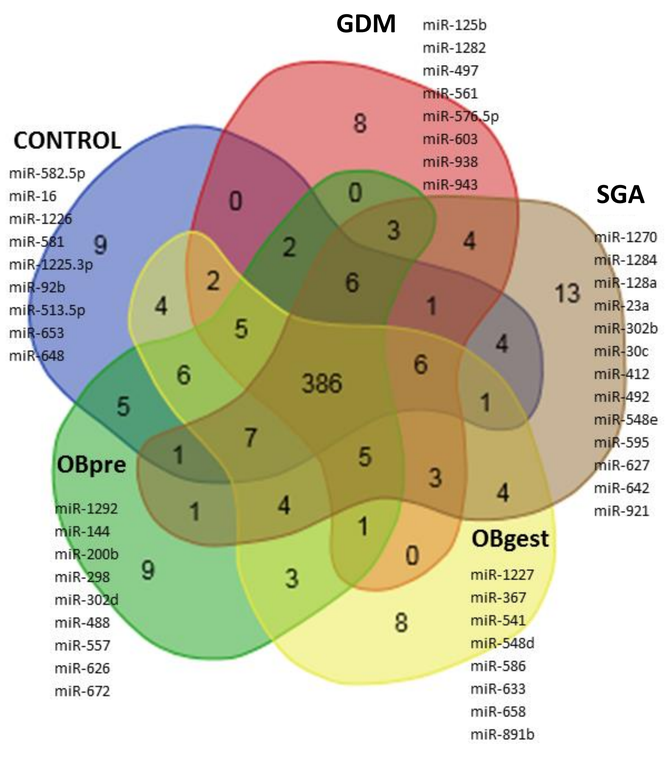

Figure 1. Venn diagram showing placental miRNA expression in the studied groups.

Results:

9 miRNAs were specific of placentas from women with preOB; 8 miRNAs of placentas from women with gestOB, 8 miRNAs of placentas from GDM women; 13 miRNAs of placentas from women with SGA children, and 386 miRNAs were common in all groups (Fig 1). Among the common miRNAs, 8 miRNAs were decreased in preOB or gestOB (miR-100, miR-1269, miR-1285, miR-181, miR-185,miR-214,miR-296 and miR487) (all p <0.05) (Fig 2). miR-100, miR-1285, miR-296 and miR-487associated with maternal metabolic parameters (all p<0.05) and were predictors of lower birth weight (all p<0.05 and R^2>30%) and increased postnatal weight gain (all p<0.05 and R^2>15%)(Table 1). *In silico* analysis showed that these miRNAs were related with cell proliferation and insulin signalling pathway.

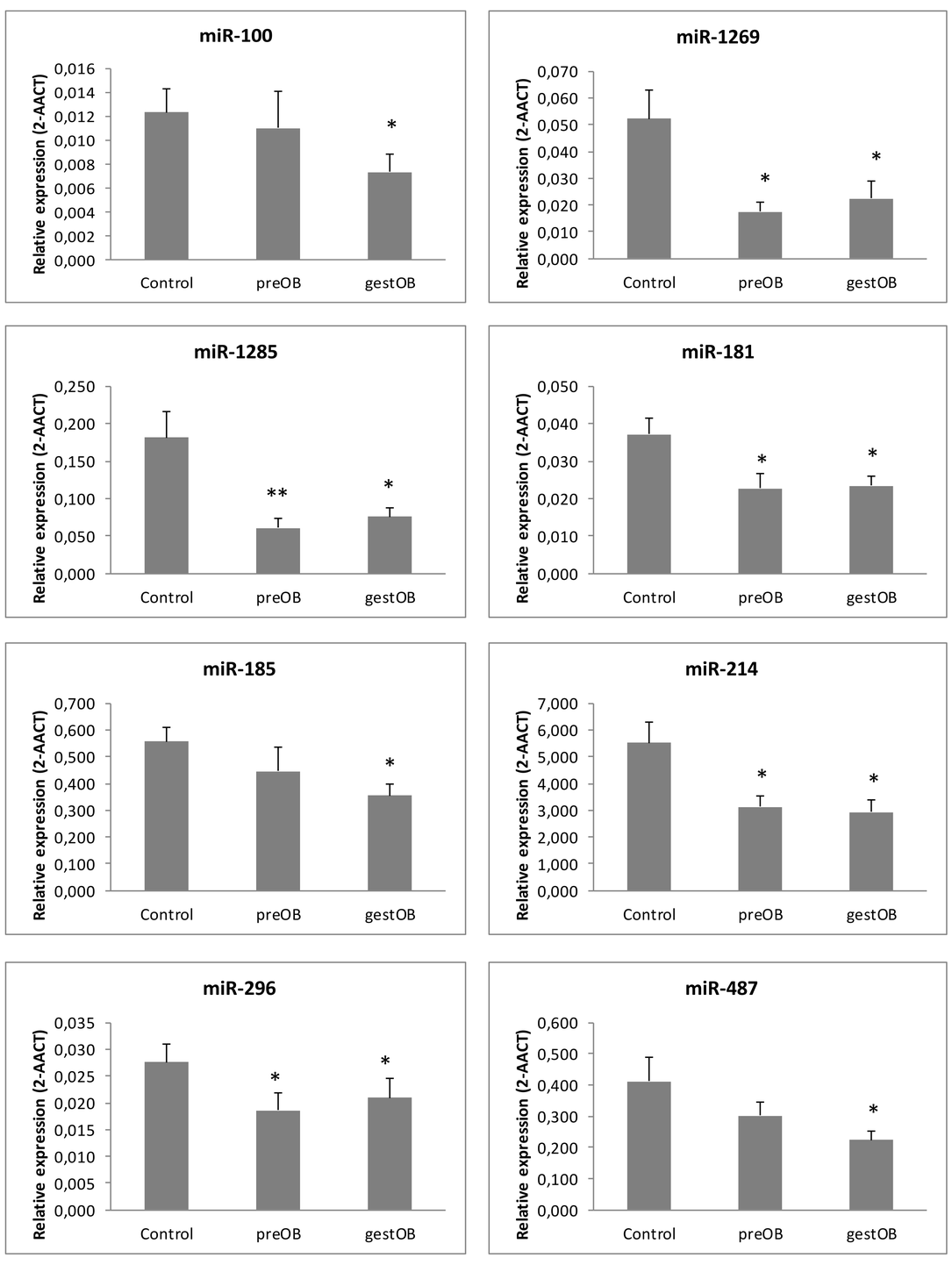

Figure 2. Error bar graphs of placental miRNAs differentially expressed in maternal obesity.

Table 1. Multivariate regression analyses of placental miRNA expression with pre- and post-natal growth parameters (n=80).

	Birth weight		Birth Height		Weight gain 12m	
	B	p	B	p	B	p
miR-100	-0.300	0.008	-0.246	0.02	0.294	0.02
EG	0.314	0.006	0.236	0.03	--	--
Pregestational BMI	--	--	0.334	0.01	--	--
Sex	--	--	-0.258	0.02	--	--
Adjusted R square	0.303		0.294		0.179	
miR-1285	-0.311	0.003	-0.298	0.006	--	--
EG	0.319	0.003	0.257	0.01	--	--
Sex	-0.209	0.04	-0.239	0.02	--	--
Adjusted R square	0.294		0.295			
miR-296	-0.222	0.01	--	--	0.377	<0.0001
EG	0.490	<0.0001	--	--	--	--
Sex	-0.184	0.04	--	--	--	--
Adjusted R square	0.307				0.198	
miR-487	-0.273	0.01	-0.218	0.03	0.400	0.006
EG	0.333	0.002	0.318	0.003	--	--
Sex	--	--	-0.258	0.01	--	--
Adjusted R square	0.312		0.304		0.160	

Conclusion:

We identified a specific placental miRNA profile in several pregnancy disorders including maternal obesity, GDM and SGA. The dysregulation of placental miRNAs may mediate the growth promoting effects of maternal obesity on the offspring.

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