

**66 Obesity alters pregnancy-related maternal cardiovascular remodeling through a miR-29 related mechanism**

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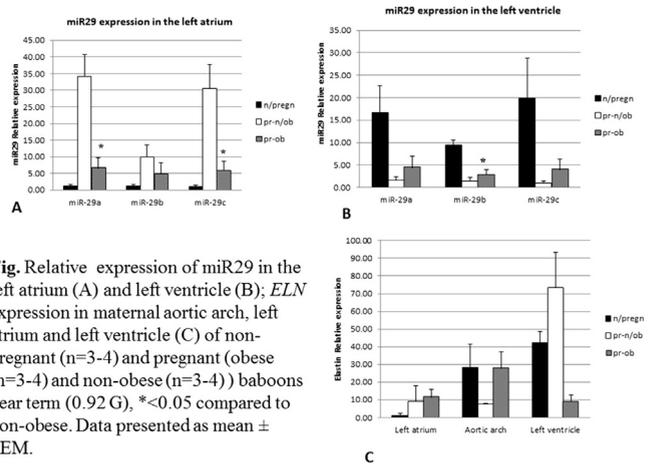
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**OBJECTIVE:** Adequate local (spiral arteries) and systemic cardiovascular system (CVS) remodeling is the key to successful adaptation to pregnancy. Maternal obesity (MO) is a major risk factor for preeclampsia (PE), fetal growth restriction (FGR) and is associated with decreased CVS compliance through a yet to be determined mechanism. The miR-29 microRNA family is a powerful regulator of at least 16 extracellular matrix genes involved in CVS remodeling. Vascular miR-29 expression is decreased in FGR in humans and in overfed non-human primates and its placental expression is increased in patients with PE. The goal of this study was to evaluate CVS miR-29 (subgroups a, b, and c) and elastin (ELN) expressions in MO. We hypothesized that MO would increase miR-29 and decrease elastin (ELN) mRNA expression in maternal heart.

**STUDY DESIGN:** Three groups of baboons (*Papio* spp.) were studied: non-pregnant (two obese, two non-obese, NP, n=4), pregnant obese (POb, n=4), and pregnant non-obese (PnOb, n=4). The tissues (left ventricle (LV), left atrium (LA), aortic arch) were collected at the end of gestation (0.92G). ELN and miR-29 expressions were quantified by qRT-PCR. miR-29 RNA expression was analyzed using the formula:  $2^{-\Delta\Delta\text{miRNA } 21 - \Delta\text{tU6}}$ . Statistical analyses were performed with ANOVA and significance was set at  $p < 0.05$ .

**RESULTS:** LA miR-29 (a, c) expressions were lower in POB compared to the PnOb baboons (Fig. A), while in the LV miR-29b expression was higher (Fig. B). The expression of ELN was decreased in the LA and LV of POB compared to PnOb baboons (Fig. C).

**CONCLUSION:** This is the first report documenting differential regulation of miR-29 family by MO. The ELN expression in the LV, paralleling changes in the miR-29, is in agreement with published data, which documented dramatic increase of ELN with the suppression of miR-29 in experimental models. Pharmacological tissue-specific targeting of miR-29 might represent a pioneering strategy for prevention and treatment of complications of MO, including PE.



**Fig.** Relative expression of miR29 in the left atrium (A) and left ventricle (B); ELN expression in maternal aortic arch, left atrium and left ventricle (C) of non-pregnant (n=3-4) and pregnant (obese (n=3-4) and non-obese (n=3-4)) baboons near term (0.92 G), \* $p < 0.05$  compared to non-obese. Data presented as mean  $\pm$  SEM.

**67 Fasting glucose levels during pregnancy and long-term childhood growth in the offspring**

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**OBJECTIVE:** Studies on the long-term health impact of intrauterine exposure to hyperglycemia on childhood growth in the offspring are relatively limited and findings are inconsistent.

**STUDY DESIGN:** We performed a prospective study among 665 women who were suspected to have gestational diabetes from the Danish National Birth Cohort, as part of the ongoing Diabetes & Women's Health Study, to investigate the association of maternal fasting glucose levels in pregnancy with childhood growth in the offspring. Weight and height at birth, 5 months, 12 months, and 7 years in the offspring were used to calculate age and gender specific BMI Z-scores and percentiles. Multivariable linear regression models adjusted for maternal age, parity, and BMI were used to examine the associations. Modified Poisson regression was used to estimate risk ratios of child overweight/obesity (BMI  $\geq$  85th percentile).

**RESULTS:** Each 10 mg/dl increment in maternal fasting glucose was associated with a 0.1 unit increase in BMI Z-score at birth ( $P=0.02$ ) in the offspring. Similar findings were observed at 7 years; corresponding to a 0.4 kg increase of weight ( $P=0.02$ ) and 0.1 unit of BMI Z-score ( $P=0.03$ ). Moreover, each 10 mg/dl increment in glucose was related to a 1.64-fold increased risk of overweight/obesity at 7 years. However, no significant association was observed for maternal glucose with any of the growth measurements at 5 and 12 months.

**CONCLUSION:** Maternal fasting glucose levels in pregnancy were positively and significantly related to fetal growth and childhood growth at 7 years in the offspring, independent of maternal pre-pregnancy BMI.