HEPATIC LIPID METABOLISM MODULATION BY MICRORNAS

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Abstract
We have shown that offspring from obese dams present elevated hepatic triacylglycerol synthesis, diminished fat acid oxidation, lower miR-370 and higher miR-122 expression. Here we overexpressed miR-122 in hepatic cells in the presence or absence of palmitate. Overexpression of miR-122 reverted deleterious effects observed when cells are treated with palmitate. Our data suggests that miR-122 expression may be related with the epigenetic modifications in lipid metabolism of obese dams offspring.

Key words: miR-122, metabolic programming, lipid metabolism

Introduction
Recently, our group demonstrated that offspring of dams with diet-induced obesity present higher triacylglycerol synthesis and lower fatty acid oxidation in liver, compared to offspring of control dams. Furthermore, offspring of obese dams showed diminished miR-370 expression and a raise in miR-122 expression, the most important microRNA in liver, known for its many regulation activities (Benatti et al., 2014). Thus, in the present study we aimed to modulate miR-122 expression in vitro, through a synthetic mimic in a mouse hepatic cell line (Hepa1c1c7), in the presence or in the absence of palmitic acid, in order to simulate the effects we had shown in vivo.

Results and Discussion
Preliminary results show that transfection with miR-122 mimic seems to revert some phenomena observed when cells treated only with fatty acid. When treated with palmitate, cells showed lower expression of miR-122 and higher expression of miR-370. miR-122 mimic transfection reverted the Cpt1a decrease, as well as lead to a lower expression of Agpat and raised the expression of HNF4a, a transcription factor for miR-122. Cpt1a is an important enzyme involved in fatty acid transport for oxidation and Agpat is one of the main enzymes that participate of triacylglycerol synthesis. Thus, miR-122 seems to participate in fatty acid oxidation and triacylglicerol synthesis and its expression may be related to the epigenetic programming we had previously shown in vivo.

Conclusions
Taken together, our results suggest that miR-122 expression may be related to epigenetic modifications in the metabolic programming we observed in offspring from obese dams. However, new experiments will be performed to endorse the results we previously obtained.

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