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MiR-34a regulates mitochondrial content and fat ectopic deposition induced by resistin through the AMPK/PPARα pathway in HepG2 cells

Running title: MiR-34a regulates fat deposition induced by resistin

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Abstract

Resistin is an adipocyte-derived cytokine and was named for its role in the development of insulin resistance. Increased serum resistin levels are also associated with steatohepatitis and non-alcoholic fatty liver disease. In a previous study, resistin was observed to reduce mitochondrial content and upregulate miR-34a significantly in the liver. In this study, male C57BL/6 mice were injected with agomir-34a or control agomir, and HepG2 cells were transfected with miR-34a mimics or inhibitors to assess their role in resistin-induced fat deposition. The overexpression of miR-34a increased liver and HepG2 cell TAG content, decreased mitochondrial content, changed mitochondrial morphology and impaired mitochondrial function. In contrast, a miR-34a inhibitor significantly restored the TAG content and mitochondrial transmembrane potential. A study of transcriptional regulation revealed that C/EBPβ is essential for upregulating miR-34a by resistin. Furthermore, miR-34a inhibited the PPARα signaling pathway by binding to sites in the 3'UTR of AdipoR2 genes and the AMPK pathway. Consequently, this increased the fat content and decreased the mitochondrial content in HepG2 cells. This paper reveals a novel mechanism for mitochondrial regulation, which suggests that normal mitochondrial content and function is crucial for lipid metabolism in the liver.

Keywords: miR-34a; mitochondria content; fat ectopic deposition; resistin; AdipoR2