Hepatic microRNAs in Type II Diabetes Pathogenesis

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Background/Objective:

Diabetes mellitus is a disease with increasing incidence worldwide affecting more than 435 million patients, most of whom have Type II diabetes (T2D). Of the many organs affected by T2D, the liver is responsible for much of the dysregulated metabolic pathways in response to insulin signaling. These include, but are not limited to gluconeogenesis, glycogen storage, fatty acid and cholesterol biosynthesis and transport, and fatty acid oxidation. Recent studies show significant differences in miRNA expression profiles between healthy and disease states of T2D. This implicates an important role of miRNAs in T2D pathogenesis and makes miRNAs an attractive therapeutic target and diagnostic marker for T2D patients. The aim of this review is to provide an overview of the hepatic miRNAs relevant to T2D pathogenesis.

Methods:

We compiled and reviewed articles from the PubMed database that were relevant to miRNAs and T2D pathogenesis in the liver.

Results:

We found that hepatic miRNAs affect most if not all dysregulated metabolic pathways in T2D pathogenesis, which we categorized into carbohydrate metabolism, lipid metabolism, and insulin signaling. The miRNAs that are most represented in our literature include miR-122, miR-33a/b, miR-29, and miR-21. These miRNAs target a variety of molecules, including transcription factors that are master regulators of metabolic pathways (FOXO1, HNF4α), lipid transporters (ABCA1, ABCG1), or key insulin signaling molecules (IRS1/2, caveolin-1). In addition, circulating miR-122 is associated with the risk of developing metabolic syndrome and T2D in the general population.

Conclusion and Potential Impact:

Multiple miRNAs are dysregulated in the liver of animal models of T2D. Administration of miRNA mimics or antagomirs to correct aberrant miRNA expression improved the pathophysiology *in vivo*. miRNAs are also promising tools as markers for disease development. Ultimately, the identification of miRNAs can guide future research to facilitate the diagnosis and improve the treatment of T2D.