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Review Article

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The Role of miR-181c in the Development of the tri-metabolic Disorders: Diabetes, Obesity and Aging

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Abstract

In the past decades, miRNAs were considered pivotal cellular rheostats that control many critical and fundamental signaling pathways. These small noncoding RNAs play a fundamental role in regulating gene expression, with accumulating evidence of the miRNAs ability to modulate diverse signaling pathways that once altered can lead to the development of many metabolic disorders. In addition, miRNAs were shown to have a crucial role in maintaining mitochondrial homeostasis and inflammatory responses. Of the many studied miRNAs, the highly conserved miR-181 family, particularly miR-181c represents an interesting research area. In the current review, we will provide an overview of the tri-pathways miR-181c is involved in, its function, and its role in developing diabetes, obesity, impaired angiogenesis, and aging. Additionally, this review will provide key insights into the key markers miR-181c triggers or targets in these disease models. Finally, this review aims to provide a better understanding of the miR-181c family with the hope that it may open new therapeutic avenues for different metabolic conditions.

Keywords: MicroRNA, Diabetes, Ageing, Obesity, Metabolic Disorders

Introduction

MicroRNAs (miRNAs) are endogenous small non-coding RNAs (20–22 nucleotides in length); they are pivotal for cellular behavior as they regulate various fundamental biological pathways that maintain the developmental processes and homeostasis of mature tissues/organs; by regulating the gene expression. miRNAs usually down-regulate the expression of their target genes, through their imperfect binding to the seed regions of the target sequences often located in 3′-untranslated regions [1]. Depending on the recognition site, the binding of the miRNA-induced silencing complex to the cognate target can have different outcomes [2]. In the majority of cases, the binding is partially complementary to the target sites and leads to the repression of translation, whereas when it is fully complementary, it leads to the degradation of the target transcript [1, 3, 4]. In the vast majority of cases, miRNAs are grouped in families consisting of several members that only differ in few nucleotides outside the seed region. Subsequently, each family member is clustered in specific chromosomal regions that can be present in two or more copies [5]. Of the different miRNA families, lately the miR-181 [6] family has been drawing a lot of interest in the biomedical research. Intriguinely, it was revealed that miR-181 family modulates various important cellular events including cellular proliferation, mitochondrial function, autophagy, programmed cell death, and immune responses [7-12]. MiR-181 family consists of four different 5p mature forms: (i) miR-181a-5p; (ii)

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