



Therapeutic Significance of MicroRNAs in Cardiovascular Diseases

Ravinder Reddy Gaddam*

Cardiovascular Division, Department of Medicine, Abboud Cardiovascular Research Center, Carver College of Medicine, University of Iowa, Iowa City, USA

*Corresponding author: Ravinder Reddy G, Cardiovascular Division, Department of Medicine, Abboud Cardiovascular Research Center, Carver College of Medicine, University of Iowa, IA City, IA, 52242, USA, Tel: +13194715767; E-mail: ravinderreddy-gaddam@uiowa.edu

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Editorial

Cardiovascular Diseases (CVDs) are the most common cause of morbidity and mortality in humans despite significant therapeutic improvements in the past few decades. Although classical pharmacological treatment strategies have improved cardiovascular outcome and survival, the prognosis of affected individuals with CVDs remains poor. Cardiovascular diseases account for nearly 836,546 deaths per each year (one of every three deaths are associated with heart diseases) in the USA. The cost of CVDs to the United States health care system is estimated to be as high as \$329.7 billion (Heart Disease and Stroke Statistics 2018) [1]. This necessitates the current need for further understanding of underlying mechanisms and development of innovative effective therapies for heart diseases. Since CVDs are hard to cure, several investigations have focused on different mechanisms underlying CVD in order to manage the symptoms. MicroRNAs (miRNAs) have emerged as one of the most favorable molecular targets in this regard. MicroRNAs (miRNAs, miRs) are a family of novel small non-coding regulatory RNA molecules of approximately 20-23 nucleotides long capable of modulating many target genes either by repression or degradation of targeted mRNA sequences often located within 3' UTR regions (post-transcriptional gene silencing). They play an important role in the regulation of fundamental cellular mechanisms such as cell differentiation, proliferation, growth and apoptosis. Recent advances in research uncovered the importance and emerging roles of miRNAs in diverse aspects of cardiovascular diseases and found their way to clinic due to their pathological and therapeutic significance. The miRNA expression patterns change in various cardiovascular diseases including cardiac hypertrophy and heart failure suggests miRNAs critical role heart diseases. Recent animal studies have shown pathological and therapeutic significance of few miRNAs (miR-19b, miR-21, miR-29, miR-98, miR-133, miR-195, miR-199b, in different cardiovascular diseases [2-8]. Similarly, human studies in cardiovascular-diseased patients showed altered (upregulated and downregulated) circulatory microRNA expression which may serve as biomarkers and function as mediators of disease [9]. Circulatory miRNAs are newly identified miRNAs which serve as strong molecular biomarkers for detection of myocardial hypertrophy, infarction, angiogenesis and fibrosis [9-11]. Therefore, development of therapeutic strategies based on miRNA modulation will benefit from cardiac diseases. Easy manipulation, high intracellular stability and ability to influence whole cellular processes make miRNAs as excellent therapeutic targets for cardiovascular diseases. Antagomirs or antimirs (miRNA silencing oligonucleotides) and miRNA mimics (double stranded miRNA-like RNA fragments) are a new form of miRNA-based drugs which act through miRNA silencing and enrichment, respectively, and counteract altered gene expression and impaired function in cardiac diseases. One of the first

studies that used an antagomir against miR-133, which is involved in cardiac hypertrophy, was performed by Care and coworkers [5]. This group implanted the cholesterol based miR-133 antagomir osmotic pumps subcutaneously in mice and showed marked increase in cardiac hypertrophy suggests therapeutic relevance of miR-133. Similarly, other studies based on antagomirs or miRNA mimics (of miR-21, miR-29, miR-99 and miR-199) revealed their pathological relevance and therapeutic implication in cardiac remodeling, such as cardiac hypertrophy, heart failure and fibrosis [2,3,7].

In conclusion, transforming miRNA targets into useful therapeutics is extremely exciting propositions that will continue stretching the limits of current technology in the cardiology field.

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