

10. Circulating MicroRNA-423-5p Attenuates the Phosphorylation of Calcium Handling Proteins in Atrial Fibrillation

Hyewon Park, Hyelim Park, Bo Kyung Jeon, Yeji Kim, Junbeom Park, Ewha Womans University College of Medicine, Seoul, Republic of Korea

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Background: MicroRNAs (miRNAs) are small non-coding RNAs that control patterns of gene expression by inducing the degradation of mRNAs. In addition, miRNAs are known to play an important role in the pathogenesis of atrial fibrillation (AF). In general, AF is diagnosed using electrocardiography. This study investigated whether specific miRNAs derived from microarray analysis of human urine could regulate AF through the inhibition of calcium handling protein phosphorylation in an AF model.

Methods: Microarray analysis of the transcriptome in the human urine of PSVT and AF patients revealed that 7 differentially expressed miRNAs were significantly downregulated (miR-3613, 6763, 423, 3162, 1180, 6511, 3197) in AF patients.

Results: Real-time PCR results showed that collagen I, collagen III, fibronectin, TGF- β , which are fibrosis-related genes, were significantly upregulated in AF patients. Moreover, fibrosis-related genes were upregulated in angiotensin II-induced atrial myocytes, which demonstrated that these genes may be targets of miR-423. In the AF cell model transfected with miR-423, the expression of calcium handling proteins including phosphorylated CaMKII was reduced. The transfection of miR-423 attenuated damage to cardiac cells caused by calcium handling proteins.

Conclusion: The findings highlight the importance of calcium handling protein phosphorylation changes in fibrosis-induced AF and support miR-423 detection in human urine as a potential novel approach of AF diagnosis.

Clinical Implications: My study will help enable cardiovascular clinicians to play an important role in the pathogenesis of AF.