**MICRORNA-328 CONTRIBUTES TO ADVERSE REMODELING IN ATRIAL FIBRILLATION**

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Background: Atrial electric remodeling and fibrosis are the key characteristics of atrial fibrillation (AF). The possibility that microRNAs (miRNAs) may be involved in atrial electric remodeling and fibrosis has not been tested.

Methods and Results: The miRNA transcriptome was analyzed by microarray and verified by real-time reverse-transcription polymerase chain reaction with left atrial samples from dogs with AF established by right atrial tachypacing for 8 weeks and from human atrial samples from AF patients. miR-328 level was elevated in AF dogs and AF patients relative to non-AF subjects. Forced expression of miR-328 through adenovirus infection in canine atrium and transgenic approach in mice recapitulated the phenotypes of AF, exemplified by enhanced AF vulnerability, diminished L-type Ca(2+) current, and shortened atrial action potential duration. Normalization of miR-328 level with antagomiR reversed the conditions, and genetic knockdown of endogenous miR-328 dampened AF vulnerability. CACNA1C and CACNB1 as the cognate target genes for miR-328 were confirmed by Western blot and luciferase activity assay. On the other hand, forced expression of miR-328 resulted in collagen secretion in cultured cardiac fibroblasts, which was abolished upon depletion of miR-328 by its antisense. We then established TGFBRIII as a direct target for miR-328.

Conclusions: miR-328 contributes to the adverse atrial electric remodeling and fibrosis in AF through targeting L-type Ca(2+) channel genes and TGFBRIII. The study uncovers a novel molecular mechanism for AF and indicates miR-328 as a potential therapeutic target for AF.