INCREASED EXPRESSION OF HCN CHANNELS AND ENHANCED IF CURRENT IN THE ATRIAL MYOCARDIUM CONTRIBUTES TO ATRIAL FIBRILLATION TRIGGER IN TRANSGENIC ATRIAL FIBRILLATION MICE

Poster Contributions
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Background: Over the last 20 years, much attention has focused on If in nonpacemaker cells and its potential role in triggering atrial and ventricular arrhythmias in both patients and various experimental animal models. But little is known regarding the If current underlying the pathogenesis of atrial fibrillation (AF). Thus, we aimed to investigate the If current and the HCN channels on the pathogenesis of AF.

Methods and Results: We firstly investigated the If current and the HCN channels expression between the wild-type (WT) mice and the transgenic mice (p(RR)-TG) overexpressing heart-specific (pro) renin receptor, a useful mouse model of AF, and then examined the effects of ivabradine, a specific HCN channel blocker, on the If current and HCN channels expression, and the prevention of AF episode. Compared with WT mice, the enhanced If current density and the faster activation kinetic, as well as the HCN4 protein were significantly increased in atrial myocytes from TG mice. After treatment with ivabradine (7 mg/kg per day orally) for 4 months, it partially reverses the electrophysiological remodeling occurring in TG mice, and If density was reduced in the atrial myocytes. The effects of ivabradine on electrophysiological remodeling were accompanied by a downregulation in overexpression of HCN2 and HCN4 protein in atrium tissue. Furthermore, we found that ivabradine significantly reduce the incidence of AF among TG mice, most likely by suppressing an increase in automaticity.

Conclusion: Our findings provide the first evidence that increased expression of HCN channels contributes to the increased arrhythmicity seen in atrial arrhythmia in vivo, and suggest that HCN channel blockade may represent a new and effective means of preventing AF.

Key Words: atrial fibrillation, transgenic mouse, funny current, ivabradine, HCN channels