C1q/TNF-Related Protein-9 ameliorates atrial inflammation, fibrosis and vulnerability to atrial fibrillation in post-MI rats

Introduction: Inflammation and fibrosis play an important role in the pathogenesis of atrial fibrillation (AF) after myocardial infarction (MI). C1q/TNF-related rotein-9 (CTRP9) as a secreted glycoprotein can reverse left ventricle (LV) remodeling post-MI, but its effects on MI-induced atrial inflammation, fibrosis, and associated AF are unknown.

Methods: MI model rats received adenoviral supplementation of CTRP9 (Ad-CTRP9) by jugular-vein injection. The cardiac function, inflammatory, and fibrotic indexes and related signaling pathways, electrophysiological properties, and AF inducibility of atria in vivo and ex vivo were detected in 3 or 7 days after MI. shCTRP9 and shRNA were injected into rat and performed similar detection at day 5 or 10. Adverse atrial inflammation and fibrosis, cardiac dysfunction were induced in both MI and Ad-GFP+MI rats.

Result: Systemic CTRP9 treatment improved cardiac dysfunction post-MI. CTRP9 markedly ameliorated macrophage infiltration and attenuated the inflammatory responses by downregulating interleukin (IL)-1β and IL-6, and upregulating IL-10, in 3 days post-MI; depressed left atrial fibrosis; and decreased the expressions of collagen types I and III, α-SMA, and TGF-β1 in 7 days post-MI through depressing the TLR4/NF-κB and Smad2/3 signaling pathways. Electrophysiologic recordings showed that the increased incidence and duration of AF inducibility and prolongation of interatrial conduction time (IACT) induced by MI were attenuated by CTRP9; moreover, CTRP9 was negatively correlated with IL-1β and AF duration. Downregulation of CTRP9 aggravated atrial inflammation, fibrosis and susceptibility of AF, and prolonged IACT, without affecting cardiac function.

Conclusion: CTRP9 is effective at attenuating atrial inflammation and fibrosis, and may be an original upstream therapy for AF in early phase of MI, possibly via its inhibitory effects on the TLR4/NF-κB and Smad2/3 signalling pathways.