**Arrhythmias and Clinical EP**

**Alpha B-Crystallin Suppress Ventricular Arrhythmia by Increasing Conduction Velocity and Attenuating Oxidative Stress in Rat Autoimmune Myocarditis**

Poster Contributions
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**Background:** Myocarditis is a major cause of heart failure and arrhythmia. Despite a lack of direct evidence that inflammation causes ventricular arrhythmia, reversal of inflammation is considered a plausible therapy. This study evaluated whether a small heat shock protein, alpha B-crystallin (CryAB), could suppress arrhythmia in experimental autoimmune myocarditis (EAM) rats.

**Methods:** Porcine cardiac myosin (1 mg) was injected into footpads of adult Sprague-Dawley rats on day 1 and 8 (EAM, n=10). In 14 EAM rats, CryAB (1 mg/kg) with TAT-protein transduction domain (EAM+CryAB, n=8) or GFP (EAM+G, n=6) were injected via intraperitoneum for 2 weeks. Hearts were perfused, mapped optically to analyze action potential durations (APD), and restitution kinetics, and tested for VF vulnerability. The intracellular calcium concentration was measured in H2C9 rat cardiomyocyte with inflammation induced by TNF-alpha (10 ng/ml) treatment.

**Results:** In EAM groups, 4 (40%) rats died and had ventricular arrhythmia. However, no rat died and had arrhythmia in EAM+CryAB group (p=0.04). EAM hearts had slower conduction velocity (CV; P<0.01 versus control), steeper CV restitution kinetics, greater fibrosis, higher levels of transcripts for Cox2, iNOS, TNF-α, IL-6, HMGB1 (P<0.05 versus control). Programmed stimulation triggered VF in EAM (n=4/10) and EAM+GFP (n=2/6), but not in control (n=0/10) and EAM+CryAB (n=1/8; P<0.01). CryAB treatment reversed the transcripts for inflammation, flattened CV restitution kinetics, reduced APD at 90% recovery to baseline, increased CV (P<0.01), and reversed ventricular enlargement of EAM (P<0.05). While the intracellular calcium concentration was increased in H2C9 cells with inflammation (P<0.01 versus control), it was decreased after CryAB treatment.

**Conclusions:** CryAB treatment suppressed ventricular arrhythmia in EAM hearts by increasing CV and preventing intracellular calcium overloading from a combination of reversal of inflammation and hypertrophy and by attenuating oxidative stress. This study provides compelling evidence that CryAB may provide a novel therapy to manage myocarditis in human by reversing inflammation and oxidative stress.