Acute Coronary Syndromes

SELECTIVE INHIBITION OF THE MASTER REGULATOR TRANSCRIPTION FACTOR EGR-1 USING CATALYTIC OLIGONUCLEOTIDES REDUCES MYOCARDIAL INJURY AND IMPROVES LV SYSTOLIC FUNCTION IN A PRECLINICAL MODEL OF MYOCARDIAL INFARCTION

Poster Contributions
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Background: Egr-1 is implicated in the pathogenesis of myocardial ischemia reperfusion (I/R) injury. The aim of this study was to ascertain the effectiveness of the delivery of DNAzyme specifically targeted against Egr-1 transcription at reperfusion following myocardial ischemia.

Methods: Pigs (30-40 kg) were subjected to balloon occlusion of the left anterior descending (LAD) coronary artery for 60 min, followed by reperfusion and recovery. Pigs received functional DNAzyme (DZF) targeting Egr-1 or a size-matched scrambled control (DZFSRc) via intracoronary delivery immediately upon reperfusion. At 48 h post-I/R, 3-T cardiac magnetic resonance imaging (MRI) was performed and comparative analysis of ejection fraction (EF) and percentage of salvaged heart tissue determined. Echocardiography was performed and left ventricular (LV) fractional area change (FAC) determined. Following the in vivo studies, hearts were excised and examined for molecular and histological markers of inflammation including ICAM-1, VCAM-1, tissue factor (TF), and apoptotic markers including p53, PTEN, and Complement 3.

Results: Delivery of DZF led to the significant decrease in the expression of the ICAM-1, VCAM-1, TF, p53, PTEN, and complement 3. Furthermore, within the DZF treated group there was a significant 29% increase in EF volume coupled with 40% increase in FAC and 82% increased LV salvage compared to the DZFSRc group.

Conclusions: Silencing of Egr-1 through the intracoronary delivery of DNAzymes immediately upon reperfusion following acute myocardial I/R injury decreases markers of inflammation and apoptosis within the heart tissue and subsequently reduces cardiac tissue damage and dysfunction following I/R injury.