**EXOGENOUS GDF11 PROTECTS AGAINST MYOCARDIAL ISCHEMIA-REPERFUSION INJURY VIA ATTENUATION OF TGF-** **β SIGNALING PATHWAY**

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Growth Differentiation Factor 11 (GDF11) is a member of TGF-β1 superfamily that reverses age-related cardiac hypertrophy, improve muscle regeneration and angiogenesis, and maintain the progenitor cells in injured tissue. Recently, overexpression GDF11 was found to reduce heart failure and enhance the proliferation of cardiac progenitor cells after myocardial ischemia-reperfusion (I-R) in aged mice. However, there is no study focusing on the cardioprotective effect of exogenous recombinant GDF11, which is convenient to apply in clinical therapeutics, in acute I-R injury. This study was designed to investigate whether application of recombinant GDF11 protect against acute myocardial I-R injury and analyze its underlying mechanism. GDF11 was administrated before the left anterior descending coronary artery (LAD) occlusion in rats. GDF11 reduced arrhythmia, myocardial infarction, increased the cardiac systolic function, suppressed the programmed cell death, inflammation, oxidative stress, and reduced the Wnt signaling, which might regulate cardiac fibrosis or remolding. GDF11 activated canonical pathway of TGF-β, however, the non-canonical pathway of TGF-β, ERK and JNK were inactivated. In addition, the activation of Smad2/3 signaling and cardioprotective effects of GDF11 were blockaded by pretreatment with follistatin (FST), the inhibitors of GDF11 and activin subfamily. These data suggested that exogenous GDF11 has cardioprotective effects and it reduced the detrimental effect of TGF-β signaling pathway in the acute stage of I-R injury. Exogenous recombinant GDF11 therapy has potential translatable into morphologic and functional recovery in early stage of myocardial I-R injury. Our study implicates the potential of GDF11 to be a therapeutic approach against myocardial I-R injury.