INOSITOL HEXAKISPHOSPHATE KINASES’ (IP6KS) SELECTIVE INHIBITION ENHANCES MESENCHYMAL STEM CELLS ENGRAFTMENT AND IMPROVES THERAPEUTIC EFFICACY FOR MYOCARDIAL INFARCTION

Poster Contributions
Poster Sessions, Expo North
Saturday, March 09, 2013, 10:00 a.m.-10:45 a.m.

Session Title: Acute Coronary Syndromes: Basic I
Abstract Category: 2. Acute Coronary Syndromes: Basic
Presentation Number: 1127-188

Authors: Feng Cao, Zheng Zhang, Dongdong Sun, Haichang Wang, Xijing Hospital, Xi an, People’s Republic of China

Background: Poor viability of engrafted stem cells hampers therapeutic efficacy for treatment of myocardial infarction (MI). This study is to investigate the role of Inositol phosphates 6 kinase (IP6Ks) for improving mesenchymal stem cells (MSCs) functional survival and cardiac protective effects after transplantation into infarcted mice hearts.

Methods: and results: Bone marrow derived MSCs, isolated from dual-reporter firefly luciferase and enhanced GFP positive (Fluc+ eGFP+) transgenic mice, were preconditioned with IP6Ks inhibitor TNP (0.5μmol/L, 1μmol/L, 5μmol/L, 10μmol/L) for 2 h followed by 6 h of hypoxia and serum deprivation (H/SD) injury. TNP at 10μM significantly decreased IP7 production with increased Akt phosphorylation. Moreover, TNP (10μM) improved the viability and enhanced the paracrine effect of MSCs after H/SD. Furthermore, MSCs were transplanted into infarcted hearts with or without selective IP6Ks inhibition. Longitudinal bioluminescence imaging and immuno-staining revealed that TNP pretreatment enhanced survival of engrafted MSCs, which overtly promoted the anti-apoptotic and pro-angiogenic efficacy of MSCs in vivo. Furthermore, MSCs therapy with IP6Ks inhibition significantly decreased fibrosis and preserved heart function.

Conclusion: Inhibition of IP6Ks promotes MSCs engraftment and paracrine effect in infarcted hearts by down-regulating IP7 production and enhancing Akt activation, which might attribute to preserved myocardial function after MI.