Multimodality Molecular Imaging Monitors Bone Marrow Mesenchymal Stem Cells for the Treatment of Ischemic Heart Disease in Rats

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OBJECTIVES The aim of this study was to explore multimodality molecular imaging to monitor transplanted stem cells with a triple-fused reporter gene in acute myocardial infarction rat models.

METHODS Rat myocardial infarction was established by ligating the left anterior descending coronary artery. A recombinant adenovirus carrying TGF (Ad5-TGF) was constructed. After transfection with Ad5-TGF, 5 × 10^6 bone marrow mesenchymal stem cells (BMSCs) were transplanted into the anterior wall of the left ventricle (n = 14). Untransfected BMSCs were as controls (n = 8). MicroPET/CT, fluorescence and bioluminescence imaging were performed. Continuous images were obtained at day 2, 3 and 7 after transplantation with all three imaging modalities and additional images were performed with bioluminescence imaging until day 15 after transplantation.

RESULTS High signals in the heart area were observed using microPET/CT, fluorescence and bioluminescence imaging of infarcted rats injected with Ad5-TGF-transfected BMSCs, whereas no signals were observed in controls. Semi-quantitative analysis showed the gradual decrease of signals in all three imaging modalities with time. Immunohistochemistry assays confirmed the location of the TGF protein expression was the same as the site of stem cell-specific marker expression, suggesting that TGF tracked the stem cells in situ.

CONCLUSIONS TGF could be used as a reporter gene to monitor stem cells in a myocardial infarction model by multimodality molecular imaging.

GW26-e1336 Myocardial Protection by MiR-126 Against Ischemia/Reperfusion Injury Through Suppression of GSK-3β

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OBJECTIVES MiR-126 is considered to play an active role in cardioprotection against ischemia/reperfusion (I/R) injury, as studies suggest that it facilitates vascular regeneration and ameliorates myocardial I/R injury by modulating angiogenic signaling. In this study, the critical role of miR-126 in cardiomyocyte survival and the underlying molecular mechanism were investigated.

METHODS Male Wistar rats were randomly divided into sham operation group and I/R group (in which the left anterior descending coronary artery of the rats were ligated for 30 min and then reperfused for 120 min). Lentivirus expressing miR-126 (LmiR-126) was constructed and transfected into rat through the right common carotid artery. Western blotting and quantitative PCR methods were applied to detect protein and mRNA expressions. Myocardial apoptosis and infarct size were analyzed by in situ apoptosis assay and triphenyltetrazolium chloride (TTC) staining, respectively.

RESULTS Our study demonstrated that the expression of miR-126 was decreased in I/R group compared with sham operation group (p < 0.01). Stretch or enforced expression of miR-126 significantly decreased I/R-induced myocardial infarct size by 42% and attenuated I/R-induced myocardial apoptosis, together with down-regulation of glycogen synthase kinase 3 beta (GSK-3β) (p < 0.05). The results of luciferase assays suggested that GSK-3β may be a direct target of miR-126. Knockdown of GSK-3β inhibited cell apoptosis and afforded cardioprotection during I/R injury, while its overexpression abolished the effects of miR-126. In addition, miR-126 increased both protein and mRNA levels of β-catenin, which is the downstream effector of GSK-3β in Wnt/β-catenin signaling pathway, and subsequently elevated the expressions of β-catenin targets cyclin D1 and c-Myc.

CONCLUSIONS These findings illustrated that miR-126 played an important role in cardioprotection against I/R injury through targeting GSK-3β and subsequently activating Wnt/β-catenin signaling pathway.

GW26-e1435 Tanshinone IIA Reduces Atrial Fibrillation by Inhibiting Left Atrial Fibrosis Via MMP-9 / TIMP-1 Pathway in Isoproterenol-Induced Myocardial Infarction Rats

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OBJECTIVES Atrial fibrillation is a major contributing factor of atrial fibrillation (AF). Tanshinone IIA (TSN) is a lipophilic diterpene extracted from the Chinese herb Salvia miltiorrhiza Bunge with anti-fibrotic effect. We used isoproterenol-induced myocardial infarction (MI) rats together with transesophageal programmed electrical stimulation AF inducing technology to investigate the effects of TSN on AF and the underlying mechanisms.

METHODS MI rat model was induced by isoproterenol. One week after the first injection, 100 mg/Kg/d TSN was gavaged for 4 weeks. AF inducibility and duration were detected by transesophageal programmed electrical stimulation AF inducing technology. The expression of I and III collagen and the change of MMP-9/TIMP-1 balance in left atrial were measured by western blot.

RESULTS After 2 hours of injection isoproterenol, the ST segment elevated and serum CK-MB levels increased. Four weeks after the administration of TSN, the AF inducibility was lower than the MI group (47.1% in TSN vs. 70.6% in MI) and the AF duration was reduced (58.1±25.7s in TSN vs. 441.5±737.5s in MI, P < 0.05). Type I (0.95±0.94% in TSN vs. 1.69±0.14% in MI, P < 0.05) and III (1.45±0.20% in TSN vs. 3.19±0.36% in MI, P < 0.05) collagen in left atrium were decreased in administration group, compared with MI group. The matrix metalloproteinase (MMP)-9 and tissue inhibitor of metalloproteinase 1 (TIMP-1) protein levels were lower than MI group, MMP-9/TIMP-1 ratio (0.20 in TSN vs. 0.27 in MI) decreased.

CONCLUSIONS TSN reduces the inducibility rate and duration of AF after MI by inhibiting left atrial fibrosis via regulating MMP-9/TIMP-1 balance.

GW26-e1522 Effect of EGB 761 on the Cardiac Fibrosis in a Rat Model of Myocardial Infarction

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OBJECTIVES Cardiac fibrosis is a common feature of advanced coronary heart disease and is also a hallmark of heart diseases.