GW28-e0375

Rosuvastatin improves CRP-induced reendothelialization of late endothelial progenitor cells by repairing RAGE/ eNOS signaling pathway

Junlin Zhong,[1] Jinlai Liu,[2] Hui Zhang,[1] Yanling Zhang,[1] Suhua Li[2]
[1]Department of Ultrasonography, the Third Affiliated Hospital, Sun Yat-sen University; [2]Department of Cardiology, the Third Affiliated Hospital, Sun Yat-sen University

OBJECTIVES To investigate whether rosuvastatin improve reendothelialization of late endothelial progenitor cells (EPCs) induced by C reactive protein (CRP) through the advanced glycation end products (RAGE)/eNOS signaling pathway.

METHODS 1.Human late EPCs were treated with CRP of different concentrations (0, 10, 25, 50ug/mL) to explore the CRP-induced RAGE/ eNOS signaling pathway. 2.EPCs were pre-incubated with rosuvastatin of different concentrations (0, 10-8M, 10-7M, 10-6M) and then stimulated with 50ug/mL CRP, with EPCs incubated with 50ug/mL CRP as positive control. The mRNA levels of eNOS for EPCs were measured by quantitative PCR. NO secretions were detected by NO nitrate reductive enzymatic. RAGE protein expressions were checked by western blotting. MTT assay was used to test Proliferation of EPCs, transwell assay for migration, and adhesiveness assay for adhesion.

RESULTS 1.When EPCs were incubated with CRP at different dosages, the expression of eNOS mRNA and NO secretions dropped gradually compared with normal control ($P < 0.05$). In contrast, RAGE protein expressions increased in a dose-dependent manner ($P < 0.05$). 2. The RAGE proteins expressions in positive control raised to 121%±4% ($P < 0.01$) when compared with normal control. After pre-incubated with increasing concentrations of rosuvastatin, RAGE proteins expressions declined gradually to 115%±10%, 110%±10% and 87%±4% ($P < 0.01$). The eNOS mRNA level in positive control declined to 44%±19% when compared with normal control, and raised to 58%±13%, 82%±32% and 203%±52% ($P < 0.01$) with increasing concentration of rosuvastatin. Similarly, NO secretions in positive control significantly declined compared with normal control, and up-regulated gradually in a dose-dependent manner when treated with rosuvastatin. Simultaneously, the migration and adhesion of CRP-induced EPCs were up-regulated along with increasing concentration of rosuvastatin. However, the proliferation of EPCs had no changes.

CONCLUSIONS CRP could influence expressions of eNOS/NO though signaling pathway mediated by RAGE. Rosuvastatin improves EPCs' reendothelialization induced by CRP though restraining RAGE.

GW28-e0383

Low-level laser therapy to the bone marrow reduces scarring and improves heart function post-acute myocardial infarction in pigs

Jie Qin,[1] Chuangfeng Li,[1] Lingrong Peng,[1] Wenjie Tang[1]
[1]Department of Radiology, the Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES The aim of the present study was to determine whether low-level laser therapy (LLLT) application to stem cells in the bone marrow (BM) could affect the infarcted porcine heart and reduce scarring following myocardial infarction (MI).

METHODS MI was induced in farm pigs by percutaneous balloon inflation in the left coronary artery for 90 min. Laser was applied to the tibia and iliac bones 30 min, and 2 and 7 days post-induction of MI. Pigs were euthanized 90 days post-MI. The extent of scarring was analyzed by histology and MRI, and heart function was analyzed by echocardiography.

RESULTS The number of c-kit+ cells (stem cells) in the circulating blood of the laser-treated (LT) pigs was 2.62- and 2.4-fold higher than in the non-laser-treated (NLT) pigs 24 and 48 h post-MI, respectively. The infarct size [% of scar tissue out of the left ventricle (LV) volume as measured from histology] in the LT pigs was 3.2 ± 0.82%, significantly lower, 68% ($p < 0.05$), than that (16.6 ± 3.7%) in the NLT pigs. The mean density of small blood vessels in the infarcted area was significantly higher [6.5-fold ($p < 0.025$)], in the LT pigs than in the NLT ones. Echocardiography (ECHO) analysis for heart function revealed the left ventricular ejection fraction in the LT pigs to be significantly higher than in the NLT ones.

CONCLUSIONS LLLT application to BM in the porcine model for MI caused a significant reduction in scarring, enhanced angiogenesis and functional improvement both in the acute and long term phase post-MI.

GW28-e0384

MR targeted imaging for the expression of tenascin-C in myocardial infarction in vivo

Jie Qin,[1] Chuangfeng Li,[1] Lingrong Peng,[1] Wenjie Tang[1]
[1]Department of Radiology, the Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES To investigate the presence of viable myocardium in mice with acute myocardial infarction (MI) using a molecular targeted probe.

METHODS Super paramagnetic iron oxide (SPIO) nanoparticles and tenascin-C antibody were conjugated as an MRI probe. Fifteen mice with infarction were injected with SPIO-anti-tenascin-C (3 days [d], 5d, 7d after infarction; $n = 5$ for each group). Another five mice with infarction (5d, $n = 5$) were injected with SPIO for comparison. In vivo MR (7 Tesla, fast low-angle shot multi-slice T2* sequence) was performed for tracing. Histological analysis was used to compare surviving cardiomyocytes with signal changes on MR.

RESULTS The mRNA expression of tenascin-C increased directly after MI and peaked at the fifth day (5d 24.29 ± 1.41 versus 3d 10.63 ± 0.72, 7d 6.56 ± 0.12; $P < 0.01$). T_2 relaxation rate of synthesized SPIO-anti-tenascin-C was $r2 = 338\ mM^{-1}\ s^{-1}$. After MR, the signal changes (contrast-to-noise ratio) of the research group were 3d 6.51 ± 1.13 versus 5d 14.06 ± 3.19 versus 7d 5.02 ± 2.65, $P < 0.05$. The MR signal showed a small decrease in the contrast group on 5d (research group 14.06 ± 3.19 versus contrast group 1.75 ± 0.59, $P < 0.05$).

CONCLUSIONS Tenascin-C was expressed by surviving cardiomyocytes within the infarcted region. MR imaging with SPIO-anti-tenascin-C might be used to evaluate myocardial viability of MI patients before therapy.

GW28-e0385

Multimodal imaging for in vivo evaluation of induced pluripotent stem cells in a murine model of heart failure

Jie Qin,[1] Chuangfeng Li,[1] Lingrong Peng,[1] Wenjie Tang[1]
[1]Department of Radiology, the Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES To assess viability and cardiac retention of induced pluripotent stem cells after intramyocardial delivery using in vivo bioluminescence analysis (BLI) and magnetic resonance imaging (MRI).

METHODS Murine induced pluripotent stem cells (iPSCs) were transfected for luciferase reporter gene expression and labeled intracellularly with supraparamagnetic iron oxide particles. 5×10^5 cells were transplanted intramyocardially following left anterior descending coronary artery ligation in mice. Cardiac iPSCs were detected using BLI and serial T2* sequences by MRI in a 14-day follow-up. Additionally, infarct extension and left ventricular (LV) function were assessed by MRI. Controls received the same surgical procedure without cell injection.

RESULTS MRI sequences showed a strong MRI signal of labeled iPSCs correlating with myocardial late enhancement, demonstrating engraftment in the infarcted area. Mean iPSC volumes were 4.2 ± 0.4 mm^3 at Day 0; 3.1 ± 0.4 mm^3 at Day 7; and 5.1 ± 0.8 mm^3 after 2 weeks. Thoracic BLI radiance decreased directly after injection from 1.0×10^6 $\pm 4.2 \times 10^4$ (p/s/cm^2 /sr) to 1.0×10^5 $\pm 4.9 \times 10^3$ (p/s/cm^2 /sr) on Day 1. Afterward, BLI radiance increased to 1.1×10^6 $\pm 4.2 \times 10^4$ (p/s/cm^2 /sr) 2 weeks after injection. Cardiac graft localization was confirmed by ex vivo BLI analysis and histology. Left ventricular ejection fraction was higher in the iPSC group (30.9 ± 0.9%) compared to infarct controls (24.0 ± 2.1%; $P < 0.05$).

CONCLUSIONS The combination of MRI and BLI assesses stem cell fate in vivo, enabling cardiac graft localization with evaluation of LV function in myocardial infarction.

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Prediction of infarct transmurality from C-reactive protein level and mean platelet volume in patients with ST-elevation myocardial infarction

Jie Qin,[1] Chuangfeng Li,[1] Lingrong Peng,[1] Wenjie Tang[1]
[1]Department of Radiology, the Third Affiliated Hospital of Sun Yat-sen University