**e0072 CARDIOPROTECTIVE EFFECT OF β3 ADRENORECEPTOR AGONISM IN PRESSURE OVERLOAD INDUCED HYPERTROPHY**

doi:10.1136/hrt.2010.208967.72

Niu Xiaolin, Zhang Qiangsun, Zhang Lihua, He Yong, Cingolani Oscar, Bedja Djahida, Kass David, Barouch Lil. Department of Cardiology, Tangdu Hospital, Fourth Military Medical University, Xian, China

**Objective** β3-adrenergic receptors (β3-AR) and its downstream signalling are recognised as novel modulators of heart function. We have recently shown impaired cardiac functional compensation in a model of pressure overload. We therefore hypothesised that the selective β3-AR agonist, BRL37344 (BRL), would protect the heart from pressure overload induced cardiac remodelling.

**Methods and results** C57BL/6J mice underwent transverse aortic constriction (TAC) for 3 weeks, resulting in increased cardiac hypertrophy and dysfunction assessed by echocardiography. 3 weeks of BRL treatment (0.1 mg/kg/day via subcutaneous osmotic infusion pump) starting from 1 day post TAC reduced hypertrophy, with lower heart weight normalised to tibia length (100±4 vs 120±7 g/cm), LV mass (156±7 vs 165±5 g), wall thickness (1.08±0.02 vs 1.16±0.02 mm) and systolic dimension (1.56±0.09 vs 1.28±0.03 mm; p<0.05 for both) and completely restored systolic function back to normal (58±2 vs 62±1%; p=NS vs sham, p<0.05 vs TAC). BRL reduced myocyte width by H&E staining, but had no effect on fibrosis scale. These benefits from β3-AR stimulation were associated with increased nitric oxide (NO) production (13.73±1.84 vs 5.05±0.52 μM/mg protein) and suppressed superoxide generation (14017±583 vs 21459±783 CPM/mg tissue; p<0.01 vs TAC for both). Neuronal NO synthase (nNOS) protein expression was up-regulated ~3 fold by BRL treatment (1.11±0.22 vs 0.39±0.17; p<0.05). More interestingly, the suppressive effect of BRL on superoxide generation was abolished by acute nNOS inhibition by specific nNOS inhibitor N5-(1-imino-3-butanyl)-L-ornithine, monohydrochloride (L-NVNO).

**Conclusions** These results are the first to show in vivo the cardio-protective effect of β3-AR specific agonism in pressure overload hypertrophy and heart failure, and support nNOS as a downstream molecule favouring NO and reactive oxygen species (ROS) balance in this pathologic process in the failing heart.

**Corresponding author** Niu Xiaolin, Department of Cardiology, Tangdu Hospital, Fourth Military Medical University, Xian, China

---

**e0073 EFFECT OF BONE MARROW MESENCHYAL STEM CELLS TRANSPLANTATION ON EXPRESSION OF NFB AND PCNA AND VASCULAR STENOSIS AFTER CAROTID ARTERY BALLOON INJURY OF RABBIT**

doi:10.1136/hrt.2010.208967.73

Zhi-jiang Liu, Bei Shi, Guan-xue Xu, Ran-zun Zhao, Chang-yin Shen, Dong-mei Wang. The First Affiliated Hospital of Zunyi Medical College

**Objective** To investigate effect of bone marrow mesenchymal stem cells transplantation on expression of nuclear factor kB (NF-kB) and proliferating cell nuclear antigen (PCNA) and vascular stenosis after carotid artery balloon injury of rabbit.

**Methods** 36 carotid artery atherosclerotic stenosis rabbits were randomly divided into the control group (balloon injury+PBS solution) and the MSCs transplantation group (balloon injury +MSCs transplantation). MSCs (5×10^7/ml) were pre-labelled by DAPI and then infused into MSCs transplantation group rabbits by the ear vein, and control group was infused with the same amount of PBS solution. 1 week after MSCs transplantation, DAPI labelled cells were detected under immunofluorescence microscope; The plasma tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6) levels were detected with ELISA on the 1st, 2nd and 4th week after MSCs transplantation. After 2 weeks and 4 weeks, the injured vessels were stained by HE and the immunohistochemical analysis of NF-kB and PCNA.

**Results** The DAPI-labelled MSCs could be detected on impaired intima 1 week after MSCs transplantation. NF-kB and PCNA expression was not seen in the normal blood vessels after 2 weeks, the expression of NF-kB and PCNA in MSCs transplantation group decreased significantly compared with control group. The plasma TNF-α and IL-6 levels in MSCs transplantation group were significantly lower than those in control group. The intimal area, the ratio of the intima/media area and the luminal stenosis ratio were significantly lower in MSCs transplantation group than control group at 4 weeks.

**Conclusions** MSCs are capable of decreasing the inflammatory reaction of injured vessels and lighten the restenosis of injured vessels.

---

**e0074 EFFECTS OF TRANSPLANTATION OF PERIPHERAL BLOOD MESENCHYAL STEM CELLS WITH HYPOXIA PRECONDITIONING ON POSTANGIOPLASTY RESTENOSIS IN RABBITS**

doi:10.1136/hrt.2010.208967.74

Bei Shi, Yan Guo, Zhang-long Wang, Dong-mei Wang, Chang-yin Shen. The First Affiliated Hospital of Zunyi Medical College

**Objective** To investigate the function and the mechanism of transplanting bone marrow derived peripheral blood mesenchymal stem cells (PBMSCs) on restenosis after carotid balloon angioplasty in the model of carotid atherosclerosis rabbits and to determine if the functions of PBMSCs are enhanced after hypoxia preconditioning.

**Methods** Bone marrow cells were mobilised by granulocyte colony-stimulating factor (G-CSF), and PBMSCs were connected through density gradient centrifugation and adherent culture, labelled with enhancement type green fluorescent protein (EGFP) genes. All animals with carotid atherosclerosis stenosis were randomly divided into three groups: hypoxia preconditioning group (n=24, received intravenous transplantation of PBMSCs with hypoxia preconditioning), non-hypoxia preconditioning group (n=24, received normal culture of PBMSCs) and control group (n=24, only received equal-volume of culture medium). Vascular endothelial growth factor (VEGF) was determined by enzyme linked immunosorbent assay (ELISA) at 7 d, 14 d and 28 d post-angioplasty, respectively. The vessel morphology, the homing of MSCs and the reendothelialization were analysed with Weigert staining and immunohistochemistry.

**Results** Compared to control group, the level of VEGF significantly increased in both hypoxia preconditioning group and nonhypoxia preconditioning group at all time points (p<0.01). The level of VEGF in hypoxia preconditioning group was higher than that in nonhypoxia preconditioning group (p<0.05) at 7 d and 14 d, but no difference at 28 d postangioplasty was observed. At 7 d, GFP-positive cells were found in both hypoxia preconditioning group and nonhypoxia preconditioning group. Neointima thickening and the rate of restenosis were lower in hypoxia preconditioning group than those in non-hypoxia preconditioning group at 28 d (p<0.05), but both hypoxia preconditioning group and nonhypoxia preconditioning group were markedly lower than that in control group (p<0.01). The reendothelialization in hypoxia preconditioning group outweighed that in nonhypoxia preconditioning group (p<0.05), but both two groups were lower than that in control group (p<0.01).

**Conclusions** Intravenous transplantation of PBMSCs contributes to the reendothelialization, and attenuates neointima thickening after carotid balloon induced injury in the rabbit model. Further, hypoxia...
preconditioning may strengthen the above function of MSCs, which is correlated with the increase in cytokines induced by hypoxia preconditioning to MSCs.

**e0075** EVALUATION THE ROLE OF PRENATAL CHRONIC HYPOXIA ON CARDIAC FUNCTION IN ADULT RABBITS OFFSPRING USING ECHOCARDIOGRAPHY

doi:10.1136/hrt.2010.208967.75

Ziyang Huang, Yang Jingyang, Wang Zhenhua. The Second Affiliated Hospital of Fujian Medical University

**Objective** To evaluate the role of prenatal chronic hypoxia on cardiac function in adult rabbits offspring via echocardiography.

**Methods** 16 New Zealand rabbits were divided randomly into two groups: prenatal chronic hypoxia group (12% O₂, n=8) and normal oxygen group (21% O₂, n=8). After delivery, two male offspring of each maternal rabbit were selected and breast-fed for 3 months. Then they were randomly divided into high-fat diet and normal diet respectively. Therefore, four groups were included: Prenatal Chronic Hypoxia with High Fat Diet (n=8), Non-Prenatal Chronic Hypoxia with High Fat Diet (n=8), Prenatal Chronic Hypoxia with Normal Diet (n=8) and Normal Control (n=8). At 6 months of age, the offspring rabbits were undergoing echocardiography examination for left ventricular (LV) dimensions, shortening fraction, ejection fraction and Tei index, and cardiocyte caspase-3 activity detection.

**Results** Prenatal chronic hypoxia induced a thickening of interventricular septum (main effect is 0.66 mm, p<0.01), decrease in ejection fraction of left ventricle (main effect is -4.84%, p<0.05), increase of Tei index (main effect is 0.08, p<0.01) and cardiocyte caspase-3 activity (main effect is 0.47 unit, p<0.05) in 6-month-old prenatal chronic hypoxia offspring. All these effects were aggravated significantly when hyperlipaemia was imposed (p<0.05).

**Conclusions** Echocardiography is a useful tool to evaluate the role of prenatal chronic hypoxia on cardiac function in adult rabbits offspring. Prenatal chronic hypoxia leads to cardiac dysfunction in adult rabbits offspring. This effect is aggravated by hyperlipidaemia.

**e0076** SCREENING OXIDATIVE STRESS ASSOCIATED GENES BY GENECHIP ON PERIPHERAL BLOOD MONONUCLEAR CELLS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

doi:10.1136/hrt.2010.208967.76

Ruan Hufen, Chen Zhibin, Tang Hao, Liang Yanbing. The First Affiliated Hospital of Sun Yat-sen University

**Objective** GeneChip is one of the low-throughput gene screening tools, which is quite suitable for detecting target genes associated with certain pathophysiologic process. Our team has applied such technique into the studying of oxidative stress during the Acute Myocardial Infarction (AMI) and the following ischaemia/reperfusion injury (IRI) after PCI.

**Methods** 11 patients with confirmed STEMI were admitted to our ER and CCU were involved into our study. 10 healthy volunteers with matching age and sex were set as the controlled group. Blood samples were collected immediately after the diagnosis and the same procedure was done on the 3rd and 7th day. Peripheral blood mononuclear cells (PBMCs) were extracted for RNA extraction. Human Stress & Toxicity Pathway Finder PCR Array was applied for corresponding gene screening. Real Time PCR was applied to confirm the candidate genes mRNA expression.

**Results** 12 genes were detected with significant changes in the PBMCs of STEMI patients. GADD45A (associated with cell growth/aging), PRDX2 (associated with oxidative stress), HSPD1, DNAJB1, DNAJB2 (associated with heat shock process), RAD50 (associated with DNA restoration), TNFSF6, TRADD (associated with apoptosis) displayed up-regulated expression. CCNG1 (associated with cell proliferation/cancer), CAT, CYP1A1 (associated with oxidative stress), ATM (associated with DNA restoration) were down-regulated. Further RT-PCR confirmed the previously findings.

**Conclusions** Sophisticated mechanism was involved during the pathophysiology of STEMI and the following IRI after PCI. Oxidative stress, heat shock reaction, cell restoration and apoptosis play an important role in the process of injury and repair.

**e0077** EFFECT OF PULSED ALTERNATING MICROCURRENTSTIMULATION ON COMMUNICATION JUNCTION FUNCTION OF COCULTURED RAT MESENCHYMAL STEM CELLS AND CARDIAC MUSCLE CELLS

doi:10.1136/hrt.2010.208967.77

Yao Qing, Yindai Jiajia, Ma Xiangang, Sun Wei, Wang Liting, Song Zhiyuan. Southwest Hospital

**Objective** This study was to investigate the effect of pulsed alternating micro-current (PAMC) stimulation on the communication junction function of co-cultured rat mesenchymal stem cells (MSCs) and cardiac muscle cells by simulating the physiological electrical environment for cardiac muscle cell growth.

**Methods** Healthy SD rat bone marrow was subjected to 5-azacytidine induced culture. MSCs not induced (IPAMC) and MSCs cultured for 7 (IIIPAMC), 14 (IIIIPAMC), and 28 days (IVPAMC) after induction were co-cultured with Hoescht33258 labelled cardiac muscle cells, and stimulated with PAMC. Morphological changes in the gap junction were observed, and the following parameters were determined in each group: intracellular Cx43 distribution and content, the function of intercellular junction communication, the intracellular free calcium concentration and CaMKII expression levels. The results were also compared with those of the group not treated with PAMC.

**Results** There was a number of typical gap junction structures in group IIIIPAMC. Compared to the groups not subjected to PAMC stimulation, group IIIIPAMC showed a greater increase in the Cx43 expression (78.59±6.72 vs 66.48±9.69, p<0.01), the highest fluorescence recovery rate after photobleaching in the co-culture cells (50.25%±4.08% vs 45.89%±3.94%, p<0.05), an increase in [Ca2+]i (101.21±11.56 vs 96.97±9.71, p<0.05), and a significant enhancement of the CaMKII expression (754.35±20.16 vs 596.32±13.45, p<0.01).

**Conclusions** Appropriate PAMC stimulation will effectively promote the formation of typical intercellular gap junction structures, increase and accelerate the synthesis of gap junction protein, and enhance the intercellular communication junction function.

**e0078** THE EFFECT OF ACUTE ATORVASTATIN ON CARDIOPROTECTION OF ISCHAEMIC POSTCONDITIONING IN DIABETES MELLITUS

doi:10.1136/hrt.2010.208967.78

Fan Ying, Yang Shunsen, Cao Yang, Ma Lei, Liu Shangjun, Huang Yanglin, Li Weimin. The First Affiliated Hospital of Haerbin Medical University

**Objective** This study was to investigate if the low dose of acute atorvastatin treatment could affect the cardioprotection of ischaemic post-conditioning (Ipost) in type 2 diabetes mellitus (T2DM) during ischaemia and reperfusion.

**Methods** Male Wistar rats and diabetic rats were randomly assigned to four groups: (1) nonconditioning group, (2) Ipost group, (3) acute atorvastatin—treated group (2 mg/kg/day atorvastatin for 3 days),...