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e0199 PERSIMMON PEEl IMPROVED DYSLIPIDEMIA AND ITS RELATED PRODUCTION OF ATHEROGENIC AUTOANTIGEN COMPLEXES IN LOW-DENSITY LIPOPROTEIN RECEPTOR-DEFICIENT MICE

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Objective Roles of persimmon peel were investigated on possibility of developing atherosclerosis in low-density lipoprotein receptor (LDLR)-deficient mice in view of lipid metabolism, physico-biological oxidation, production of its related atherogenic autoantigen, and anti-atherogenic natural antibody production.

Method Male LDLR-deficient mice fed a high fat diet or a high fat diet supplemented with 10% dried and powdered persimmon peel (PP) for 12 weeks.

Result The PP supplementation significantly reduced the increment of plasma cholesterol and triglyceride levels. The high fat diet feeding increased plasma level of oxidised LDL/2GPI) complexes as an atherogenic autoantigen, while the expression of calsarcin-1 and the activity of calcineurin-NFAT signalling pathway may be the most important mechanism involving in pathological cardiac hypertrophy in cTnIR146W /+- mice.

Conclusion cTnIR146W /+- mice had typical pathological cardiac remodelling and heart dysfunction, especially in the older ones. The expression of calsarcin-1 and the activity of calcineurin-NFAT signalling pathway may be the most important mechanism involving in pathological cardiac hypertrophy in cTnIR146W /+- mice.

e0200 EFFECTS OF MESENCHYMAL STEM CELLS ON MATRIX METALLOPROTEINASE SYNTHESIS OF CARDIAC FIBROBLASTS

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Objective Mesenchymal stem cell (MSC) transplantation has been known to decrease matrix metalloproteinase (MMP) synthesis in the myocardium after myocardial infarction (MI) and to improve ventricular remodelling. However, the underlying mechanisms behind MSC have not been clearly demonstrated yet. This study investigated the effects of MSCs through paracrine actions on the MMP synthesis of cardiac fibroblasts (CFs).

Method CFs were placed under hypoxia conditions for 24 h before co-culture with MSCs or hypoxia preconditioning MSCs (HP-MSCs) in transwell. CFs and MSCs/HP-MSCs shared the same medium, in which erythropoietin (EPO) antibody and EPO receptor (EPOR) were/were not added. Gelatin Zymography was used to detect the gelatinolytic activity of matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) in culture media of CFs with different conditions. Western-Blotting was used to assay MMP-2, MMP-9 and TIMP-1 synthesis of CFs. The ERK1/2 signalling pathway was also investigated.

Result Protein expression and activity of MMP-2 produced by CFs significantly increased by about 1.4-fold (p<0.01) through hypoxia and decreased after co-culture with MSCs or H-MSCs. This is not the case with MMP-9. Mediation of effects may involve phosphorylation of ERK1/2. Tissue inhibitors of metalloproteinases-1 (TIMP-1) had reverse effects on regulation of MMP-2. Either exogenous EPOAb or EPOSR partially inhibited MSCs effect on MMP-2 protein expression and activity by CFs.

Conclusion MSCs may influence MMP/TIMP expression by CFs via the ERK1/2 pathway and EPO may acts as a key factor in the paracrine actions of MSCs.

e0201 HEAT SHOCK PROTEIN 90 PROTECTS RAT MESENCHYMAL STEM CELLS AGAINST HYPOXIA AND SERUM DEPRIVATION-INDUCED APOPTOSIS VIA PI3KAK AND ERK12 PATHWAYS

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Objective Mesenchymal stem cells (MSCs) transplantation has been shown therapeutic potential to repair the ischaemic and infarcted myocardium, but the effects are limited by apoptosis and loss of donor cells in host cardiac microenvironment. The aim of this study is to explore the cytoprotection of Hsp90 against hypoxia and serum deprivation induced apoptosis and the possible mechanisms.

Method Cell viability was determined by 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide assay. Apoptosis was assessed by Hoechst 33258 nuclear staining and flow cytometric analysis with annexin V/PI staining. The gene expression of TLR4 and ErbB2 were detected by Western blot and RT-PCR. We also assessed the activity of calcineurin in cTnIR146W /+- mice, in order to elucidate potential mechanisms involving in the cardiac remodelling in cTnIR146W /+- mice.

Results The total expression of cTnI in cTnIR146W /+- mice was significantly higher than that of cTnIR146W /+- mice (p<0.01), while other cardiac hypertrophy-related signalling pathway protein, such as calcineurin, GSK-3β, AKT, SERCA2 did not change. The mRNA expression of PLB was reduced significantly by RT-PCR (p<0.05). Meanwhile, the calcineurin activity of cTnIR146W /+- mice increased significantly (p<0.01).

Conclusion cTnIR146W /+- mice had typical pathological cardiac remodelling and heart dysfunction, especially in the older ones. The expression of calsarcin-1 and the activity of calcineurin-NFAT signalling pathway may be the most important mechanism involving in pathological cardiac hypertrophy in cTnIR146W /+- mice.

elucidate the signalling pathway involving in heart remodelling of cTnIR146W /+- mice.

Methods Cardiac hypertrophy-related signalling pathway protein, such as calcineurin, calcin-1, GSK-3β, AKT, SERCA2, PLB were detected by Western blot and RT-PCR. We also assessed the activity of calcineurin in cTnIR146W /+- mice, in order to elucidate potential mechanisms involving in the cardiac remodelling in cTnIR146W /+- mice.

Results The total expression of cTnI in cTnIR146W /+- mice was significantly higher than that of cTnIR146W /+- mice (p<0.05), while the phosphorylation of cTnI decreased significantly (p<0.05), resulting in an obvious decrease of the ratio of phos-cTnI to cTnI (p<0.05). Pathological changes such as myocardial cell proliferation, cardiac hypertrophy, and interstitial fibrosis were observed by optical microscope in cTnIR146W /+- mice. Markers of cardiac hypertrophy, such as ANF, BNP, β-MHC increased significantly in cTnIR146W /+- mice (p<0.05). The expression of calcineurin-1 in cTnIR146W /+- mice was significantly higher than that of cTnIR146W /+- mice (p<0.01), while other cardiac hypertrophy-related signalling pathway protein, such as calcineurin, GSK-3β, AKT, SERCA2 did not change. The mRNA expression of PLB was reduced significantly by RT-PCR (p<0.05). Meanwhile, the calcineurin activity of cTnIR146W /+- mice increased significantly (p<0.01).

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