GWICC Abstracts 2010

E0200 EFFECTS OF MESENCHYMAL STEM CELLS ON MATRIX METALLOPROTEINASE SYNTHESIS OF CARDIAC FIBROBLASTS

doi:10.1136/hrt.2010.208967.200

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Objectives 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).

Methods CFs were placed under hypoxia conditions for 24 h before co-culture with MSCs or hypoxia pre-conditioning MSCs (HP-MSCs) in transwell. CFs and MSCs/HP-MSCs shared the same medium, in which erythropoietin (EPO) antibody and EPO receptor (EPO-R) 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.

Results 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.

Conclusions 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.

E0199 PERSIMMON PEEL IMPROVED DYSLIPIDEMIA AND ITS RELATED PRODUCTION OF AHEROGENIC AUTOANTIGEN COMPLEXES IN LOW-DENSITY LIPOPROTEIN RECEPTOR-DEFICIENT MICE

doi:10.1136/hrt.2010.208967.199

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

Method Male LDL-R-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/B2-glycoprotein I (oxLDL/B2GPI) complexes as an atherogenic autoantigen, and anti-atherogenic natural antibody production.

Conclusion Thus, these results demonstrate that persimmon peel may have an anti-atherogenic property through normalisation of lipid metabolism and may be able to reduce production of the atherogenic complexes.

HEAT SHOCK PROTEIN 90 PROTECTS RAT MESENCHYMAL STEM CELLS AGAINST HYPOXIA AND SERUM DEPRIVATION-INDUCED APOPTOSIS VIA PI3KAKT AND ERK12 PATHWAYS

doi:10.1136/hrt.2010.208967.201

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Objective Mesenchymal stem cells (MSCs) transplantation has 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.

Methods 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 was detected by real-time PCR. The protein levels of cleaved-caspase3, bcl-2, bcl-xl, bak, total-Erk, phospho-Erk, total-Akt, phospho-Akt and hsp90 were detected by western-blot. The production of nitric oxide was measured by spectrophotometric assay.

Results Hsp90 improves MSCs viability and protects MSCs against apoptosis induced by serum deprivation and hypoxia. The

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