

protective role of Hsp90 not only elevates bcl-2/bax and bcl-xL/bax expression but also decrease cleaved-caspase3 expression via down-regulating TLR-4 and ErbB2 membrane receptors. By binding to TLR-4 and ErbB2, Hsp90 activates the PI3K/Akt and ERK1/2 pathways. Hsp90 also down regulates the pro-apoptotic protein bax. It is demonstrated that exogenous Hsp90 elevates the expression levels of bcl-2/bax and bcl-xL/bax by activating the TLR-4 and ErbB2 downstream PI3K/Akt and ERK1/2 pathways, which decreases cleaved caspase-3.

Conclusion Hsp90 significantly protects MSCs against apoptosis induced by hypoxia and serum deprivation. These findings demonstrates a novel and effective treatment strategy against MSC apoptosis in cell transplantation.

e0202 EFFECTS OF RANOLAZINE ON ACTION POTENTIAL AND CONTRACTION FORCE IN GUINEA PIG PAPILLARY MUSCLES

doi:10.1136/hrt.2010.208967.202

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Objective To observe the effects of ranolazine on the action potential and contraction force in guinea pig papillary muscles. To explore the mechanism of ranolazine anti-arrhythmia and myocardial ischaemia.

Methods 18 healthy adult guinea-pigs were randomly divided into H₂O₂ (200 mmol/l) groups, ranolazine (10 mmol/l) +H₂O₂ groups and TTX (2 mmol/l) +H₂O₂ groups, with six guinea pigs in each group compared before and after administration to observe the effects of ranolazine on the papillary muscles.

Results H₂O₂ could increase action potential durations measured at 50% repolar... moreization levels and 90% repolarisation levels were prolonged (p<0.001). There was reduced myocardial contractility (p<0.05) in contraction force in the guinea pigs compared to before administration. Ranolazine can inhibit action potential durations measured at the 50% repolar... moreization levels and the 90% repolarisation levels were prolonged by H₂O₂, but the effect was weaker compared to that of TTX. Ranolazine and TTX could improve myocardial contractile force by reducing the H₂O₂-induced.

Conclusion ranolazine could reduce action potential duration the H₂O₂-induced and increase contraction force. TTX performs a similar role.

e0203 ATHEROSCLEROSIS IMPAIRS CXCR4 EXPRESSION AND FUNCTION IN BONE MARROW CELLS

doi:10.1136/hrt.2010.208967.203

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Objectives The chemokine stromal cell-derived factor-1 (SDF-1) plays a critical role in mobilising CXCR4-positive precursor cells in the bone marrow and may be essential for efficient vascular regeneration and repair. We recently reported that CXCR4 and the angiogenic potential of bone marrow derived cells (BMCs) were regulated positively by calcium and negatively by ageing. We hypothesise that atherosclerosis may also affect CXCR4 surface expression and functions. This study is to determine that atherosclerosis defects BMCs both on the decreased population of CXCR4 + progenitor cells and on the impaired mobility as well as to explore possible mechanisms.

Methods We established atherosclerosis model on ApoE^{-/-} mice under at least 6-month High Fat Diet (group Ath), and used 3~4-week aged ApoE^{-/-} mice as control (group Ctrl). In order to evaluate

impact of the disease on CXCR4 expression from gene transcription to protein synthesis, surface CXCR4 expression on BMCs from the two groups of mice were analysed with FCM; the mRNA of CXCR4 was detected by real-time PCR. To compare the inducibility of CXCR4 expression in response to environmental change, 1 mM CaCl₂ was applied as an extracellular stimuli to treat BMCs for 4 h. To examine how BMC_{Ath} are defect on calcium-induced CXCR4 surface expression, calcium influx was analysed by measuring the increase of intracellular calcium after BMCs were mixed with CaCl₂. Cell-cell adhesion assays were used to detect the SDF-1 mediated adhesion of BMCs to the HUVEC monolayer and vertical invasion assays were used respectively to quantify trans-endothelial migration of BMCs in response to a gradient of SDF-1.

Results BMC_{Ath} have less number of cells expressing CXCR4 as compared to BMC_{Ctrl} (8.54±1.96% vs 13.75±3.94%; n=10, p<0.01). CXCR4 expression on BMC_{Ctrl} could be enhanced by calcium, but CXCR4 surface expression in BMC_{Ath} increased significantly lesser than BMC_{Ctrl} (11.24±1.31% vs 26.59±4.92%; n=10, p<0.01). It is partly because of the defective calcium influx in BMC_{Ath} which reduced the CXCR4 gene transcription, consequently leading to impaired responses on calcium-induced CXCR4 surface expression. BMC_{Ath} showed weaker lower mobility and lower trans-endothelial migration (0.80±0.11 mm vs 1.17±0.15 mm; n=4, p<0.05), and this was not enhanced by calcium pretreatment.

Conclusions Atherosclerosis impairs CXCR4 surface expression on BMCs and related cell functions.

e0204 HEAT SHOCK PROTEIN 90 ENHANCES RAT MESENCHYMAL STEM CELLS MIGRATION VIA PI3K/AKT AND ERK12 PATHWAYS

doi:10.1136/hrt.2010.208967.204

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Objective Heat shock protein 90 (HSP90) is a chaperone for several client proteins involved in transcriptional regulation, signal transduction, and cell cycle control. HSP90 is abundantly expressed by a variety of tumour types and has been recently targeted for cancer therapy. The objective of this study is to determine the role of Hsp90 in regulating the migration of Mesenchymal stem cells and to determine the mechanism. We hypothesised that inhibition of Hsp90 impairs the MSCs migration via PI3K/Akt and ERK1/2 signalling pathways.

Methods The MSCs were cultured from femoral and tibia. The ability for MSCs cells to migrate is to be determined by the wound healing assay and transwell assay. The activity of matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) were estimated by gelatin-zymography. The mRNA levels of MMP-2, MMP-9, CXCR4 and VCAM-1 were detected by real-time PCR. The protein expression of MMP-2, MMP-9 and ERK1/2, phospho-ERK1/2, Akt and phospho-Akt were determined by Western-blot.

Results Treatment with RhHsp90 α significantly enhances MSCs migration from 9.83±2.48 to 48.65±2.81 cells. Treatment with sirhsp90 α significantly decreased MSCs migration compared with treatment of hsp90 α from 63.33±9.61 to 13.00±4.38 cells. Pretreat with 17-AAG, wortmannin, U0126, decreased MSCs migration to 13.33±1.29, 15.33±2.1, 16.5±3.3 cells, respectively. Treatment with RhHsp90 α enhanced the MSCs secretion of MMP-2 and MMP-9, as well as significantly increasing the activity of MMP-9, and increasing the expression of CXCR4 and VCAM-1. PI3K/Akt and ERK signalling pathways mediate the promotion of MSCs migration by RhHsp90 α .