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 demonstrate 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

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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 ranolazine administration to observe the effects of ranolazine on the papillary muscles.

**Results** H2O2 could increase action potential durations measured at 50% repolarization levels and 90% repolarization levels compared to BMCCtrl (8.54±1.96% vs 15.75±5.94%; n=10, p<0.01). CXCR4 expression on BMCControl 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 PI3KAKT AND ERK12 PATHWAYS

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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. HS90 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 RhHsp90x significantly enhances MSCs migration from 9.83±2.48 to 49.65±2.81 cells. Treatment with sirhsp90x significantly decreased MSCs migration compared with treatment of hsp90x from 63.33±9.61 to 13.00±4.38 cells. Pretreat with 17-AAG, vorinostat, U0126, decreased MSCs migration to 13.33±1.29, 15.33±2.1, 16.5±5.3 cells, respectively. Treatment with RhHsp90x 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 signaling pathways mediate the promotion of MSCs migration by RhHsp90x.