Aims We hypothesized that SDF-1 α is a potential mediator of RIPC-induced protection.

Methods and Results Rats were anaesthetized and subjected to RIPC, consisting of 3 cycles of 5 minutes ischaemia by application of a tourniquet around the hind limb followed by 5 minutes of reperfusion. SDF-1 α levels in rat plasma were measured using an ELISA kit. There was a 50% increase ($p<0.01$) in SDF-1 α levels in plasma obtained from rats subjected to RIPC (890 ± 70 pg/ml, $n=8$) compared to the control group (590 ± 50 pg/ml, $n=8$). Pharmacological inhibition using AMD3100, a highly specific antagonist of CXCR4 signalling, was used to investigate the involvement of SDF-1 α in RIPC. Rats were treated intraperitoneally with AMD3100 ($10\text{ }\mu\text{g/kg}$), prior to the RIPC protocol. The hearts were then excised and subjected to IR injury using the in vitro isolated Langendorff perfusion model. RIPC decreased the infarct size from $53\pm3\%$ to $27\pm3\%$ ($n=6$, $p<0.05$). Cardioprotection was abolished by AMD3100 ($40\pm4\%$ vs $53\pm3\%$, $n=6$, $p<0.05$). In separate experiments using myocytes isolated from rat hearts, SDF-1 α was shown to reduce cell death, as measured by propidium iodide, following 3 h hypoxia and 1 h re-oxygenation ($20\pm5\%$ vs. $34\pm5\%$). RIPC also improved functional recovery of cardiac papillary muscle from $53\pm13\%$ ($n=4$) to $84\pm5\%$ ($n=6$, $p<0.05$) and was similarly blocked by AMD3100 ($46\pm7\%$, $n=6$). Further, the direct application of SDF-1 α was shown to be protective in this model ($89\pm9\%$ vs. $55\pm9\%$ control, $n=4$, $p<0.05$) and was blocked by AMD3100 ($60\pm11\%$). We also measured the serum levels of dipeptidase (DPPIV) which is known to cleave and inactivate SDF-1 α . We observed no change in DPPIV activity after RIPC. This suggests that increased synthesis and release of SDF-1 α caused the increase in plasma levels.

Conclusion RIPC increases circulating levels of SDF-1 α , which acts via the CXCR4 receptors in the heart to attenuate IR injury. These results suggest that this chemokine might be an essential mediator of RIPC.

253

REMOTE ISCHAEMIC PRECONDITIONING IS MEDIATED VIA THE SDF 1 α /CXCR4 SIGNALLING AXIS

P Selvaraj, D He, C Boi-Doku, J Kearney, R Yellon, S Davidson, D Yellon *The Hatter Cardiovascular Institute, UCL*

doi:10.1136/heartjnl-2013-304019.253

Background Ischaemic preconditioning is one of the most potent experimental modalities known to decrease infarct size following ischaemia-reperfusion (IR) injury. Much interest has been stimulated by the phenomenon of Remote Ischaemic Preconditioning (RIPC) which occurs when a preconditioning stimulus is applied to a limb remote from the heart to stimulate cardioprotection. The protection is believed to be mediated by an unidentified humoral factor between 3.5 and 30 kDa. Stromal cell-derived factor-1 α (SDF-1 α or CXCL12) is a chemokine of 10 kDa that is induced by hypoxia and recruits stem cells. However it also exerts a direct and acute cardioprotection via its receptor, CXCR4.