

P005 Inhibition of mitochondrial permeability transition accompanies protection of ischaemic reperfused hearts by urocortin
Samantha Clarke, Paul Townsend, Igor Khaliulin, Jo Parker & Andrew P Halestrap
University of Bristol & University of Southampton

Urocortin, a 40 amino acid peptide, protects hearts from ischaemia / reperfusion injury. Recovery of left ventricular developed pressure following 35 min ischaemia and 30 min reperfusion was $38 \pm 9\%$ in control and $75 \pm 5\%$ in Langedorff-perfused hearts treated with 10^{-8} mol.l⁻¹ urocortin (means \pm S.E.M., $p < 0.01$), whilst the end diastolic pressure decreased from 48 ± 6 mmHg to 21 ± 4 mmHg ($p < 0.01$). Total LDH release during 30 min reperfusion (an indicator of necrotic cell damage) decreased from 5.85 ± 1.04 to 1.88 ± 0.42 Units ($p < 0.02$). Mitochondrial permeability transition pore (MPTP) opening *in situ*, using deoxyglucose entrapment, was decreased by Ucn-treatment from 38.1 ± 3.1 to 31.2 ± 1.5 DOG-units ($p < 0.05$). Mitochondria were rapidly isolated from hearts following 35 min control perfusion with or without Ucn or following 30 min ischaemia and 3 min reperfusion. MPTP opening was determined in the isolated de-energised mitochondria in response to $80 \mu\text{M}$ Ca^{2+} . There was no difference in the extent of MPTP opening between mitochondria isolated from control and Ucn-treated hearts prior to ischaemia but a significant decrease following 3 min reperfusion. In conclusion, protection of the heart from ischemia/reperfusion injury by urocortin is associated with inhibition of the MPTP, but the effect may be secondary to other changes such as calcium overload and oxidative stress.