Abstract: **P269**

**Hearts subjected to ischemia-reperfusion benefit from adenine nucleotide translocase 1 overexpression**

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**Introduction:** The occlusion of coronary vessels interrupts the blood supply (ischemia) in the heart and impedes the perpetuation of cells with oxygen and substrate to generate ATP, leading to myocardial infarction (MI). Reperfusion of the occluded vessel is essential for the survival of the heart. However, reperfusion also conveys an additional damage. Oxygen deficiency during ischemia induces mitochondrial membrane depolarization and reperfusion provokes opening of MPTP. The adenine nucleotide translocase (ANT) – a protein of the inner mitochondria membrane - has a physiologic key function in cellular energy metabolism and regulates MPTP opening. Thus, ANT1 is highly involved in mitochondria function.

**Purpose:** ANT1 is down regulated during I/R. This down-regulation may contribute to I/R injury. Therefore, we analysed if ANT1-overexpressing (ANT1-TG) rat hearts are protected against I/R injury.

**Methods:** Hearts of 5 - 8 month old wildtype (WT) and ANT1-TG rats were mounted on the Langendorff apparatus and retrograde perfused in vitro via the aorta at a constant pressure of 50 mm Hg. Hearts were perfused continuously with Krebs–Henseleit buffer for 20 min prior to global ischemia for 45 min followed by two hours of reperfusion. Heart rate, systolic and diastolic pressure, aortic pressure and flow were continuously recorded. Mitochondria were isolated after basal Langendorff perfusion for 25 minutes or after I/R. Respiration of mitochondria, membrane potential, and calcium retention capacity were measured. To determine the infarct size (IS), the whole heart was removed rapidly at the end of reperfusion, cut into slices from apex to base and directly incubated in buffered 1% 2,3,5-triphenyltetrazolium chloride (TTC).

**Results:** After ischemia/reperfusion ANT1-TG hearts displayed improved LVDP recovery (WT: 41.7 ± 7.1 %; ANT1: 55.3 ± 5.0 %) by trend and a significant decrease in diastolic (WT: 29.8 ± 3.9 mmHg; ANT1: 20.6 ± 2.5 mmHg, p<0.05) and aortic pressure (WT: 98.7 ± 4.3 mmHg; ANT1: 80.7 ± 3.4 mmHg, p<0.01) in comparison to WT hearts. In line with the better hemodynamics, ANT1-overexpressing mitochondria from ischemic/reperfused hearts exhibit a higher calcium retention capacity (WT: 50.0 ± 6.3 nM CaCl2; ANT1: 97.5 ± 8.5 nM CaCl2; p<0.01) and an attenuated decrease in membrane potential (WT: 37.2 ± 0.6 a.u.; ANT1: 25.5 ± 1.7 a.u.; p<0.01 than WT mitochondria. Additionally ANT1-overexpressing mitochondria are not restricted in oxygen consumption after I/R. (Complex 1: WT 18.9 ± 1.4 basal vs 12.9 ± 1.7 I/R, p<0.05; ANT1 18.3 ± 1.2 basal vs 17.4 1.6 I/R; in nmol O2*min-1 *mg protein-1). However, there is no difference in infarct size between both groups.

**Conclusion:** ANT1-overexpressing hearts can better cope with the outcome of I/R injury that was shown by better hemodynamics and more robust mitochondria. This is based on a better energy management and calcium handling, resulting in less rigor contracture of surviving ANT1-TG cardiomyocytes.