OS004
ADMINISTRATION OF MESENCHYAL STROMAL CELLS BEFORE RENAL ISCHAEMIA/REPERFUSION ATTENUATES KIDNEY INJURY AND MODULATES RENAL LIPID METABOLISM IN RATS
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Background: Mesenchymal stromal cells (MSC) have been demonstrated to attenuate renal ischemia/reperfusion (IR) damage in rodents. The mechanisms of such nephroprotection remain unclear.

Materials and Methods: Male Lewis rats aged 8-10 weeks received tail i.v injection of 1.5x10^6 MSC in 1 mL saline (MSC-7, n = 11) or saline alone (SD-7, n = 6) 7 days before renal I/R. Left renal ischemia (by clamping the renal pedicle) lasted 45 min. Right nephrectomy was simultaneously performed. Blood sample was collected from inferior vena cava 48 h post reperfusion. Renal function was assessed by measuring serum creatinine (SCr) levels. Expressions of inflammatory and apoptotic markers by real-time (RT)-qPCR were comparatively quantified. High-throughput RNA sequencing was applied to MSC-7 vs. SD-7 non-ischemic right kidneys. Relevant pathways were detected using Gene-Expression Analysis with WebGestalt, and confirmed by RT-qPCR.

Results: Scr levels reached 1.4 ± 0.7 vs. 2.4 ± 0.8 mg/dL in MSC-7 vs. SD-7 group (p < 0.05). Infiltration significantly reduced mRNA expression of Casp3, Hsp 70, Kit, Mcp1 and Il-6 and increased mRNA expression of Bcl compared to saline. Among 25 908 genes, 748 were identified as significantly differentially expressed (False Discovery Rate (FDR), <0.05) between MSC-7 vs. SD-7 non-ischemic kidneys. Among the most detected metabolic pathways, renal lipid metabolism was significantly altered, with down-regulation of fatty acid biosynthesis and an up-regulation of PPARα pathway in MSC-7 vs. SD-7 groups. By immunoblotting, PPARα and phosphorylated-PPARα were significantly increased in MSC-7 vs. SD-7 kidneys, in both non-ischemic and ischemic conditions. Moreover, levels of malondialdehyde-derived lipid peroxidation products were decreased in MSC-7 ischemic kidneys in comparison to SD-7 ischemic kidneys.

Conclusion: MSC infusion at day 7 prior injury critically impacts renal lipid metabolism, which may condition kidney parenchyma against I/R.

OS005
COLLECTIN-11 PROMOTES RENAL TUBULINTERSTITIAL FIBROSIS FOLLOWING RENAL ISCHEMIA REPERFUSION
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Collectin-11 (CL-11) is a newly identified collection of the innate immune system and recently has been suggested to play a pathogenic role in acute kidney injury induced by renal ischemia reperfusion (IR). However, the impact of CL-11 on the late phase of renal IR injury is unknown. In the present study, we investigated whether CL-11 is involved in the pathogenesis of renal tubulointerstitial fibrosis following renal IR and the underlying mechanisms.

We employed a murine model of renal IR injury and CL-11−/− mice to determine the roles of CL-11 in renal inflammation and tubulointerstitial fibrosis. To investigate cellular mechanisms that CL-11 contributes to renal inflammation and the development of tubulointerstitial fibrosis we performed a series of in vitro experiments using freshly prepared peritenal neutrophils or monocytic/macrophages and primarily cultured renal fibroblasts.

We show that CL-11 deficiency protected mice from the development of tubulointerstitial fibrosis following renal IR. Compared to the wild littersmates, CL-11−/− mice had significantly reduced renal fibrosis, as evidenced by reduced renal function impairment, tubular injury, renal leucocyte infiltration (i.e. CD45, neutrophils, macrophages), collagen deposition in the kidney as well as intrarenal gene expression of proinflammatory (TNFα, IL-1β, IL-6) and profibrotic (TGF-beta) molecules. In vivo study showed that CL-11 had potent effects in promoting leucocyte migration and stimulating renal fibroblast proliferation.

Therefore, our findings demonstrate a pathogenic role for CL-11, particularly locally produced, in renal tubulointerstitial fibrosis following renal IR and suggest a novel mechanism for CL-11 in promoting leucocyte chemotaxis and stimulating fibroblast proliferation in renal fibrosis. CL-11 may represent a novel therapeutic target in both the early and late phases of kidney IR injury.

Translational Kidney Ischemia-reperfusion and preservation

OS006
DIRECT COMPARISON OF HYPOTHYMIC AND NORMOTHERMIC MACHINE PERFUSION IN A PORCINE EX-VIVO KIDNEY MODEL
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Background: Hypothermic machine perfusion (HMP) is a well-established method for deceased donor organ preservation, assessment and preconditioning. Normothermic machine perfusion (NMP) offers similar and perhaps greater advantages. However, data on a direct comparison of the two methods are scarce. Therefore, the aim of this study was to compare the two methods in an ex-vivo model using porcine kidneys.

Methods: 16 kidneys from 8 donor pigs retrieved at an abattoir after 25 min of warm ischaemia time were stored on ice for 24 h. They were then perfused hypothermically (4 °C) or normothermically (37 °C) for 2). Kidneys were reperfused with whole blood for 2 h at 37 °C. Physiological parameters e.g. perfusate flow rate, urinary output and oxygen consumption were compared. Levels of IL-1α and IL-1β in perfusate samples were measured by ELISA and mRNA expression of TNF-α, IL-1β, IL-1α, and EDN-1 were determined by RT-PCR. Statistical analysis was performed using ANOVA.

Results: Kidneys after HMP showed significantly higher urinary output (5.7 ± 2.26 ml/min vs. 2.15 ± 1.24 ml/min, p = 0.0046) as well as oxygen consumption (p = 0.0032) and perfusate flow rates (p = 0.036) at reperfusion than kidneys after NMP. At mRNA level, expressions of proinflammatory markers were higher for the HMP group, which reached significance for the expression of EDN-1 (p = 0.03). IL-1α levels in perfusate samples were similar between the two groups.

Conclusion: In direct comparison to normothermic machine perfusion, hypothermic machine perfusion of porcine kidneys resulted in improved physiological parameters and led to significantly increased urinary output rates despite showing a higher upregulation of inflammatory markers at mRNA level. Further investigations of the physiological and immunological parameters of both preservation methods are needed to optimise outcomes.