Abstract# B-350

Ex Vivo Normothermic Perfusion Improves Cold Ischemic Injury and DGF in an Experimental Model of DBD Kidney Transplantation

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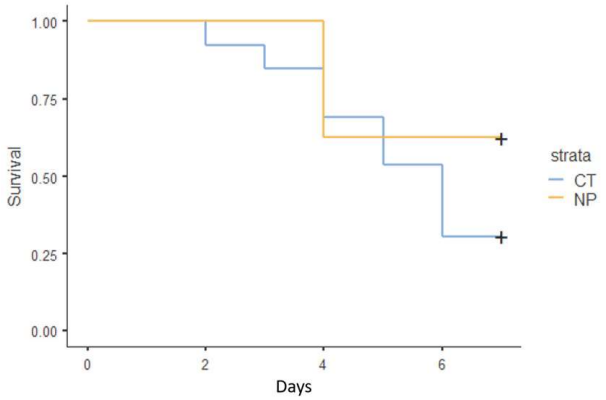
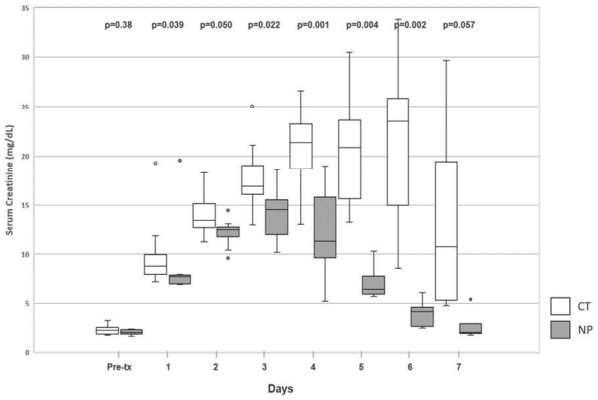
Purpose: Cold ischemic (CI) injury results in high rates of DGF, reduced graft function and survival. Ex vivo normothermic perfusion (EVNP) has shown to improve IRI in several conditions, but there is little evidence of the EVNP effects on kidney CI injury. The aim of this study was to measure the impact of EVNP after a long cold storage in a swine kidney model of DBD

Methods: Left kidneys from female pigs were cold stored for 20-hr in the control (CT) group (n=13) or the same period followed by 3-hr EVNP in the NP group (n=8). Kidneys were then reimplanted, a contralateral nephrectomy performed and renal function measured over 7 days. During EVNP kidneys were perfused with an erythrocyte-based solution, nutrients, insulin and a vasodilator. Urine volume was continuously replaced. Flow rate, arterial pressure, urine, temperature and oxygen saturation were recorded continuously.

Results: Post-transplant, 62.5% (5/8) animals survived in the NP group compared with 30.8% (4/13) in the CT group, without reach statistical differences in the survival curve (Fig. 1, Log-rank p=0.237). Deaths were mainly due to the severity of CI injury and DGF. From the first post-transplant day, renal function (creatinine (Cr) values) showed a growing difference between the 2 groups, and the NP group showed statistical inferior values until the 6th day (Fig. 2). The demonstration of statistical differences on the 7th day was limited by the small number of surviving animals in the CT group.

Conclusions: A short period of EVNP following the renal preservation period in a swine auto-transplantation model of DBD kidneys improves graft condition, diminishing CI injury and DGF.





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Abstract# B-351

Estrogen Receptor Beta Deletion in the Vascular Endothelium is Protective in Renal Ischemia Reperfusion Injury

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Purpose: Renal ischemia reperfusion injury (IRI) is a major contributor to early allograft dysfunction (EAD) in kidney transplantation. We previously identified lower rates of EAD among female renal transplant recipients in the UNOS registry. Using a murine model, we demonstrated improved IRI tolerance with administration of supplemental 17β-estradiol (E2). We also identified decreased ischemia tolerance in estrogen receptor α knockout (ERα-KO) mice. Given the therapeutic potential of E2 in renal transplantation, further clarification of E2's mechanism of action is essential. As E2 is an agonist of both ERα and estrogen receptor β (ERβ), we aim to clarify the role that ERβ plays in estrogen-mediated IRI tolerance using whole-body ERβ knockout (ERβ-KO) and selective estrogen receptor β deletion in the vascular endothelium (Tie2-Cre (+) ERβ$^{-/-}$).

Methods: In two separate experiments, female ERβ-KO mice and Tie2-Cre (+) ERβ$^{-/-}$ mice were subjected to temperature-controlled renal ischemia along with female, wild-type C57BL/6 (B6) controls. Blood urea nitrogen (BUN) and serum creatinine (Cr) were measured at 24, 48, 72, and 96 hours after surgery.

Results: ERβ-KO mice demonstrated significantly lower BUN ($p<0.0001$) and Cr ($p=0.0013$) compared to B6 mice (Figure 1). Similarly, Tie2-Cre (+) ERβ$^{-/-}$ mice portrayed significantly lower BUN ($p<0.001$) and Cr ($p=0.03$) compared to B6 mice (Figure 2).

Conclusions: Whole-body ERβ-KO is protective in warm renal IRI, and selective deletion of ERβ from the vascular endothelium is sufficient to generate the protective phenotype seen in the whole-body knockout. These previously unreported findings suggest that signaling via ERα and ERβ may have opposite effects on ischemia tolerance in renal IRI. Further investigation into the different roles that these receptors play in renal IRI will help direct the development of selective and clinically useful interventions.

Figure 1.

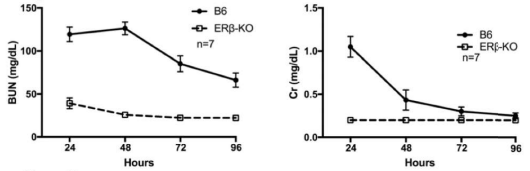
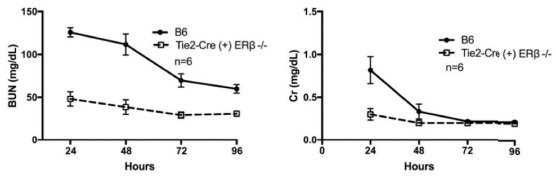


Figure 2.



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Abstract# B-352

An Immune-Modulatory Strategy to Mitigate Hepatic Ischemia Reperfusion/Injury in a Murine Model

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Purpose: Hepatic ischemia/reperfusion injury (IRI) is the leading cause of early graft dysfunction and contributes to the shortage of donor organs. However, despite its obvious clinical importance, there are no effective therapies to prevent or treat this condition. Indoleamine 2,3-dioxygenase (IDO) is an intracellular enzyme that catalyzes the catabolism of the essential amino acid tryptophan to the product kyn-