Background: The prevention/attenuation of graft ischemic injury is a challenge in kidney transplantation. We developed two rat models to investigate the impact of mesenchymal stromal cells (MSCs) in the ischemic preconditioning of kidneys from Donors after Circulatory Death (DCD) and Donors after Brain Death (DBD).

Methods: Under general anesthesia, rats underwent iv injection of saline (S-groups) or 1.5 10^6 MSCs (MSC-groups) followed by either DBD (6hr of brain death) or DCD (6hr of anesthesia and 20min warm ischemia) models, resulting in 4 groups (S-DBD, S-DCD, MSC-DBD, MSC-DCD). Kidneys were then procured after IGL1 flush. One kidney was directly fixed and the other one immersed for 14 hours in IGL1 at 4°C. Serum samples were collected before treatment (baseline) and at the time of kidney collection. Urine samples were collected by bladder puncture at the time of kidney collection. Renal function was evaluated. Kidney histology was assessed by PAS staining and KIM1 immunostaining. Total RNA was extracted from S-DCD vs S-DBD kidneys for RNAseq.

Results: BUN was increased after 6h of anesthesia (DCD) or brain death (DBD) ($p<0.01$). SCr increased in both S-DBD and MSC-DBD but was lower in MSC-treated rats (MSC-DBD 0.5±0.2mg/dL vs S-DBD 0.7±0.1mg/dL; $p=0.037$). Urinary KIM1 was lower in MSC-treated DBD (S-DBD 10.9±4.5 vs MSC-DBD 7.1±1.7; $p=0.03$). Acute Tubular Injury (ATI) and KIM1 expression were higher in S-DBD (ATI: S-DBD 65±24 % of surface vs S-DCD 39±27 % of surface ($p=0.03$) and KIM1: S-DBD 0.39±0.24 % of surface vs S-DCD 0.10±0.09 % of surface ($p=0.0002$)). In MSC groups, there was no difference in both ATI extension and KIM1 expression. There was no difference in KIM1 expression between S-DBD and S-DCD groups. RNAseq showed that proinflammatory and proapoptotic pathways were upregulated in DBD, whereas transmembrane transport and metabolic pathways were downregulated, compared to DCD.

Conclusions: The RNA profiles of the kidneys are different upon donor types, which may impact the response to MSC-based ischemic preconditioning.