RENAL INJURY RESPONSE IN AN ADULT *Pkd2* MOUSE MODEL

Sreelakshmi Cherakara, M.S; Zhang Li, Ph.D.; Courtney J. Haycraft, Ph.D. and Bradley K. Yoder, Ph.D.
Department of Cell, Developmental, and Integrative Biology
University of Alabama at Birmingham, Birmingham, Alabama, US

Introduction: Autosomal Dominant Polycystic Kidney Disease is caused by mutations in either the PKD1 or PKD2 gene, resulting in progressive renal cyst formation. Previous studies have shown that renal injury accelerates cyst formation in mouse models of PKD, suggesting PKD1 and PKD2 may be involved in regulating injury and repair responses. We are evaluating the presence of malrepaired cells, defined as persistent expression of injury markers such as SOX9 following injury, in *Pkd2* mutant mice and how loss of *Pkd2* may affect this process following injury.
Methods: Renal injury was induced by IP injection of cisplatin (9.0mg/kg BW), in adult-induced CAGG-CreERT2*;Pkd2* mutant mice. We used 10 µm frozen sections of kidneys harvested at 3-, 7-, 14-, 28-, and 35-days post-cisplatin and analyzed SOX9 expression. The percentage of SOX9-expressing renal epithelial cells in *Pkd2* mutant and control kidneys were compared using fluorescence microscope images.
Results: The number of cells expressing SOX9 peaked 7 days post-injury in both *Pkd2* mutants and controls and decreased through 28 days post-injury. At day 28, *Pkd2* mutants showed an increased number of persistent SOX9 expressing cells, indicative of malrepair, compared to controls. An increase in SOX9+ cells was observed from D28 to D35 post-injury in *Pkd2* mutants, while no change was seen in controls.
Conclusion: These data show that following renal injury, *Pkd2* mutants respond to cisplatin induced injury through upregulation of SOX9 and their response is similar to controls. The increase in number of malrepaired cells in *Pkd2* mutants as compared to controls at D28 shows a defect in repair processes suggesting that PKD2 may be involved in the repair response pathway. The increase in SOX9+ cells from D28 to D35 may indicate that the malrepaired cells are proliferating or additional cells are being further injured in *Pkd2* mutants.
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