Cisplatin-induced injury promotes cyst progression in an adult-induced PKD2 mutant mouse model

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Introduction: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most prevalent genetic kidney disease. It affects between 7 - 17.5 million people across the world and is caused by mutation of either the *PKD1* gene or *PKD2* gene. Renal injuries (e.g., ischemia reperfusion injury) have been shown to accelerate cyst formation in ADPKD animal models. Here we evaluate whether a second form of renal injury induced by cisplatin also leads to increased cyst formation in *Pkd2* mutant mouse models.

Methods: To study the effect of cisplatin-induced injury on cyst formation, adult-induced *Pkd2* mutant mice ($CAGGCre^{ERT2}$; $PKD2^{fl/fl}$) were treated with cisplatin (9.0 mg/kg body weight) by intraperitoneal injection. At 8 weeks post-injury, the kidneys were isolated for study. Paraffin sections were generated, and hematoxylin and eosin (H&E) staining was performed to visualize cystic areas using ImageJ software. Cryosections were generated, and macrophage accumulation and cell proliferation were accessed using immunofluorescence (IF) staining for F4/80 (macrophages), ki67 (proliferation), Hoechst (nuclei), LTA (proximal tubule), and DBA (distal tubule and collecting duct).

Results: Cystic index quantification showed that the *Pkd2* mutant cisplatin-induced kidneys had significantly higher cystic indices than the PBS-induced mutant kidneys. IF staining showed more macrophage accumulation around cystic areas in the mutant kidneys after cisplatin treatment, and that these kidneys had a higher level of proliferation compared to the PBS-treated group.

Conclusions: Renal injury caused by cisplatin promotes cyst progression in adult *Pkd2* mutant mice. Additionally, we observed macrophage accumulation surrounding the cysts that formed. In the future, earlier time points (4-6 weeks post-injury) will be studied to determine whether the accumulating macrophages cause cyst progression or are simply a consequence of cyst presence and expansion.

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