

PCKD, the most relevant model for ADPKD

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Abstract

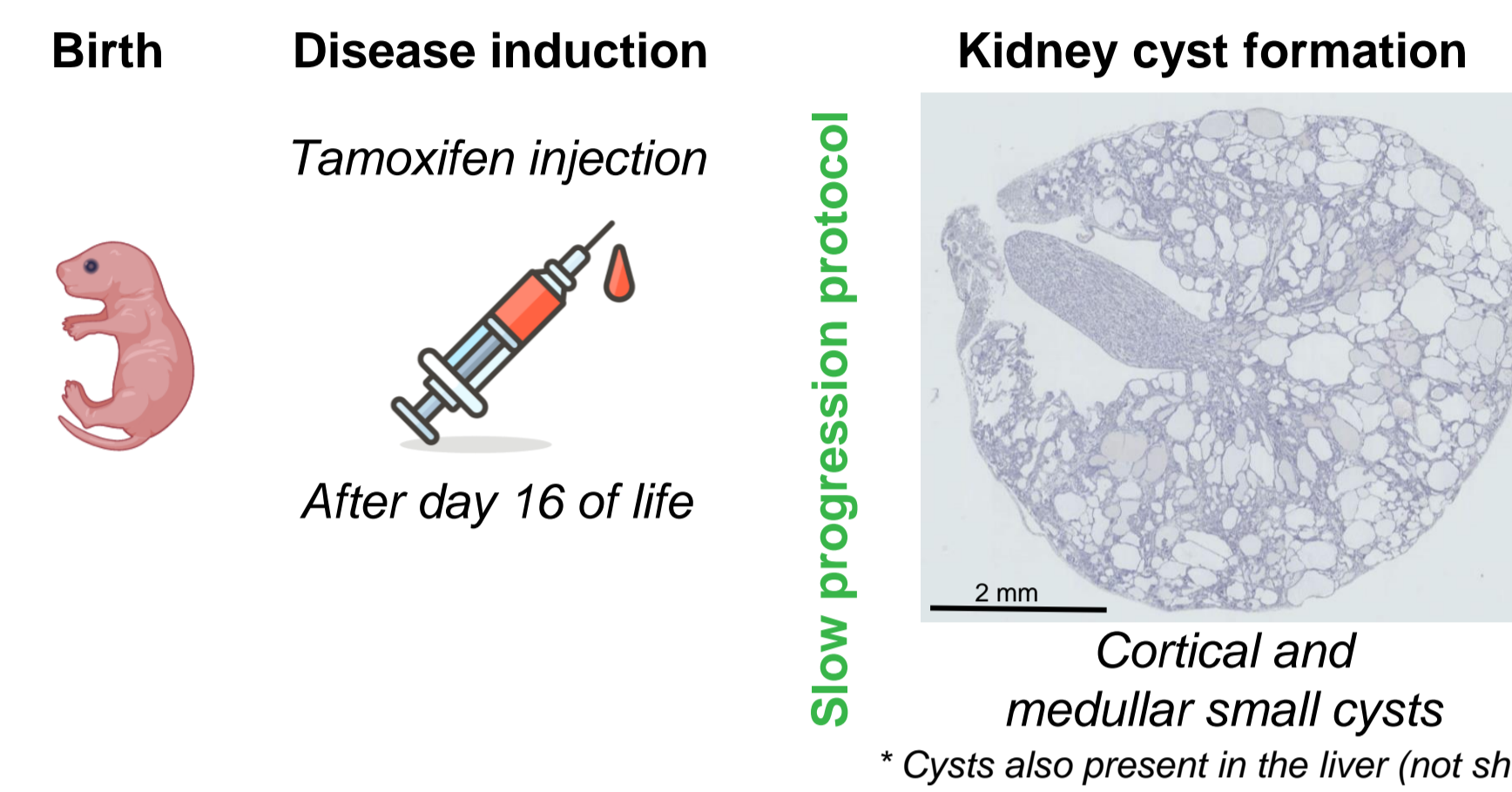
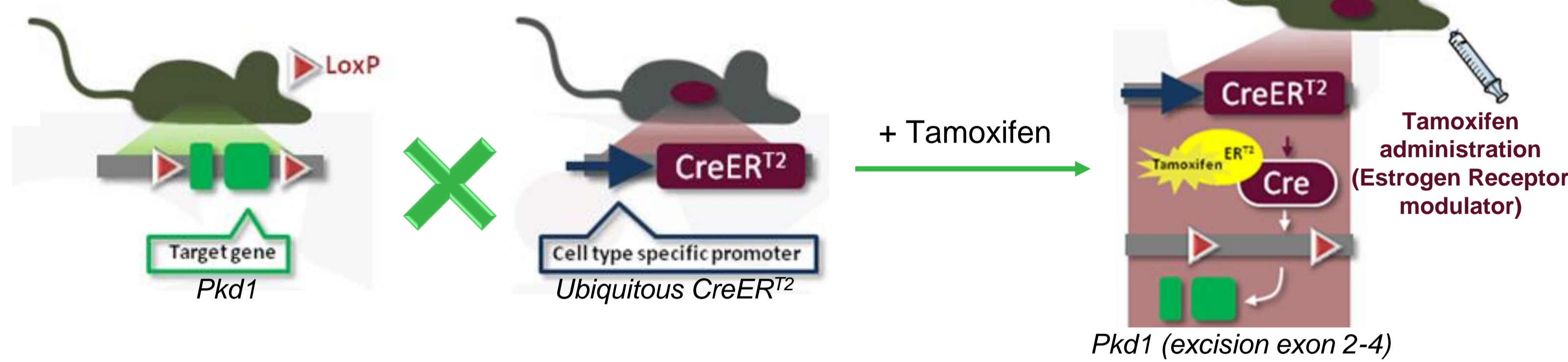
Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disorder, affecting 12 million people globally. It is characterized by the development of fluid-filled kidney cysts,

which often leads to kidney failure. The vasopressin receptor 2 antagonist, Tolvaptan, is the only approved treatment that slows the progression of ADPKD. Nevertheless, there is

still a high unmet need for treatment options for patients with ADPKD because Tolvaptan has limited efficacy and non-negligible side effects.

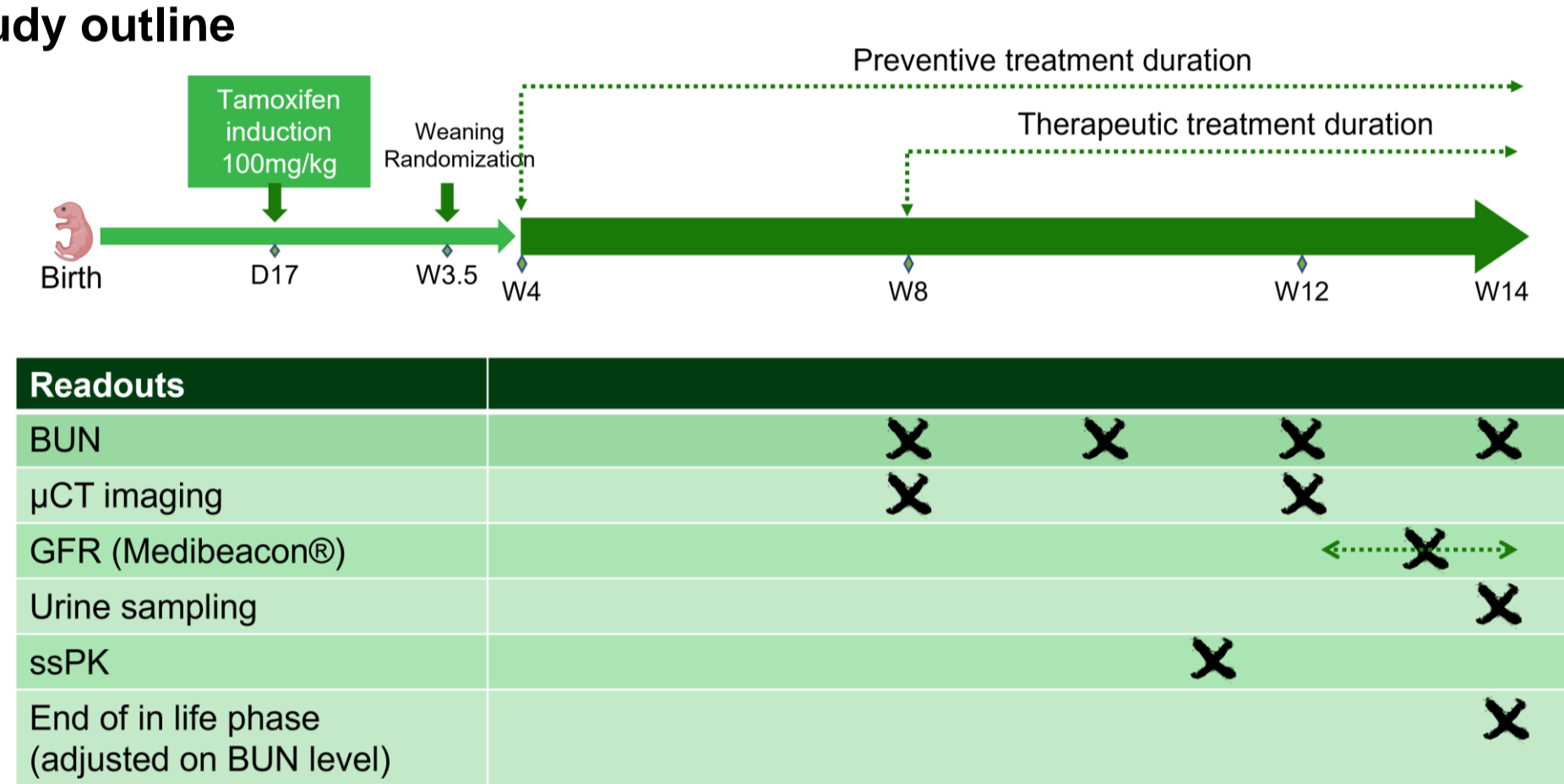
Methods

PCKD mice strain generation



Results

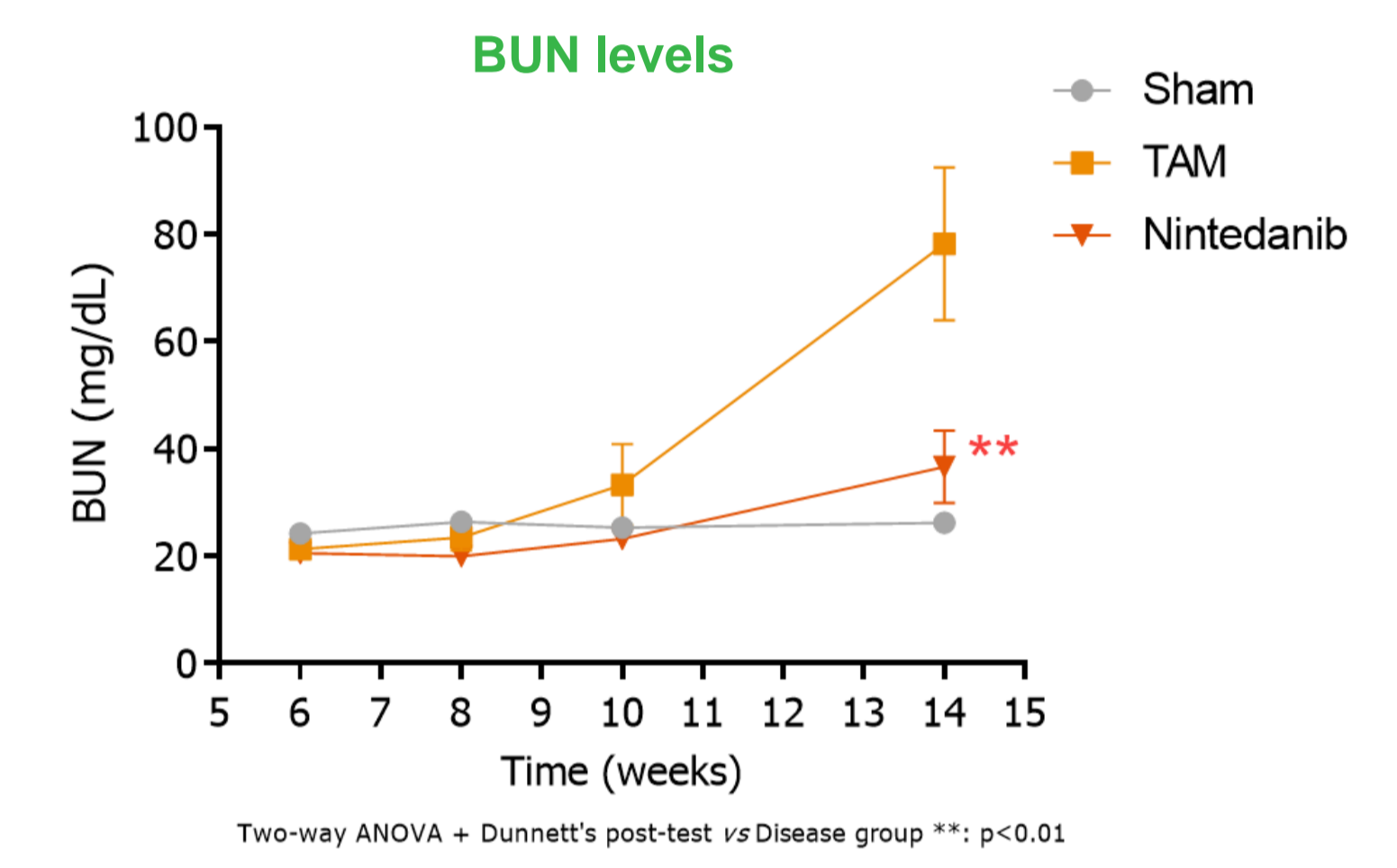
Study outline



Longitudinal BUN levels

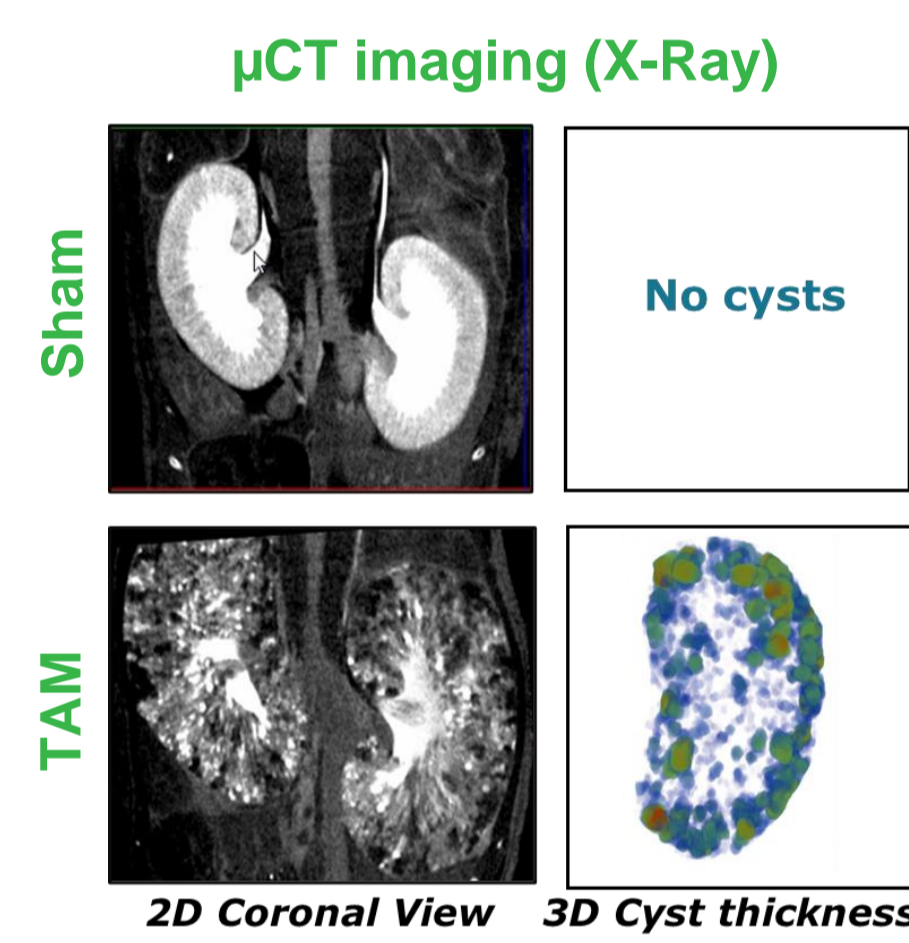
- ✓ Decreased kidney functionality (increased BUN levels) in the TAM-induced disease group
- ✓ Nintedanib protects kidney functionality

BUN: Blood Urea Nitrogen

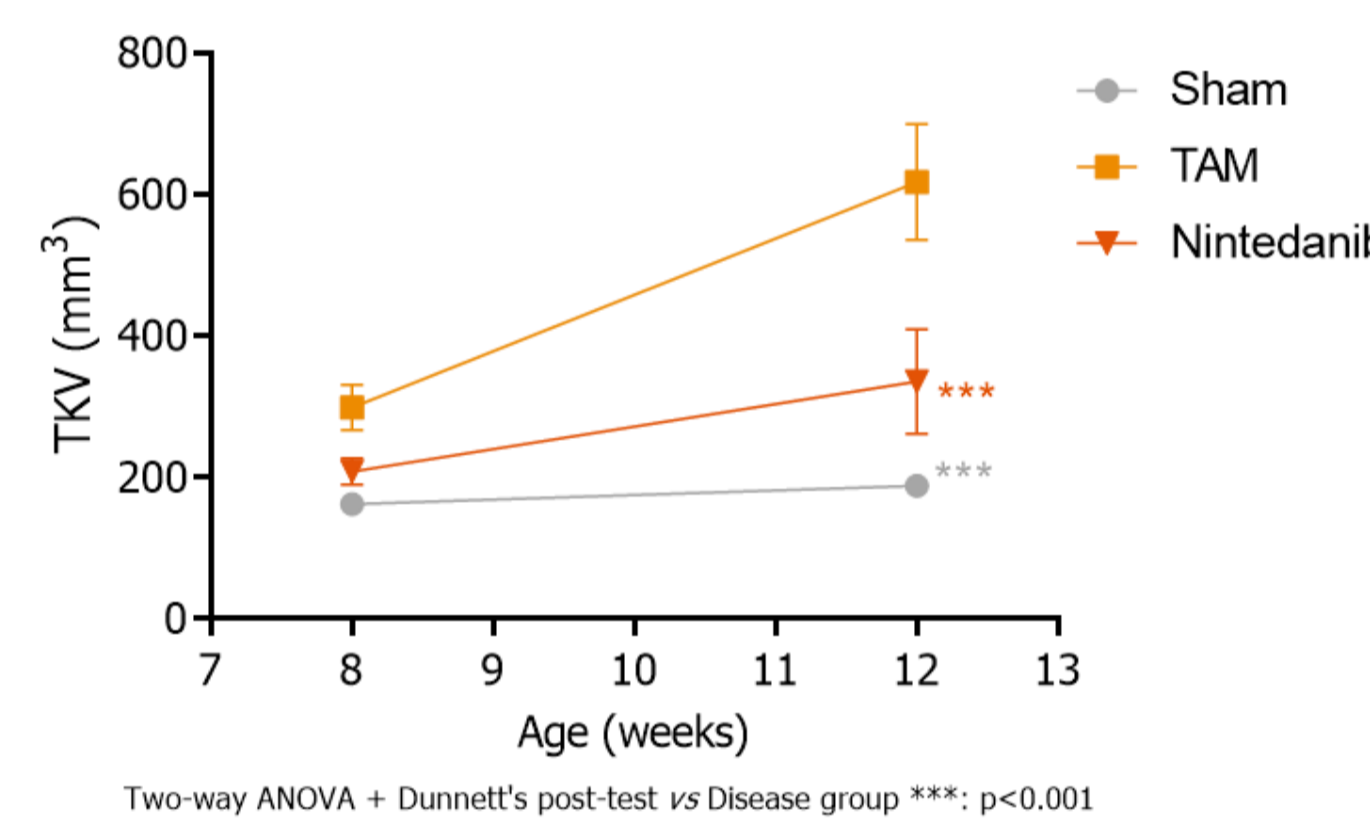


Longitudinal kidney and cyst volumes by X-Ray imaging

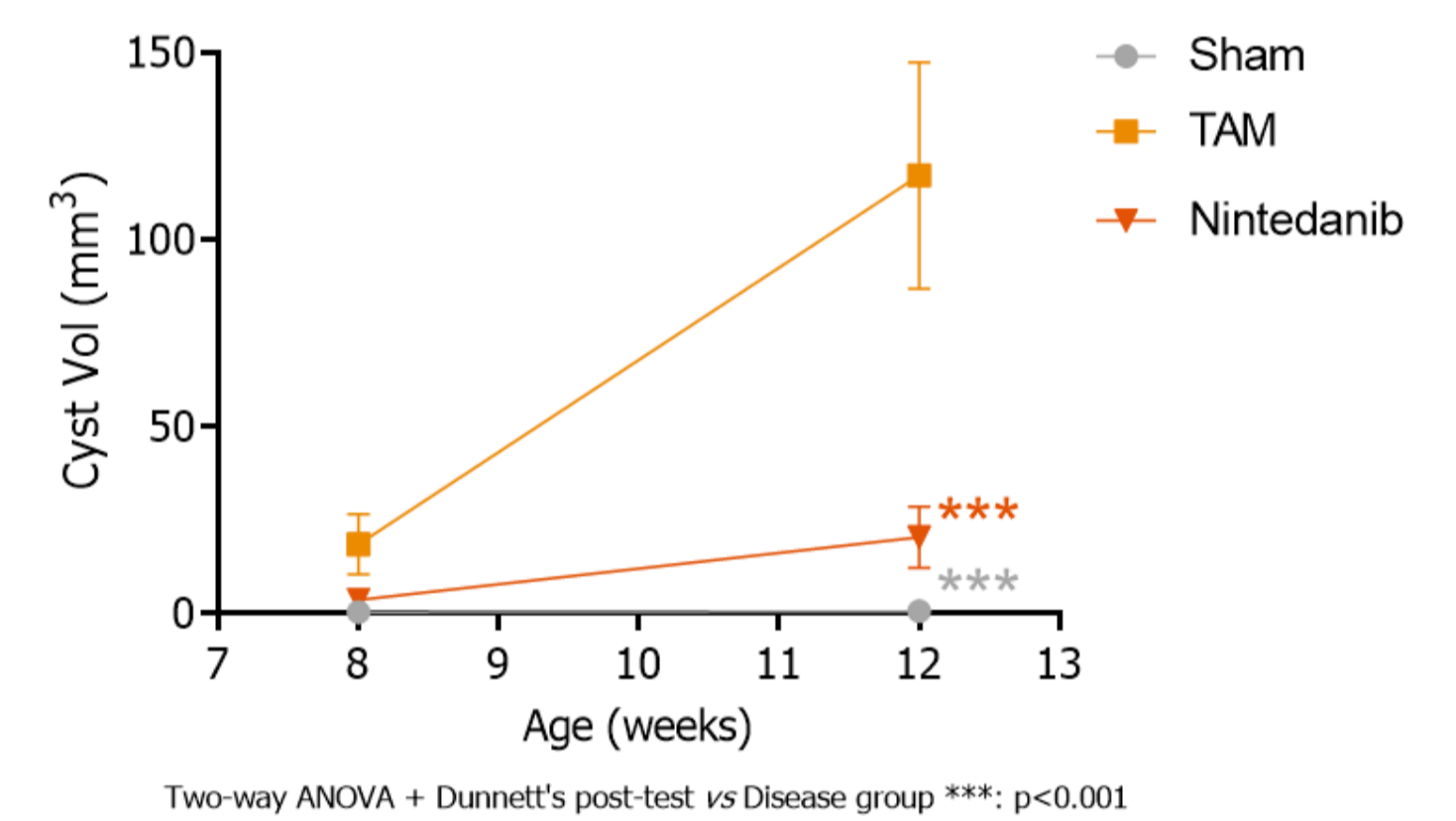
- ✓ Increased kidney volume and cyst volume in the TAM-induced disease group
- ✓ Nintedanib protects kidney structure



Total kidney volume (by µCT)

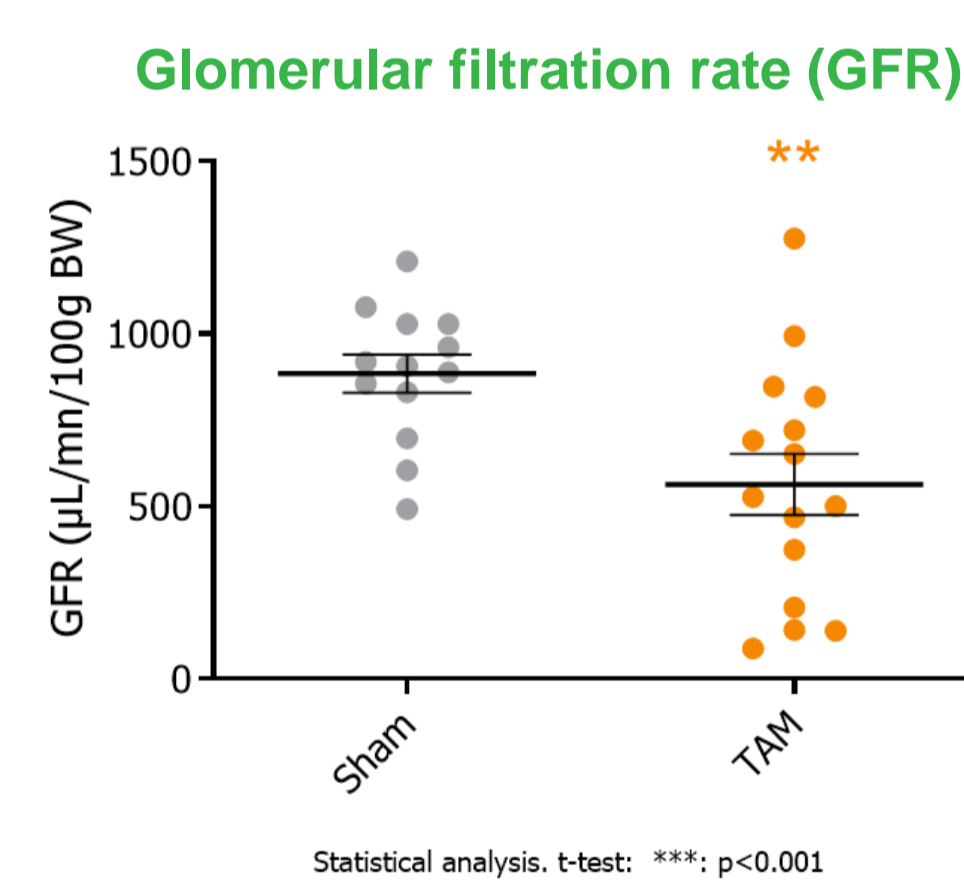


Cyst volume (by µCT)

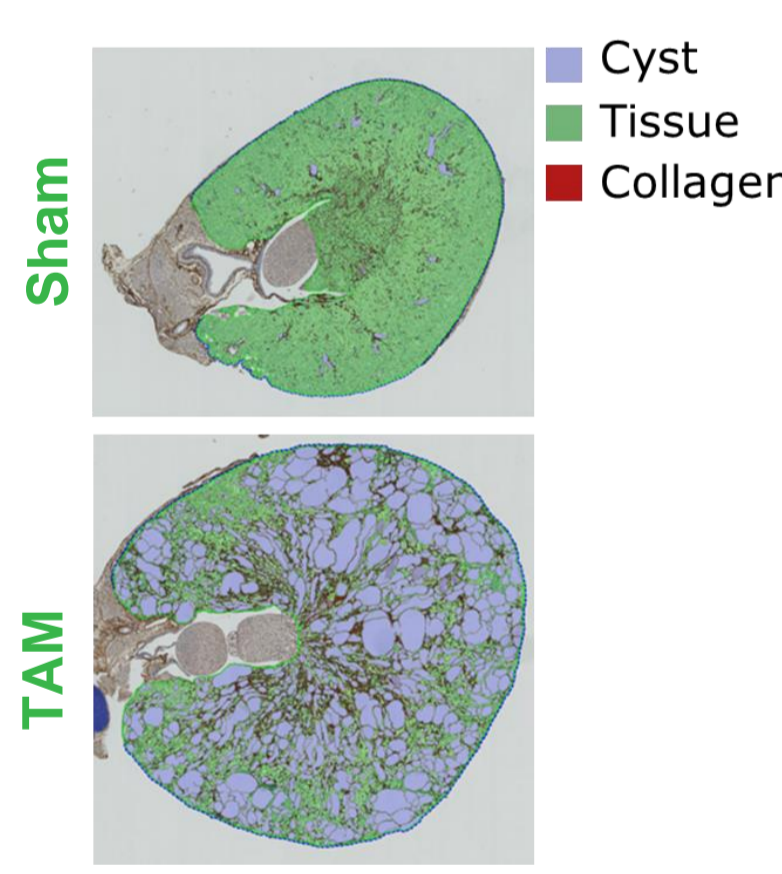


Glomerular filtration rate (GFR): kidney functionality

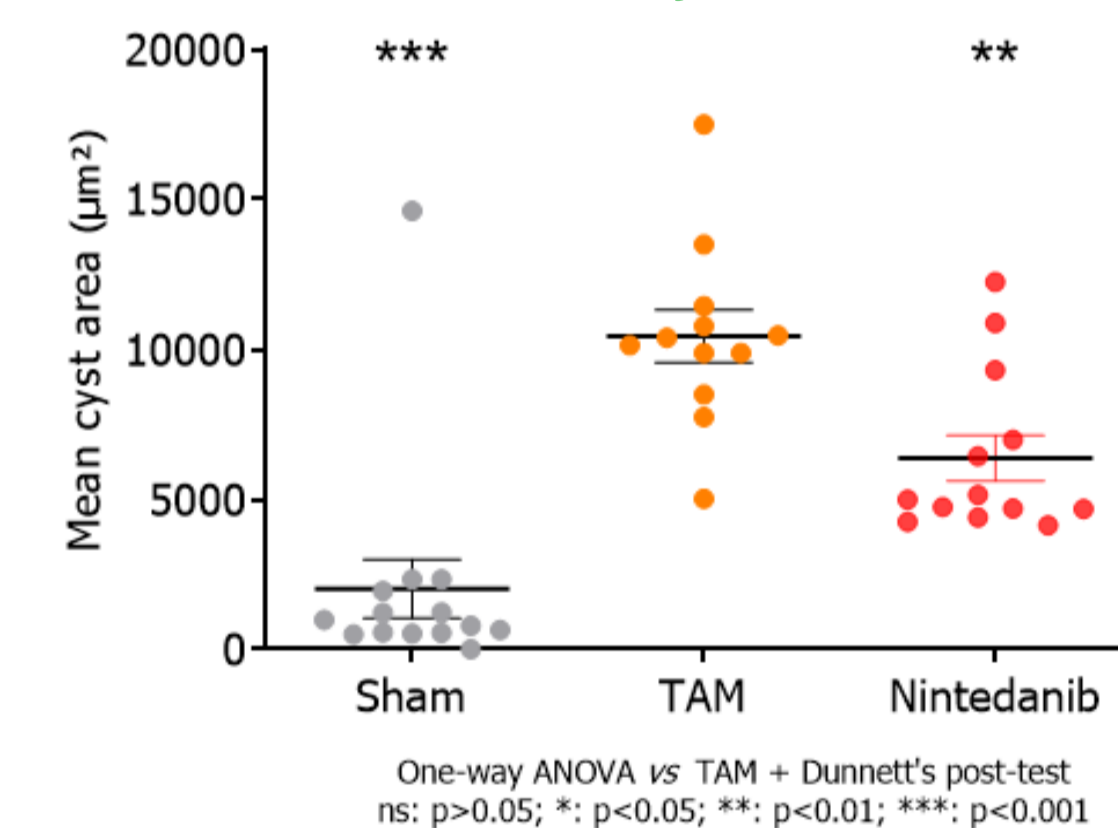
- ✓ Decreased glomerular filtration rate (GFR; kidney functionality) in the TAM-induced disease group



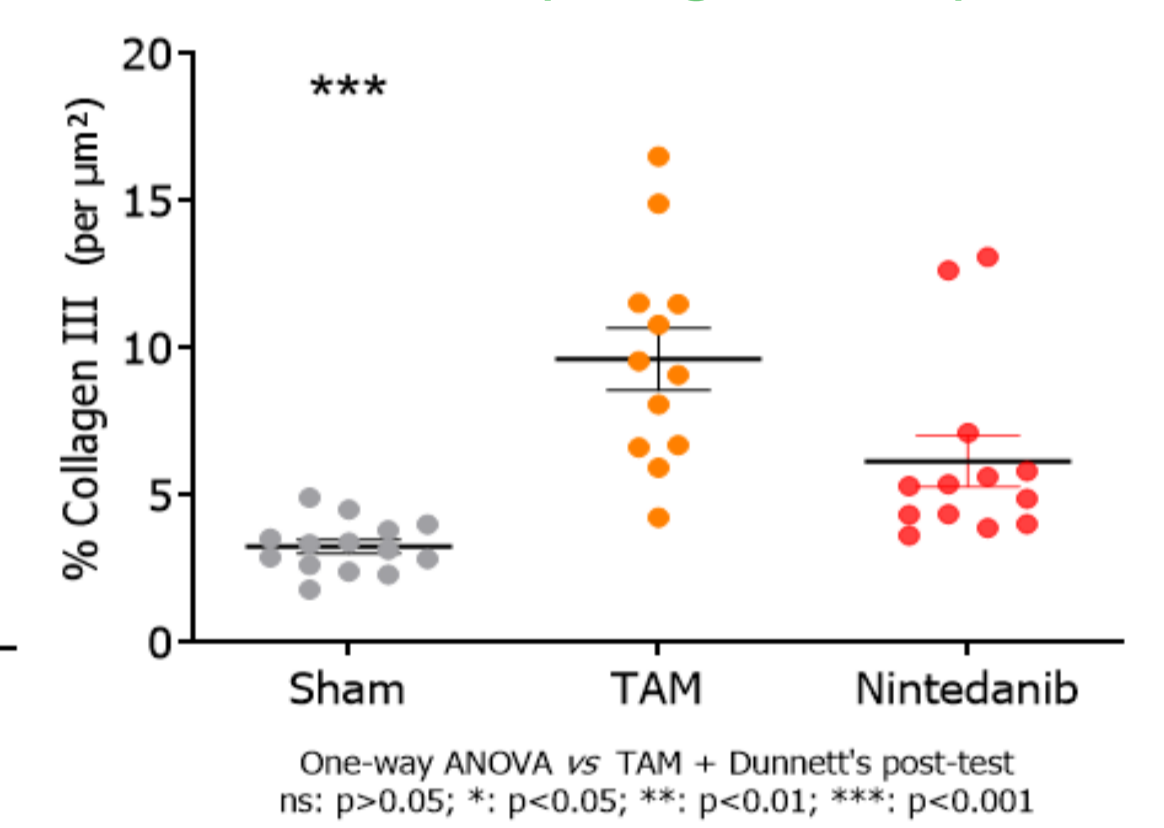
Histological analysis of PCKD model (cyst area and fibrosis)



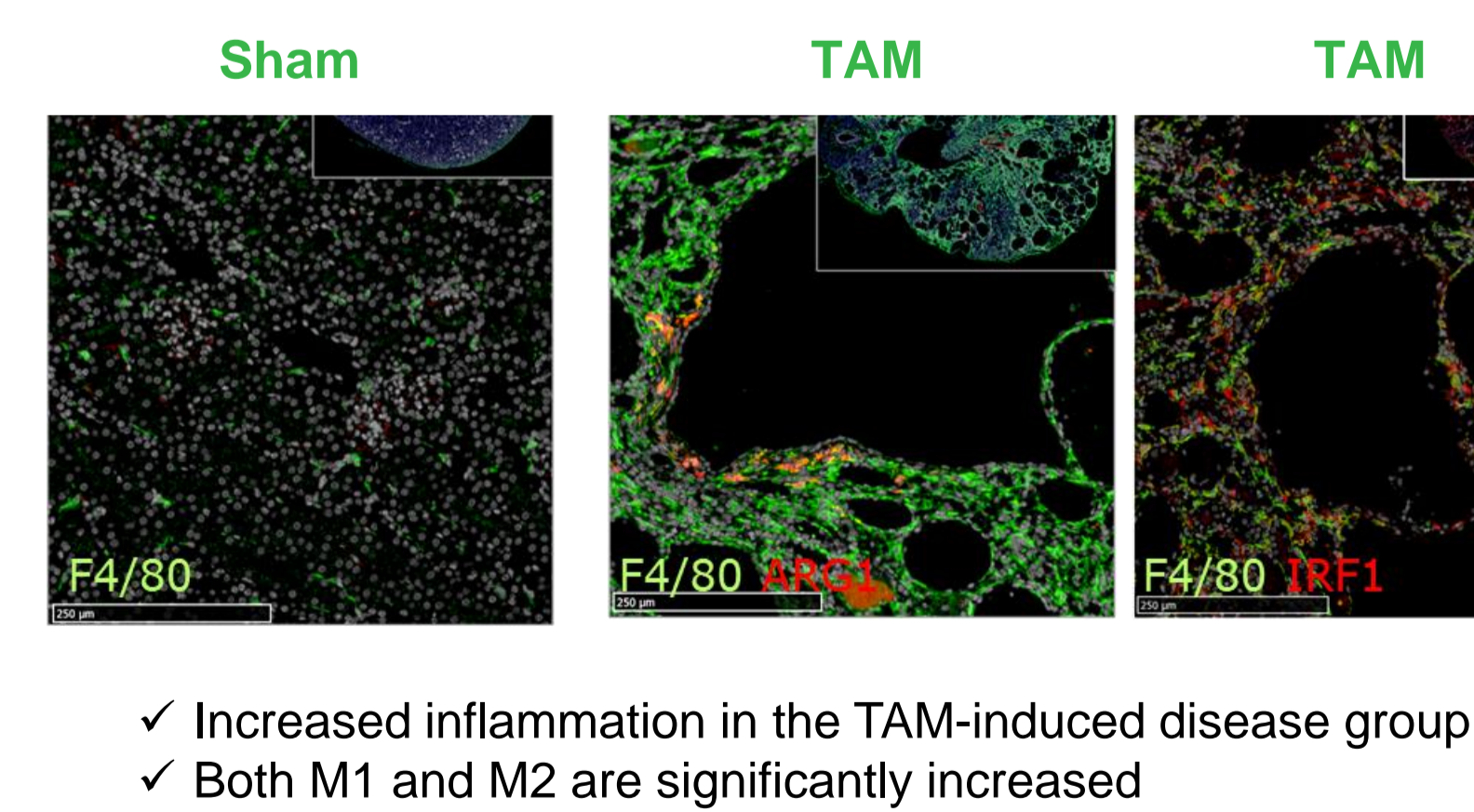
Mean cyst area



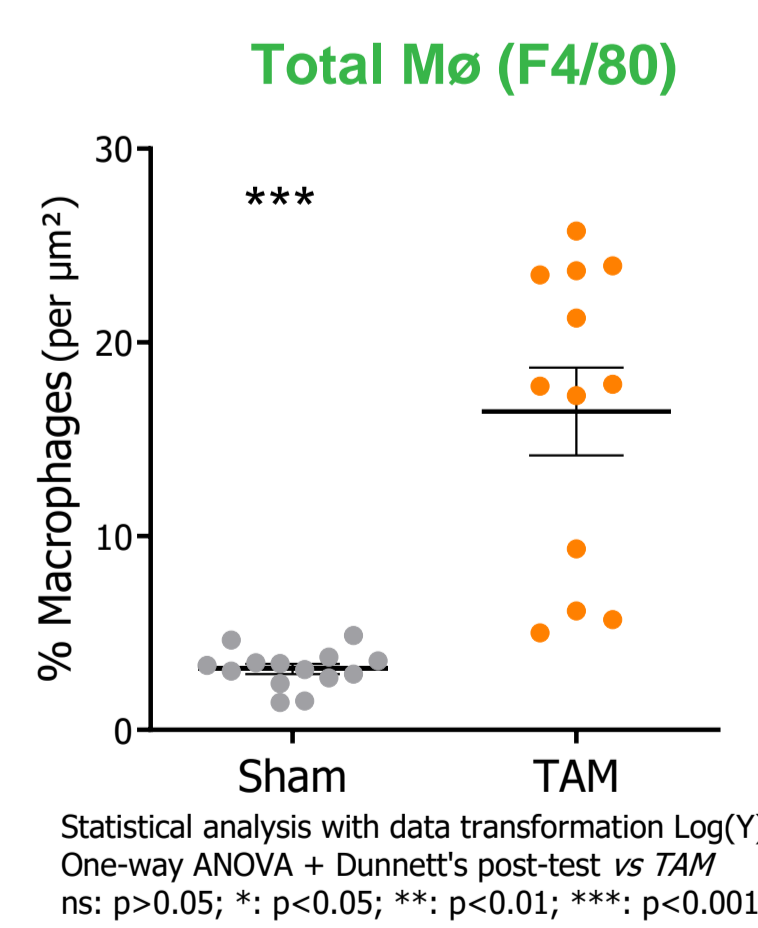
Fibrosis (collagen III IHC)



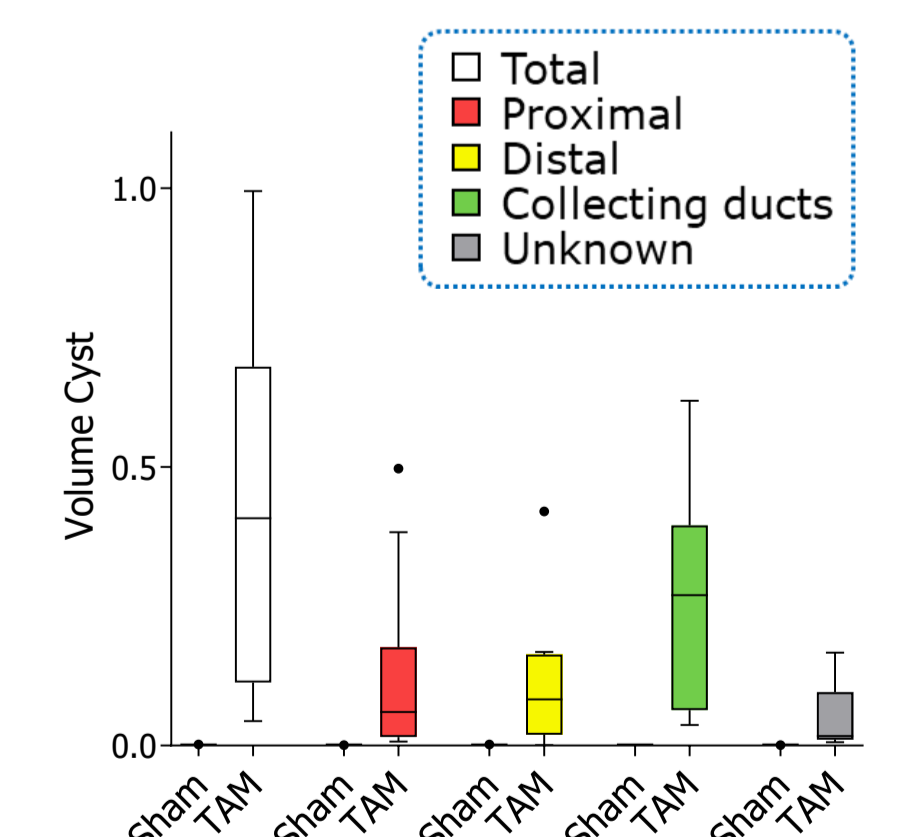
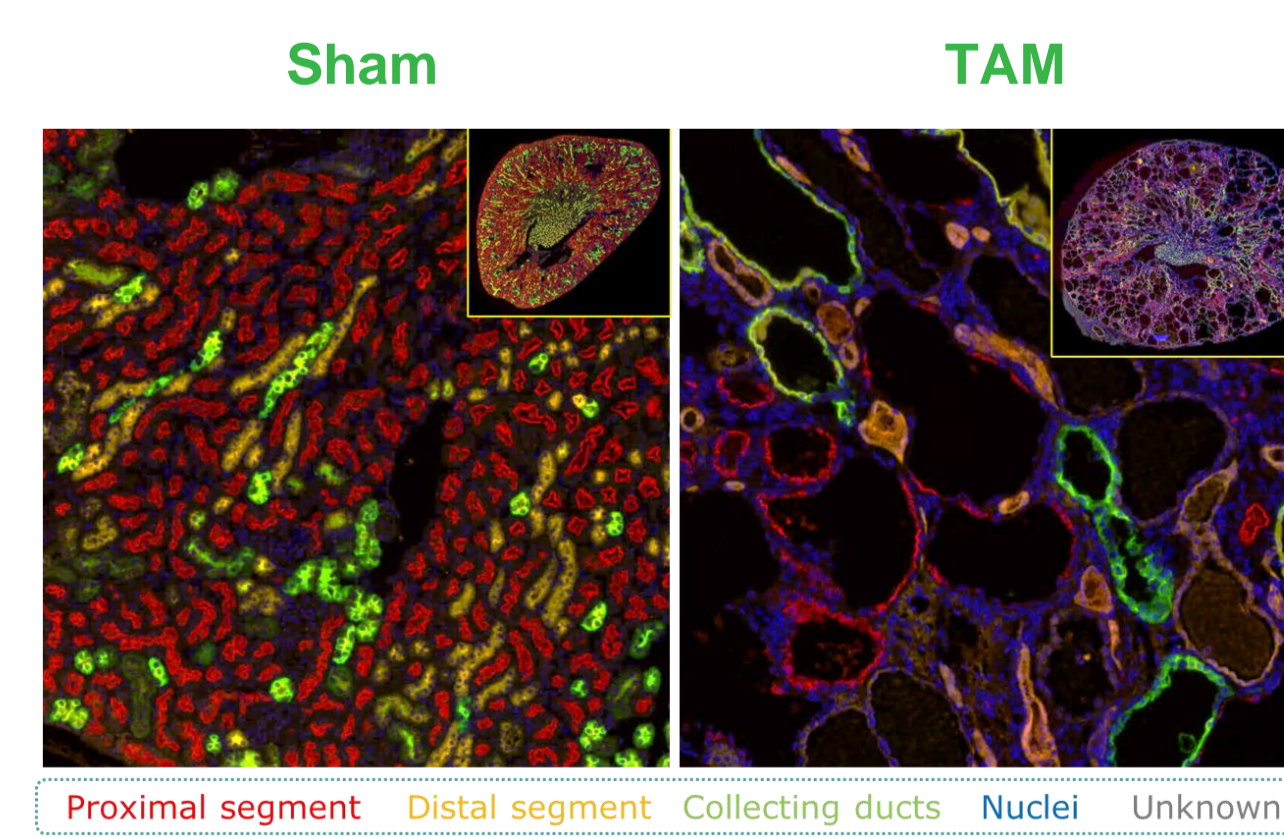
Inflammation



- ✓ Increased inflammation in the TAM-induced disease group
- ✓ Both M1 and M2 are significantly increased



Cyst origin



- ✓ Confirmation that cyst origin is mainly in the latest part of the tubule



Summary

PCKD the most relevant pre-clinical model for human ADPKD

- ✓ Ubiquitous & inducible Pkd1 KO model, representative of human ADPKD slow disease progression (kidney and liver cysts)
- ✓ Clinically relevant functional and structural readouts setup for this model
- ✓ Deep knowledge on disease mechanism: disease progression, functional and longitudinal readouts, transcriptomics, biomarkers, cyst origin, etc.
- ✓ Both preventive and therapeutic settings available
- ✓ Rapid progression model (induction before day 16 of life) also available (not shown in this poster)