

Remodeling of the Glomerular Tuft in Proteinuric Kidney Disease

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Background

Proteinuria is a marker of ongoing kidney disease, is tubulotoxic, and is prognosticative for end stage renal disease. Glomerular hypertrophy and glomerulosclerosis are hallmark features of glomerular disease. Renal ablation in adriamycin-treated rats was associated with glomerular hypertrophy and near doubling of tuft volume. Glomerular hypertrophy has been identified as an integral feature of hypertensive nephropathy and appears to precede rather than compensate for glomerulosclerosis. Glomerular expansion is associated with relapse in adult patients with minimal change disease (MCD). In fact, in MCD glomerular expansion precedes and predicts subsequent progression to focal segmental glomerulosclerosis (FSGS). A direct correlation has been observed between the number of hypertrophied vs. scarred glomeruli, and glomerular hypertrophy in FSGS is associated with more rapid progression to end-stage renal disease. Together these data support the pathogenic importance of glomerular hypertrophy in glomerular disease. Nevertheless, there is little or no investigation into the relationship between changes in glomerular structure and proteinuria. The present study sought to quantify changes in glomerular morphometry accompanying proteinuric kidney disease.

Methods

Adult male Wistar rats (sensitive strain, ~75 g) were administered puromycin aminonucleoside (PAN, 167 mg/kg, n=8) or water (n=3, sham cohort). On day 14 after PAN administration, 24-hour urine was collected for determination of proteinuria and albuminuria. Left kidneys were removed, sectioned and stained with periodic acid Schiff (PAS) and glomeruli (14 per kidney) photographed at 40X. Areas of the Bowman's capsule and glomeruli were measured using ImageJ by an observer blinded to the experiment groups and the area of the Bowman's space calculated.

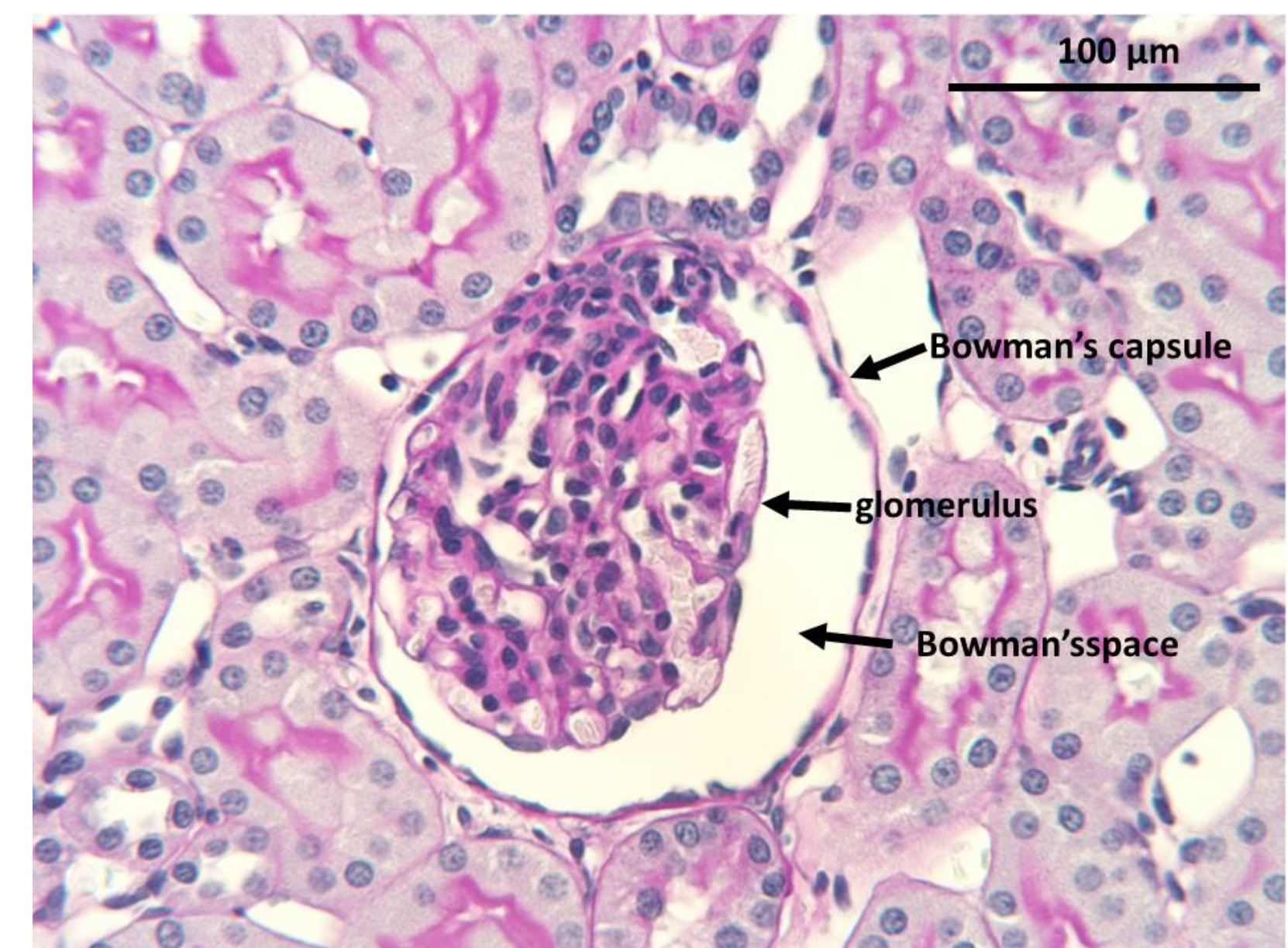


Figure 1. Glomerulus. Image (40X) of a PAS-stained rat kidney showing the Bowman's capsule, the Bowman's space and glomerulus.

Results

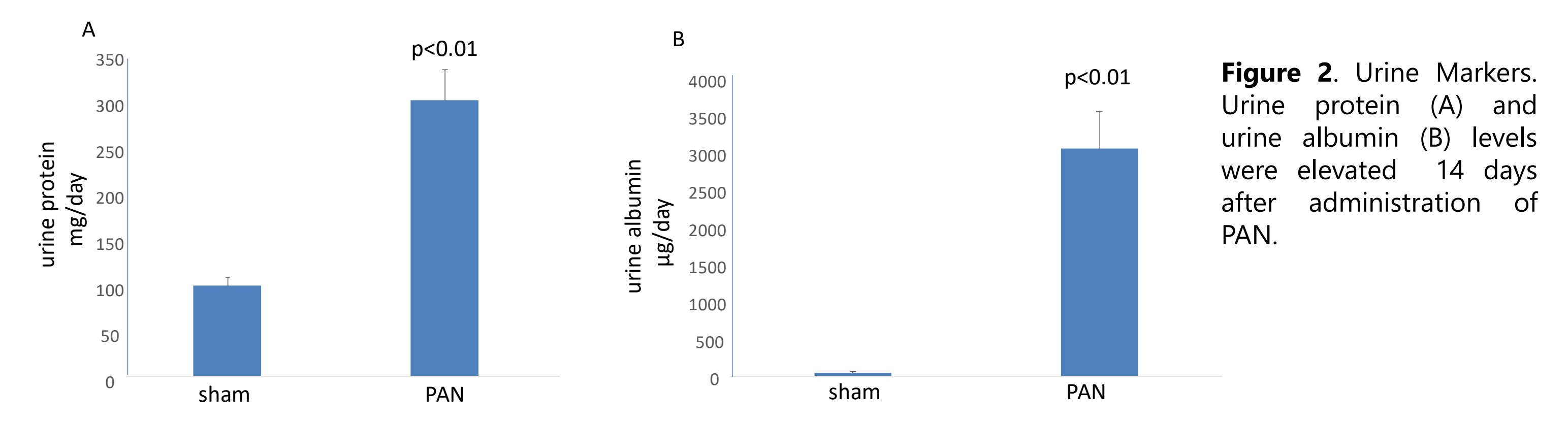


Figure 2. Urine Markers. Urine protein (A) and urine albumin (B) levels were elevated 14 days after administration of PAN.

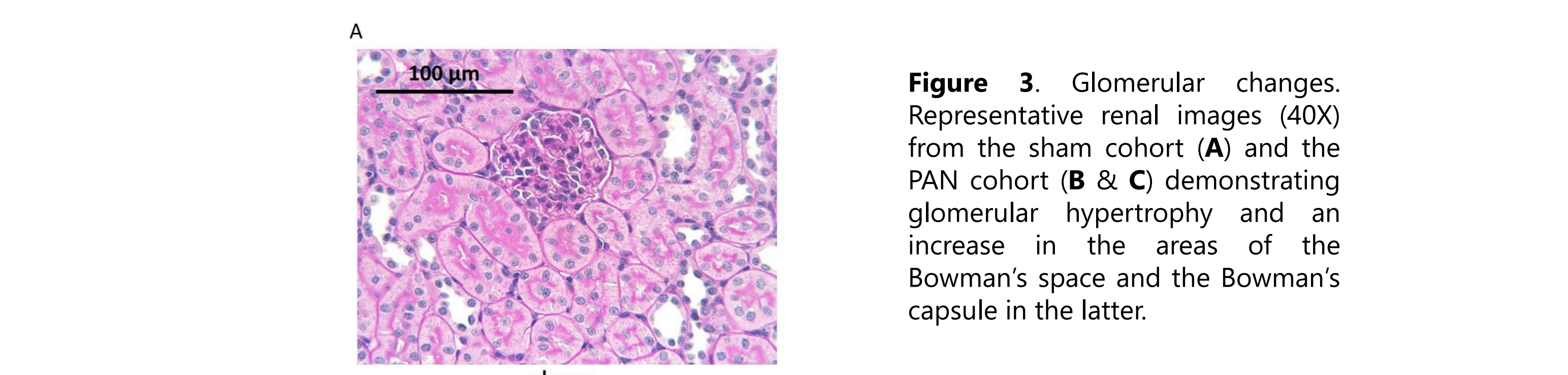


Figure 3. Glomerular changes. Representative renal images (40X) from the sham cohort (A) and the PAN cohort (B & C) demonstrating glomerular hypertrophy and an increase in the areas of the Bowman's space and the Bowman's capsule in the latter.

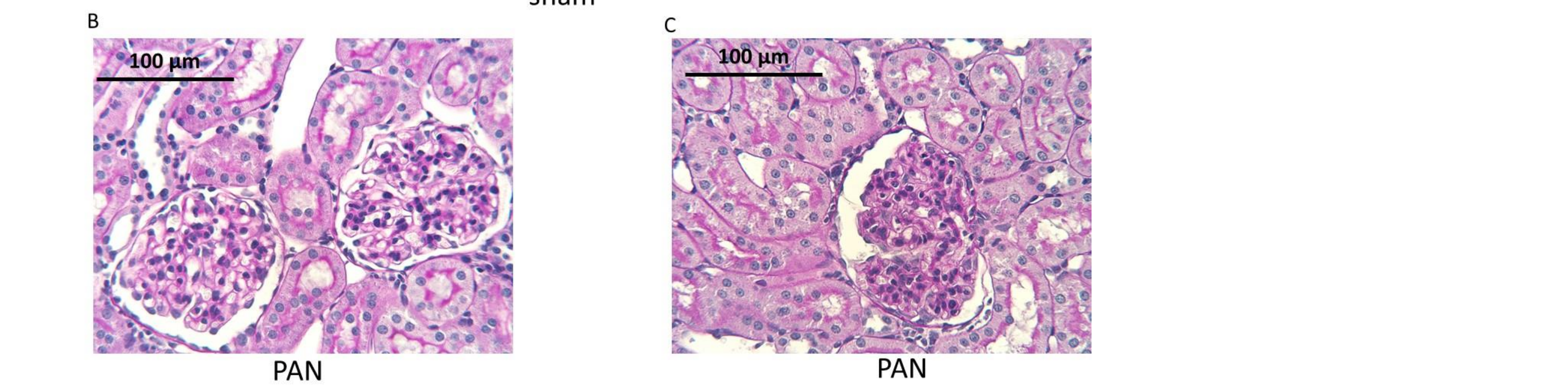


Figure 4. Glomerular morphometry. Compared to the sham cohort (A) kidneys from the PAN cohort (B & C) exhibited glomerular hypertrophy and an increase in the areas of the Bowman's space and the Bowman's capsule.

Results (2)

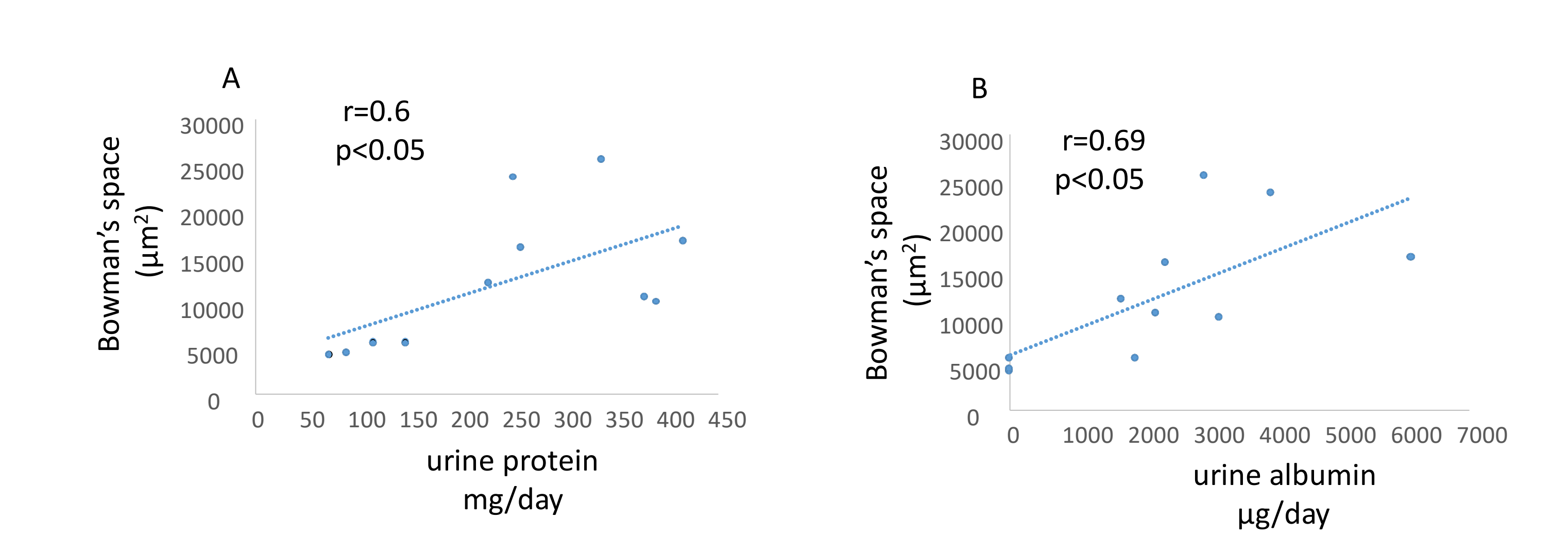


Figure 5. Urine protein/albumin & the Bowman's space. A significant and direct correlation is evident when urine protein (A) or urine albumin (B) is plotted against the area of the Bowman's space.

Summary

In PAN-administered rats, proteinuric kidney disease is accompanied by significant changes in glomerular morphometry, specifically expansion of both the Bowman's capsule and the Bowman's space, and glomerular hypertrophy. Interestingly, levels of both proteinuria and albuminuria directly correlated with area of the Bowman's space. Since MCD & FSGS are biopsy-driven, these findings are clinically significant as the extent of glomerular remodeling might inform disease outcome.

References

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