

Defects in renal papillary repair after reversible ureteric obstruction

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Background: Ureteric obstruction (UO) is a common clinical problem that results in chronic renal defects, but the cellular repair processes post-UO reversal are unclear. Using a mouse model of reversible unilateral UO (RUUO), our lab previously saw a decrease in urinary concentrating capacity 3 months post-RUUO, suggesting persistent defects in renal papillary (RP) function, which normally regulates urine concentration. The following studies evaluated the extent and kinetics of RP repair using RUUO mice.

Methods: a) Kidney sections were examined by immunofluorescence microscopy using antibodies and lectins detecting RP urinary concentrating structures: Loop of Henle (LOH) AQP1; collecting duct (CD) AQP2; Distal CD and CD-intercalated cell, LTL-Lectin; b) cell repair in normal controls, 0, 3, 7, 14, and 28 days post-RUUO, using Ki67 antibodies to detect proliferating cells. Immunofluorescence was quantified post-blinding by surface area (AQP1/AQP2/LTL), and cell numbers (Ki67), on proximal and distal renal papilla (PRP/DRP) images using ImageJ and QPath software.

Results: a)DRP showed decreased AQP1/AQP2 and consistent LTL expression at day 28. By day 84 DRP AQP2 was restored but AQP1 remained decreased; b) Ki67+ cells peaked at day 7 in PRP, however, DRP Ki67+ cells peaked earlier from days 0-7.

Conclusions: Transient AQP2 loss and persistent AQP1 loss in the DRP suggests complete repair of CD but partial repair of LOH post-RUUO. Earlier induction of Ki67-marked cellular repair in the DRP vs. PRP suggests different repair mechanisms. Further work is planned to study the mechanisms of repair of DRP vs. PRP.