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Reversal of epithelial to mesenchymal transition following relief of unilateral ureteral obstruction in the rat

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Background: Renal fibrosis begins with renal tubular epithelial mesenchymal transition (EMT); the progression thereafter depends upon a number of fibrotic factors. Unilateral ureteral obstruction (UUO) is a well-described model of EMT. We used an improved reversible unilateral ureteral obstruction (RUUO) model to investigate whether a progressive renal injury model of EMT could be reversed into the opposite direction, into mesenchymal-epithelial transition (MET) after relief of UUO in rats.

Methods: Rats were subjected to UUO or sham operation and the obstruction was removed five days later (or was left in place). Rats developed EMT after reversal of 2 or 4 weeks of ureteral obstruction as assessed by the expressions of fibrotic factors, EMT and MET markers in this post-obstructive model.

Results: We found a significant decrease in the kidney weight and renal cortical thickness in the UUO group compared with the sham groups. This rise in the RUUO group was significantly reduced. The elevated level of TGF-β1, TGF-β receptors and core fucosylation in the UUO group was significantly reduced in the RUUO groups. The EMT markers staining showed results parallel to those of TGF-β1 expression levels. In addition, UUO rats exhibited pronounced inflammatory and intrinsic proliferative cellular responses, and ultimately fibrosis. By comparison, RUUO mice had more controlled and measured extrinsic and intrinsic responses to EMT with a return to MET within several weeks after release of ureteral obstruction.

Conclusion: Our findings provide a model that allows investigation of the fibrotic factors during reversal of EMT that contribute to the development of fibrosis. EMT of the progressive renal injury could be actively reversed into MET and renal architecture is better maintained throughout injury and recovery from injury after relief of UUO in rats.

Keywords: epithelial mesenchymal transition, mesenchymal-epithelial transition, Unilateral ureteral obstruction