Sox9 Activation Highlights a Cellular Pathway of Renal Repair in the Acutely Injured Mammalian Kidney.

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Public Summary:
After acute kidney injury (AKI), surviving cells within the filtering nephron proliferate and repair. We screened injured mouse kidneys to identify regulatory genes linked to this repair process identifying a member of the Sox family, Sox9, as new factor in the injury/repair response. Sox9 encodes a regulatory factor known to control gene activity in other cell types. Mapping the relationship between Sox9 activation and nephron repair showed Sox9+ cells are the main cell source for renal repair and Sox9 is itself critical for a normal repair process. Further study of Sox9 action is predicted to give important insights into the mechanisms that switch surviving cells from functional to reparative mode in the injured kidney.

Scientific Abstract:
After acute kidney injury (AKI), surviving cells within the nephron proliferate and repair. We identify Sox9 as an acute epithelial stress response in renal regeneration. Translational profiling after AKI revealed a rapid upregulation of Sox9 within proximal tubule (PT) cells, the nephron cell type most vulnerable to AKI. Descendants of Sox9(+) cells generate the bulk of the nephron during development and regenerate functional PT epithelium after AKI-induced reactivation of Sox9 after renal injury. After restoration of renal function post-AKI, persistent Sox9 expression highlights regions of unresolved damage within injured nephrons. Inactivation of Sox9 in PT cells pre-injury indicates that Sox9 is required for the normal course of post-AKI recovery. These findings link Sox9 to cell intrinsic mechanisms regulating development and repair of the mammalian nephron.