

Macrophage Heterogeneity Regulates Kidney Injury and Repair

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The ischemically injured kidney undergoes tubular cell necrosis, apoptosis, and an interstitial inflammatory cell infiltrate. In the current study we demonstrate that classically activated M1 macrophages are the major form of macrophage present in the first 48 hours after injury, whereas alternatively activated, M2 macrophages predominate at later time points. Depletion of macrophages prior to renal ischemia/reperfusion diminishes kidney injury. Infusion of M1 macrophages, but not M2, increases the initial injuries to that seen in control animals, demonstrating that M1 activated cells selectively augment ischemic tubule injury. The appearance of M2 macrophages correlates with the proliferative phase of repair, and in vitro studies demonstrate that M2 macrophages, but not M1, stimulate renal tubular cell proliferation. Further, it is shown that renal tubular cells can induce an M1 to M2 phenotypic switch in vitro, and that M1 activated cells injected after injury can switch to an M2 expression pattern in vivo. Depletion of macrophages at 3–5 days after ischemia/reperfusion injury, when M2 cells predominate, leads to a marked reduction in tubular cell proliferation and slowing of tubule repair. Cumulatively these studies demonstrate that a phenotypic switch from M1 to M2 macrophages regulates the transition from tubule injury to tubule repair.