Topic	The role of macrophages in AKI to CKD transition
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Macrophages play an important role in both the development and recovery from acute kidney injury (AKI). They exhibit distinct phenotypes, broadly characterized as proinflammatory M1 and tissue reparative M2 phenotypes and early studies using various depletion strategies have shown that M1 macrophages promote tubular injury while M2 macrophages promote tubular rengeneration during the normal repair.

By using ischemia/reperfusion injury (IRI) in aged mice model, we recently demonstrated that senescent tubule cells with growth arrest phenotype led to defective polarization of macrophages toward persistent M1 phenotype during the recovery phase of IRI. This altered macrophage phenotype in aged mice exacerbate the progressive fibrosis, showing the important role of microenvironment in macrophage polarization as well as recovery from AKI.

While reparative M2 macrophages are critically required for normal repair during the recovery process, recent studies have shown that persistence of M2 macrophage could also promote progressive fibrosis after IRI. Macrophages in later time point after IRI or unilateral ureteral obstruction (UUO) have been shown to exhibit profibrotic gene profile. In murine models of IRI, we demonstrated that predominant macrophage population during the late recovery phase (day 7) exhibit M2 phenotypes and depletion with liposome clodronate attenuated fibrosis. Adoptive transfer of in vitro polarized M2c macrophage partially restore the fibrosis, showing that persistence of M2 macrophages are important in AKI to CKD transition. We also recently identified increased number of macrophages in 72 cases of human biopsy series of acute tubular necrosis (ATN) and observed that the density of CD163+ human M2 macrophage could predict non-recovery of AKI.

For the last several decades, our understanding of the role of macrophages in AKI has expanded. However, more studies are needed to better understand heterogenous macrophage origin, recruitment, activation, fate, and also crosstalk with intrarenal microenvironment to move forward to development of therapeutic targets.