Why do kidneys fail to repair?

Summary
The kidney has the capacity to repair from a transient insult, whereas the kidneys sometimes fail to repair and progress to chronic injury with fibrosis. The mechanism of kidney repair and the determinants of kidney prognosis remain unclear.

Proximal tubules are mainly damaged in various types of kidney injury. Recently we generated proximal tubule specific CreERT2, performed lineage tracing, and demonstrated that damaged proximal tubules are repaired by the proliferation of surviving proximal tubules (J Pathol 2015). In severe injury, however, the repaired proximal tubules become shorter, indicating the incomplete repair.

We further analyzed the impact of proximal tubule injury on other segments of the kidney, and showed that proximal tubule injury can induce the transdifferentiation of fibroblasts to myofibroblasts, leading to renal fibrosis (J Clin Invest 2011, J Am Soc Nephrol 2016).

Kidney injury in the elderly is often irreversible and leads to chronic kidney disease, however, the mechanism of impaired repair process in aged kidney has not been fully investigated. Recently, we demonstrated that aged mice, but not young mice, developed multiple renal tertiary lymphoid tissues (TLTs) after kidney injury (JCI Insight 2016). TLT size was associated with impaired renal function and increased inflammation, and, the removal of TLTs improved renal outcomes. Importantly, aged but not young human kidneys also form TLTs similar to mouse TLTs. These results indicate that the inhibition of TLT formation may offer a novel therapeutic strategy for kidney injury in the elderly.