Topic	Intervening on AKI to CKD
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The incidence of acute kidney injury (AKI) continues to rise. World-wide the estimated occurrence of AKI is 20–200 per million population in the community and the mortality is ~50% of patients admitted to the intensive care unit (ICU). In those patients with AKI who survive there is an increased risk of developing chronic kidney disease (CKD) and end-stage renal disease (ESRD). Recent studies have begun to elucidate the importance of the endothelium in the initiation and progression of fibrosis. Studies on human biopsies have associated microvascular rarefaction with progressive renal failure. Renal endothelial injury can result in a reduction of capillary density, called capillary rarefaction, occurring several weeks after AKI which may be due to hypoxia and a lack of upregulation of VEGF in response to injury. Capillary rarefaction may in turn affect tubular epithelial cells, (myo)fibroblasts, and inflammatory cells, leading to tubulointerstitial fibrosis. There is evidence that epigenetic changes are closely related to renal hypoxia and CKD progression.

During kidney recovery, renal and extrarenal cells participate in the wound healing response and can initiate fibrosis. Immune cells of the mononuclear phagocyte system, including macrophages and dendritic cells not only contribute to injury but have emerged as important cells in the recovery of kidney function during adaptive repair or fibrosis during maladaptive repair. It is the balance between wound healing and progressive fibrosis that dictates the final outcome. The intrinsic plasticity of monocytes/macrophages and dendritic cells as well as attempts to relate in vitro studies to in vivo findings makes the functional definition and phenotype of this myeloid population in kidney pathophysiology complex.

A key feature is the activation of extracellular matrix-producing myofibroblasts. Other factors important in CKD progression include endothelial cell damage and vascular damage in AKI, hypoxia-HIF, innate and adaptive immunity, cell cycle arrest and epigenetic mechanisms.

Numerous therapeutic approaches are in development, including some agents in clinical trials for diabetic nephropathy and other kidney diseases but as yet there are no approved treatments to prevent the development of kidney fibrosis or accelerate repair. The development of effective treatments requires a better understanding of the inflammatory, injury, wound healing, matrix deposition and cellular repair processes that accompany fibrosis. This presentation will focus on potential therapeutic targets on AKI to CKD transition.