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Therapeutic Target of Kidney Diseases: From Bench to Bedside

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This presentation explores innovative therapeutic strategies for kidney disease, bridging the gap between fundamental molecular research and clinical applications. We first identify the Farnesoid X receptor (FXR) as a critical regulator against renal fibrosis. Our research reveals a novel Src-mediated cross-talk between FXR and YAP in the pathogenesis of kidney injury, where FXR activation promotes an FXR-Src interaction that reduces Src phosphorylation. This modulation enhances Hippo pathway core kinase activity, leading to increased YAP phosphorylation and cytosolic sequestration, thereby suppressing pro-fibrotic gene expression. Furthermore, we discuss the significant role of dietary potassium in renoprotection; by modulating physiological responses, adequate potassium intake helps mitigate the decline in the glomerular filtration rate (GFR) and improves renal survival. These findings underscore the roles of the FXR-YAP axis and potassium-mediated signaling in protecting against both acute and chronic kidney injuries. Finally, we highlight nanomedicine-based targeting strategies designed to enhance therapeutic efficacy within the injured parenchyma. We developed hydrophobically modified glycol chitosan (HGC) nanomicelles for the targeted delivery of Tacrolimus and Olmesartan, effectively mitigating inflammation, fibrosis, and apoptosis in models of lupus nephritis and Alport syndrome. Additionally, an inflammation-sensing, ROS-responsive nanozyme platform (PTCM) and a CD44-targeting hyaluronic acid-conjugated nanoplatform (P/HA/rGO) were engineered to ensure precise drug delivery to ischemic/reperfusion-injured kidneys. Collectively, these findings provide a comprehensive perspective on kidney therapy, offering validated molecular targets and sophisticated delivery technologies to combat the global burden of renal disease.

Keywords: Kidney, Therapy, Target