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Targeting tyrosine kinase receptors as the treatment of renal fibrosis

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Abstract

The pathogenesis of chronic kidney disease (CKD) involves a complex interaction of hemodynamic and inflammatory processes that leads to a final common pathway to renal fibrosis, which is characterized by activation of renal fibroblasts and accumulation of excessive amounts of extracellular matrix (ECM) proteins. Activation of several tyrosien kinase receptors including epidermal growth factor receptor (EGFR), platelet derived grwoth factor receptors (PDGFR) and vascular growth factor receptors (VEGFR) has been reported to be involved in renal fibrogenesis. Recently, we demonstrated that treatment of cultured renal interstitial fibroblasts with suramin, a compound that inhibits the interaction of several growth factors with their receptors, inhibited their activation. In a mouse model of obstructive nephropathy, administration of a single dose of suramin immediately after ureteral obstruction abolished the expression of fibronectin, largely suppressed expression of α-SMA and type I collagen, and reduced the deposition of extracellular matrix proteins. Suramin also decreased the expression of multiple cytokines including TGF-β1 and reduced the interstitial infiltration of leukocytes. Moreover, suramin blocked phosphorylation of the EGF and PDGF receptors, and inactivated several signaling pathways associated with the progression of renal fibrosis. In a rat model of CKD, suramin abrogated proteinuria, limited the decline of renal function, and prevented glomerular and tubulointerstitial damage. Moreover, delaryed adminsteration of suramin also significantly attenuate progression of renal fibrosis. These findings indicate that inhbition of tyrosine kinase receptors with suramin may have therapeutic potential for patients with fibrotic kidney diseases.

Biography

Shougang Zhuang has completed his residency and renal fellowship in China and PhD from Yokohama City University, and postdoctoral studies from Harvard Medical School. He is an Associate Professor at Brown University and the director of Kidney Research at Rhode Island Hospital. He has published 81 papers in peer–reviewed journals and has been serving as an editorial board member of three Journals.