SIGNIFICANCE STATEMENT

Nephron damage triggers the activation of interstitial stromal fibrogenic cells, leading to progressive scarring and contributing to loss of kidney function. The signals that drive this process are not well understood. Here, we identified a molecular mechanism by which IL-1β, a major innate inflammatory cytokine, regulates the metabolism of kidney stromal cells. Mechanistically, IL-1β signaling *via* the IL-1 receptor–associated kinase 4 results in stabilization of the oncoprotein MYC and upregulation of MYC target genes, including cell cycle regulators and glycolysis enzymes. Inhibition of the pathway *in vivo* prevented fibrosis and reduced tubular injury, highlighting the therapeutic value of this novel profibrogenic molecular pathway.