SIGNIFICANCE STATEMENT

Tubulointerstitial fibrosis is associated with reduced expression of genes required for fatty acid oxidation (FAO) in renal tubular cells. Decreased FAO is proposed to cause energy deficiency and renal fibrosis. Phosphorylation of acetyl-CoA carboxylase (ACC) is a major controller of FAO. The energy-sensing AMP-activated protein kinase (AMPK) phosphorylates ACC to increase FAO and ATP generation. In this study, phosphorylation of ACC declined after kidney injury. This is likely to be deleterious, because transgenic mice with impaired ACC phosphorylation demonstrated increased fibrosis and lipid accumulation. Metformin increases phosphorylation of ACC, but this effect was absent in the ACC transgenic mice. These data suggest that metformin reduces renal fibrosis by improving lipid availability for energy generation from fatty acids in renal tubular cells.