SIGNIFICANCE STATEMENT

The conflicting roles of TGF-β create a dilemma in the treatment of human fibrotic diseases; targeting TGF-β, the principal profibrotic factor, to prevent fibrosis will also abolish its protective anti-inflammatory effects. Similarly, the use of TGF-β to reduce inflammation is prevented by its strong profibrotic effect. This study reveals for the first time that redirecting TGF-β signaling *via* β-catenin/Foxo dissociates the profibrotic from anti-inflammatory effects of TGF-β. Targeting β-catenin/Foxo provides a novel therapeutic strategy, allowing the use of TGF-β to reduce both inflammation and fibrosis.