SIGNIFICANCE STATEMENT

Impaired resolution of inflammation underlies chronic conditions, including microvascular complications of diabetes such as diabetic kidney disease (DKD). Lipoxins (LXs) are lipid mediators that promote the resolution of inflammation. Here, we investigated the potential of LXA4 and a synthetic LX analogue (Benzo-LXA4) as therapeutics in a murine model of DKD (streptozotocin diabetic $ApoE^{-/-}$ mouse). The development of diabetes-induced albuminuria, mesangial expansion, and collagen deposition was attenuated by LXs. Kidney transcriptome profiling defined a diabetic signature, and LX-mediated transcriptome responses. Using human renal epithelial cells, we demonstrate that LXs attenuate Egr-1 activation. These data demonstrate for the first time that LXs can reverse established diabetic complications and support a therapeutic paradigm to promote the resolution of inflammation.