SIGNIFICANCE STATEMENT

Low urinary citrate is an important risk factor for nephrolithiasis. Citrate is freely filtered by glomerulus, and it is reabsorbed along the proximal tubule *via* the Na^+-dicarboxylate cotransporter NaDC-1. NaDC-1 activity is one of the determinants of urine citrate levels, and it is regulated by systemic acid-base status. This study describes the signaling pathway mediating the acid-induced increase in NaDC-1 activity. We have previously shown that acid stimulation of NaDC-1 is mediated by endothelin-1 trough endothelin B receptor (ET_B). Using a cell model of proximal tubule and Pyk2 null mice, this study shows that acid stimulation of NaDC-1 activity requires two parallel pathways, Pyk2-c-Src and Raf1-ERK1,2-p90RSK, both not located downstream of ET-1/ET_B signaling.