

SIGNIFICANCE STATEMENT

In kidneys from patients with autosomal-dominant polycystic kidney disease (ADPKD) macrophage infiltration is prominent, but the role of macrophages in disease development is not well understood. This study revealed that macrophages with high expression levels of arginase-1 (ARG1) significantly promoted cyst enlargement in polycystic kidney disease (PKD) mice and that the proliferative function of macrophages was closely related to activation of the arginine-polyamine metabolic pathway. Further, L-lactic acid was secreted from cysts, stimulating macrophages to upregulate ARG1. These findings indicate that ARG1 is a novel potential therapeutic target for ADPKD and deepen our understanding of the interactions between macrophages and cysts in the polycystic kidney microenvironment.