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Lansoprazole reduces renal cyst in polycystic kidney disease via inhibition of cell proliferation and fluid secretion

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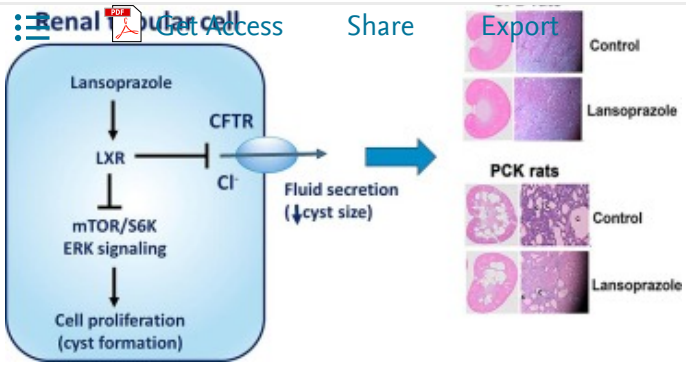
Abstract

Renal cyst development and expansion in autosomal dominant polycystic kidney disease (ADPKD) is mediated by abnormal cyst-ling cell proliferation and fluid accumulation. Liver X receptor (LXR)-activating ligands suppresses renal cyst enlargement by modulation of cysticfibrosis transmembrane conductance regulator (CFTR)-mediated fluid accumulation. Lansoprazole has been reported as agonist of LXR, and shows an anti-proliferative effect in cancer cells. Here, lansoprazole's pharmacological effect and underlying mechanism on renal cyst development and expansion in *in vitro*; human ADPKD cyst-lining epithelial cell line and Type I Mardin Darby Canine Kidney (MDCK) cells, and *in vivo* models was investigated. Lansoprazole inhibited cyst development via inhibition of cell proliferation. In renal cells, lansoprazole's anti-proliferative effect was mediated by inhibition of mTOR/S6K and extracellular signal-regulated kinase (ERK) signaling proteins. In addition, lansoprazole inhibited CFTR-mediated fluid secretion via reduction of CFTR protein expression. In PCK rats, administering lansoprazole (50mg/kgBW) for 4weeks produced significant decreases in the cystic area and improved renal function by reduction of plasma creatinine and blood urea nitrogen. Inhibition of mTOR/S6K, ERK, and CFTR protein expression was observed in PCK rat kidney following lansoprazole treatment. The findings point to potential therapeutic application of lansoprazole in ADPKD.

Graphical abstract



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Keywords

Polycystic kidney disease; Fluid secretion; Liver X receptor; mTOR; Extracellular signal–regulated kinases; CFTR