KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Oral Communication Abstract
Presentation No. OC2-03 (Abstract Submission No. 2241)

Oral Communications 2 Sep. 2 (Thu), 13:40-15:40

Involvement of Mechanosensitive Channel Piezo1 in Renal Fibrosis

Xiaoduo Zhao[1], Yonglun Kong[1], Baien Liang[1], Nan Zhou[1], Jing Li[2], Jianding Cheng[1], Weidong Wang[1], Chunling Li[1]
[1]Department of Zhongshan School of Medicine, Sun Yat-sen University, China
[2]Department of The First Affiliated Hospital, Guangzhou University of Chinese Medicine, China

Objectives: The purpose of the current study is to investigate the role of Piezo1 in renal fibrosis and potential molecular mechanism.

Methods: Unilateral ureteral obstruction was performed to establish renal fibrosis model and C57BL/6J mice were treated with or without GsMTx4. Piezo1 activity was detected by whole-cell patch clamp. Fluo-4 AM probes were used to detect intracellular calcium ion levels. Polyacrylamide hydrogels were used to mimic extracellular matrix in vitro. Western blotting, RT-PCR, Masson's staining, immunofluorescence and immunohistochemistry were used to detect fibrosis and EMT levels.

Results: In human fibrotic kidneys, Piezo1 protein expression was markedly upregulated. The abundance of Piezo1 protein in kidneys of mice was instantly increased after 30 minutes of unilateral ureteral obstruction (UUO), and persistently increased at the 3rd and the 7th days after UUO. Inhibition of Piezo1 with GsMTx4 ameliorated UUO-induced renal fibrosis. Mechanical stretch induced Piezo1 activation and epithelial-mesenchymal transition (EMT) in human proximal tubular HK2 cells, as seen in increased abundance of a fibrotic marker fibronectin and decreased expression of an epithelial marker E-cadherin, which were greatly reversed by inhibition or silence of Piezo1. Similarly, in HK2 cells, TGF-β1-induced EMT was significantly inhibited by GsMTx4. Piezo1 agonist Yoda1 evoked significant cationic currents in HK2 cells, which was associated with marked EMT. In addition, the increased expression of Piezo1 protein was found when HK2 cells were cultured in stiff polyacrylamide hydrogels, mimicking the natural accumulation of ECM. Stimulation of Piezo1 by Yoda1 caused calcium influx in association with activation of calpain2 and integrinβ1. Also, Yoda1 promoted an interaction between ECM and integrinβ1 in HK2 cells.

Conclusions: Activation of Piezo1 is involved in the development of renal fibrosis and EMT in HK2 cells, likely through calcium-calpain2-integrinβ1 pathway.