KSN 2018
Seoul, Korea · May 17 - 20

Abstract Type : Poster
Presentation No. : PDO 025

Involvement of Mas receptor In Palmitic Acid-induced Impaired Autophagy and ER Stress in HK2 cells

YongLun Kong, Miaojuan Qiu, Suchun Li, Yu Lin, Xiaoduo Zhao, Chunling Li, Weidong Wang
Department of Institute of Hypertension, Zhongshan School of Medicine, Sun Yat-sen University, China

Objectives: The local renin-angiotensin system in the kidney plays an important role in development of obesity-related kidney diseases. The purpose of current study was to investigate the role of Mas receptor in the injuries of proximal tubular epithelial cells induced by saturated fatty acid palmitic acid (PA).

Methods: $Mas^{-/-}$ mice and $Mas^{-/-}$ human proximal tubule HK2 cells were generated by CRISPR/Cas9 system, Westernblot and immunofluorescence were used to detect the protein expression of autophagy and ER stress markers.

Results: In human proximal tubule HK2 cells, PA (0.4mM) treatment induced increased LC3B and LAMP1 protein expression at 3h, suggesting an activation of autophagy. At 12h after PA treatment, LAMP1 expression was markedly reduced, indicating an impaired autophagy flux and accumulation of autophagosome. This was associated with upregulated BIP and CHOP protein expression, markers of endoplasmic reticulum stress (ER stress). The activation of Mas receptor by Ang (1-7) (an endogenous ligand) or AVE0991 (a synthetic specific Mas receptor agonist) enhanced autophagosome accumulation and ER stress caused by PA treatment for 24 hours in HK2 cells, whereas A779 (a synthetic specific Mas inhibitor) attenuated PA-induced autophagosome accumulation and ER stress. The impaired autophagy flux and ER stress were also relieved in $Mas^{-/-}$ HK2 cells treated with PA, when compared with $Mas^{+/+}$ HK2 cells. Mas gene knockout was also associated with reduced reactive oxygen species (ROS) production in HK2 cells. Moreover, $Mas^{-/-}$ HK2 cells showed better cell vitality and proliferation with PA treatment than $Mas^{+/+}$ HK2 cells. In wild type HK2 cells, PA caused elevated intracellular calcium levels, which was markedly prevented in $Mas^{-/-}$ HK2 cells,indicating an involvement of Mas- mediated calcium signalings in PA-induced injury of HK2 cells.

Conclusions: Mas receptor mediated PA-induced impaired autophagy and ER stress in HK2 cells, likely contributing to tubular injuries seen in obesity-related kidney diseases.