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

Abstract Submission No. : 2134

Transglutaminase 2 correlates with severity of kidney disease in CKD patients.

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Objectives:

Transglutaminase 2 (TG2) is a calcium dependent enzyme of the protein- glutamine γ-glutamyltransferases family that associated with fibrosis in CKD. The purpose of this study is to identify the relationship between expression of TG2 and the CKD progression in human kidney tissues, and to determine the biological activity of TG2 and TGFβ associated pathways in vitro and in vivo models.

Methods:

We conducted immunohistochemistry staining of TG2 on kidney biopsy core derived from who were diagnosed chronic kidney disease. Plasma TG2 concentrations were measured by ELISA. Analyses were performed to reveal the relationship between TG2 and pathologic, functional markers of kidney disease. TG2 mRNA were evaluated at 3, 7, 14 days after from unilateral ureteral obstruction (UUO) mice model establishment with the fibrosis aggravation. To investigate the effect of TG2 inhibition on CKD progression, we used cystamine, well known TG2 inhibitor that induces the oxidation of vicinal cysteine residues of TG2 in primary cultured human tubular epithelial cells (hTECs) that injured with rTGFβ.

Results:

Plasma TG2 concentrations showed positive relationships with CKD progression. Samples from progressed CKD patients showed higher plasma TG2 level. The tissue expression of TG2 were increased with CKD progression in human samples. After the establishment of the UUO model, elevation of TG2 mRNA levels were observed over time. TG2 inhibition by cystamine reduced 5.4% of apoptosis in hTECs that injured with rTGFβ (rTGFβ vs. rTGFβ+cystamine; 12.47% vs. 7.033%). Inhibiting TG2 using cystamine were associated with decreased fibronectin and increased E cadherin in rTGFβ inducted hTECs in a dose dependent manners.

Conclusions:

The increased expression of TG2 were associated CKD progression in kidney. Suppressing TG2 activity could protect kidney cells from CKD deterioration through its anti-apoptotic and anti-fibrotic effect.