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

Abstract Submission No. : 2405

Hyaluronan Synthase 2 plays a key role in Phenotype Transition of Peritoneal Mesothelial Cells (MCs)

Hyun-Jung Kang, Dal-Ah Kim, Min-Jeong Lee, Mina Yu, Duk-Hee Kang
Department of Nephrology, Ewha Womans University Medical Center, Korea, Republic of

Objectives: Epithelial-to-mesenchymal transition (EMT) of MC is one of the key mechanisms of peritoneal fibrosis in peritoneal dialysis (PD), which can be reversed at early stage of phenotype transition. Hyaluronan (HA) is a glycosaminoglycan component of the extracellular matrix, produced by three members of HA synthase (HAS1, HAS2 and HAS3). HAS are known to be involved in EMT of cancer cells, however there is no information on the association of HAS and peritoneal EMT.

Methods: Peritoneal MCs isolated from overnight dwell dialysates from 16 PD patients (PD_MC) at 2 months [baseline peritoneal equilibration test (PET)] and 6 months (follow-up PET) of the PD initiation. We divided PD patients into two groups based on the alteration of baseline versus follow-up PD_MC morphology (Group 1 epithelial-to-epithelial and Group 2 epithelial-to-mesenchymal). RNA-seq analysis (Ebiogen, Korea) was performed in order to detect baseline molecular markers predicting mesenchymal phenotype transition in follow-up PET. Based on RNA-seq analysis, we explored the role of HAS on TGFβ-induced EMT by evaluating the expression of HAS isoforms in MCs isolated from omentum (OM_MC).

Results: RNA-seq analysis demonstrated the difference of gene expression related to EMT (27.6%), angiogenesis (30.2 %), cell migration (27.4%), and extracellular matrix remodeling (26.3%). Among them, HAS2 expression in PD-MC of baseline PET showed the highest fold difference (28.5-folds) between group 1 and 2. In OM_MC, HAS1, HAS2 and HAS3 were constitutively expressed whereas only HAS1 and HAS2 were upregulated by TGFβ. TGFβ-induced changes in cell morphology and the expression of E-cadherin, α-SMA, and fibronectin were ameliorated by siHAS2, but not by siHAS1. HAS inhibitor (4-MU) also alleviated TGFβ-induced EMT.

Conclusions: This data suggest HAS2 plays a role in EMT of peritoneal mesothelial cells and modulation of HAS2 expression/activity can protect the peritoneal fibrosis in PD patients.