KSN SEOUL, KOREA 2023
April 27(Thu) - 30(Sun), 2023
Coex, Seoul, Korea

Abstract Type : Oral
Abstract Submission No. : 1767

uPA deficiency aggravates cBSA-induced membranous nephropathy through Th2-prone immune response in mice

Tzu-Ming Jao[2], **Jin-Shuen Chen[1]**
[1]Department of Department of Medical Education and Research, Kaohsiung Veterans General Hospital, Taiwan
[2]Department of Global Innovation Joint-Degree Program International Joint Degree Master's Program in Agro-Biomedica, National Taiwan University, Taiwan

Objectives: Urokinase plasminogen activator (uPA) is a crucial activator of the fibrinolytic system that modulates tissue remodeling, cancer progression, and inflammation. However, its role in membranous nephropathy (MN) remains unclear.

Methods: To clarify this issue, an established mouse model mimicking human MN induced by cationic bovine serum albumin (cBSA) in BALB/c mice was used, which have a Th2-prone genetic background. To induce MN, cBSA was injected into *Plau* knockout (*Plau-/-*) and wild-type (WT) mice. The blood and urine samples were collected to measure biochemical parameters, including serum concentrations of IgG1 and IgG2a, using enzyme-linked immunoassay. The kidneys were histologically examined for the presence of glomerular polyanions, reactive oxygen species (ROS), and apoptosis, and transmission electron microscopy was used to examine subepithelial deposits. Lymphocyte subsets were determined by flow cytometry.

Results: Four weeks post-cBSA administration, *Plau-/-* mice exhibited a significantly high urine protein/creatine ratio, hypoalbuminemia, and hypercholesterolemia compared with WT mice. Histologically, compared with WT mice, *Plau-/-* mice showed more severe glomerular basement thickening, mesangial expansion, IgG granular deposition, intensified podocyte effacement, irregular thickening of glomerular basement membrane and subepithelial deposits, and abolishment of the glycocalyx. Moreover, increased renal ROS and apoptosis were observed in *Plau-/-* mice with MN. B lymphocyte subsets and the IgG1/IgG2a ratio were significantly higher in *Plau-/-* mice after MN induction.

Conclusions: uPA deficiency induces a Th2-dominant immune response, leading to increased subepithelial deposits, ROS, and apoptosis in the kidneys, subsequently exacerbating MN progression in mice. This study provides a novel insight into the role of uPA in MN progression.

Working model