KSN 2017 Abstract

KSN-17-O007

Sulfatide-selective NKT cells mediate M2 to M1 polarization resulting in amelioration of kidney fibrosis.

*Seung hee YANG[1], Sunhwa LEE[1], Mi-yeon YU[2], Yong chul KIM[2], Seung seok HAN[2], Hajeong LEE[2], Jung pyo LEE[3], Ran hui CHA[4], Dong ki KIM[2], Yon su KIM[2]

[1]Biomedical Research Institute, Seoul National University Hospital, Korea,South, [2]Internal Medicine, Seoul National University Hospital, Korea,South, [3]Internal Medicine, Seoul National University Boramae Medical Center, Korea,South, [4]Internal Medicine, National Medical Center, Korea,South, [5]Biomedical Research Institute, Biomedical Research Institute, Korea,South

Objectives : Macrophage subtype polarization has been suggested as a key player related to kidney fibrosis. Moreover, myofibroblast is originated from macrophage so-called by means of macrophage-myofibroblast transition (MMT). We investigated its phenotypic skewing of these cells by sulfatide selective type II NKT cells and its impact on kidney fibrosis.

Methods : To elucidate the impact of activated type II NKT cells on phenotypic switch of M1/M2 macrophages and interstitial fibrosis, sulfatide-selective NKT II cells from B6.Jα281-/- mice were isolated, and co-cultured with primary cultured proximal epithelial cells. In addition, for in vivo study, sulfatide was injected one hour before unilateral ureteral obstruction (UUO) operation to B6 mouse. Subsequently, total cellular RNA was extracted from minced kidney, lymph nodes, and fresh blood to analyze changes in transcript expression levels using quantitative real-time PCR and microarray. Furthermore, the proportion of infiltrated αSMA+/CD206+ double positive cells in UUO kidney was compared according to application of sulfatide.

Results : Severity of renal fibrosis and the proportion of αSMA+/CD206+ double positive cells was attenuated after sulfatide injection. At the same time, sulfatide reduced senescence, shown by decreased levels of SA-β-Gal. Sulfatide stimulated polarization from M2 to M1 accompanying by increased iNOS, STAT1, SOCS3 and decreased arginase, STAT3. Pro-fibrotic transcripts, fibronectin and TGFβ, was decreased by adding sulfatide-selective NKT. Moreover, the expression level of NGAL and IL-1β, a marker of kidney damage and inflammation, was attenuated. At the same time, diminution of immunologic transcripts such as CD44, CCL5, CCL9, and macrophage mannose receptor 1 was also observed.

Conclusions : Sulfatide-selective NKT cell mediates macrophage polarization

skewing from M2 to M1 macrophage via switching on STAT1 resulting in ameliorating renal fibrosis. Infiltration of myofibroblast cells co-expressing M2 marker are also decreased by sulfatide accompanying by reduced fibrosis. Inducing the polarization of macrophages by modulation of NKT cells can be suggested as therapeutic target for curbing fibrosis.

Keywords : Chronic Kidney Disease, Kidney Fibrosis, Myofibroblast, Macrophage-myofibroblast transition (MMT), Natural Killer T cell