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

Oral Communication Abstract
Presentation No. OC2-04 (Abstract Submission No. 2307)

Oral Communications 2 Sep. 2 (Thu), 13:40-15:4

Chemokine (C-C Motif) Ligand 8 and Tubulo-Interstitial Injury in Chronic Kidney Disease

Jangwook Lee[1], Yeonhee Lee[2], Kyu Hong Kim[4], Dong Ki Kim[3], Kwon Wook Joo[3], Sung Joon Shin[1], Yon Su Kim[3], Seung Hee Yang[4]
[1]Department of Internal Medicine, Dongguk University Ilsan Hospital, Korea, Republic of
[2]Department of Internal Medicine, Uijeongbu Eulji Medical Center, Eulji University, Korea, Republic of
[3]Department of Internal Medicine, Seoul National University Hospital, Korea, Republic of
[4]Department of Kidney Research Institute, Seoul National University College of Medicine, Korea, Republic of

Objectives: Kidney fibrosis has been accepted to be a common pathological outcome of CKD. We aimed to examine serum levels of CCL8 in patients with CKD and to investigate their association with kidney fibrosis.

Methods: Total 157 patients with a diagnosis of IgAN, diabetic nephropathy, and normal healthy controls were enrolled and serum levels of CCL8 were quantified by ELISA and 83 kidney tissue samples were processed for immunohistochemistry to quantify CCL8-positive cells. To evaluate the role of CCL8 in fibrosis and apoptosis, rTGF-β-stimulated hTECs were simultaneously treated with anti-CCL8 monoclonal (m)Ab and Western blot analysis and FACs analysis were performed.

Results: Serum CCL8 levels were significantly higher in the advancing CKD stage and uPCR≥1 group and also significantly higher with interstitial fibrosis in all patients. In kidney tissues, CCL8 expression significantly increased with advancing CKD stage, proteinuria level, and pathologic deterioration. In Western blot analysis of primary cultured hTECs after induction of fibrosis with rTGF-β, CCL8 was up-regulated by rTGF-β treatment and the simultaneous treatment with anti-CCL8 mAb mitigated the rTGF-β-induced increase in fibronectin and decrease E-cadherin and BCL-2 protein levels. In FACS analysis, there were significant increase in fibronectin cell populations and decrease in E-cadherin cell populations after rTGF-β treatment. The simultaneous treatment with anti-CCL8 mAb alleviated the rTGF-β-induced increase in fibronectin in a dose-dependent manner and decrease E-cadherin cell populations. The antiapoptotic effect of the anti-CCL8 mAb was also demonstrated by Annexin V/propidium iodide staining assay. In qRT-PCR analysis, mRNA expression levels of the markers for fibrosis and apoptosis showed similar expression patterns to those observed by Western blotting.

Conclusions: CCL8 pathway is associated with increased risk of kidney fibrosis and that CCL8 blockade can ameliorate kidney fibrosis and apoptosis. Thus, therapeutic strategies that inhibit CCL8 function may be effective in preventing CKD progression.

Figure 1. Immunohistochemical photos and quantification of CCL8 expression in CKD

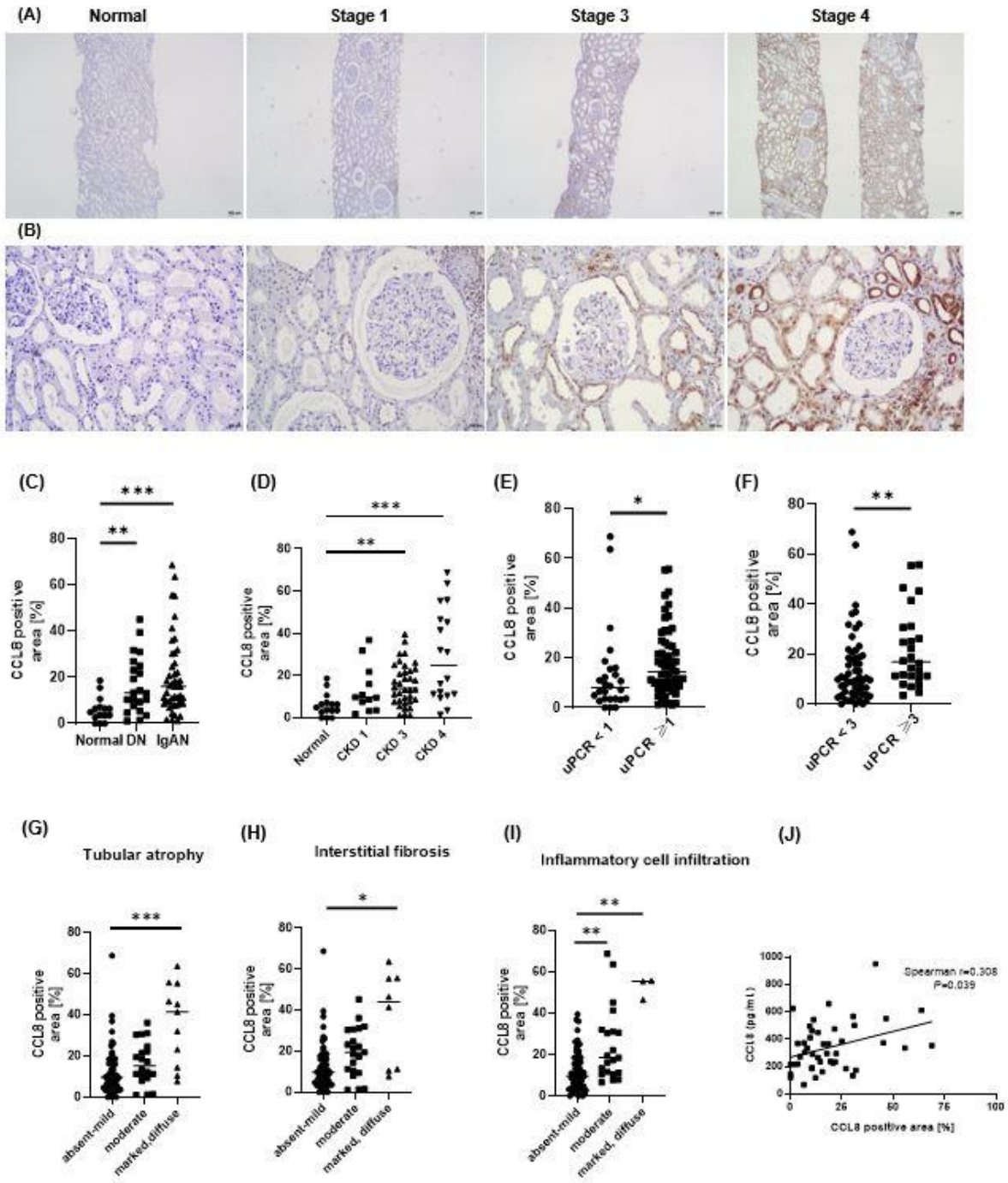

Figure 2. Effect of CCL8 blockade and rCCL8 induced by rTGF-β in hTECs