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

Oral Communication Abstract
Presentation No. OC5-02 (Abstract Submission No. 2413)

Oral Communications 5 Sep. 3 (Fri), 08:30-10:30

RNA methylation signaling pathway mediated by METTL3 affects the development of acute kidney injury and chronic kidney disease transition

Jeonghwan Lee[1], Ara Cho[1], Sung Yup Cho[2], Jung Pyo Lee[3]
[1]Department of Internal Medicine-Nephrology, SMG-SNU Boramae Medical Center, Korea, Republic of
[2]Department of Biochemistry & Molecular Biology, Seoul National University College of Medicine, Korea, Republic of
[3]Department of Internal Medicine-Nephrology, Seoul National University College of Medicine, Korea, Republic of

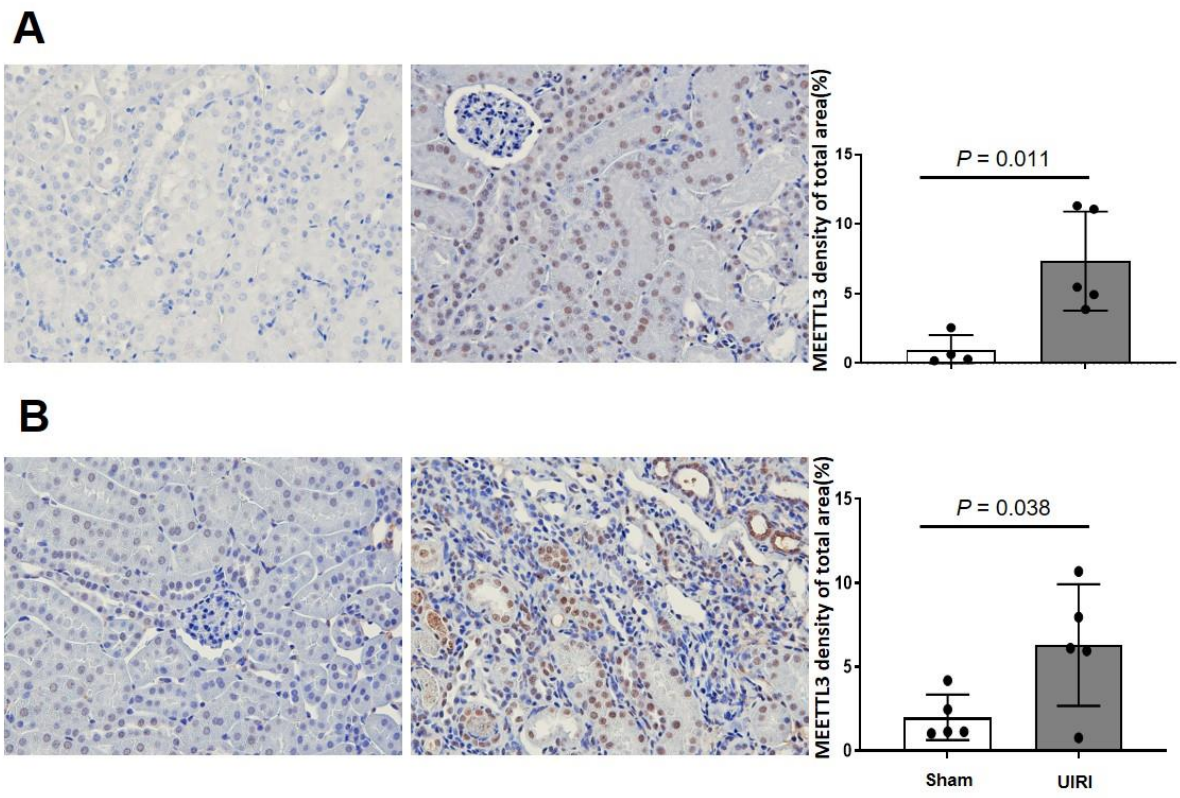
Objectives: RNA methylation is a reversible post-translational modification to RNA that epigenetically impacts numerous biological processes. In this study, we aimed to investigate the biological effects of RNA methylation in the development acute kidney injury (AKI) and subsequent AKI-to-CKD transition.

Methods: Both bilateral ischemia-reperfusion injury (IRI) and unilateral ischemia-reperfusion injury (UIRI) mice model was establish to induce AKI and AKI-to-CKD transition. C57BL/6 male mice were randomly divided into 4 experimental groups: sham-operated controls to IRI (n = 4), IRI-operated AKI group (n = 5); sham-operated controls to UIRI (n = 5), and UIRI operated mice group (n = 5). IRI-controls and IRI groups were sacrificed at 48 hours, and UIRI-controls and UIRI groups were killed 4 weeks after operation. Kidney tissue expression of METTL3 and m6A reader protein YTHDF1 were tested using immunohistochemical staining methods. To explore the transcriptomic effects of METTL3 knock-down on AKI-to-CKD transition, methylated RNA immunoprecipitation sequencing (MeRIP-seq) was tested in TGF-β challenged HK2 cells.

Results: The serum creatinine levels in the IRI groups increased significantly compared to the IRI-control groups. The degrees of kidney tissue fibrosis in the UIRI groups were significantly higher compared to the UIRI-controls at Masson's trichrome staining. In the immunohistochemical staining of METTL3, IRI groups showed higher tissue expression (7.33 ± 3.57% vs. 0.92 ± 1.11%, $P = 0.011$). In addition, UIRI groups presented higher METTL3 expression (6.29 ± 3.63% vs. 1.99 ± 1.36%, $P = 0.038$). Expression levels of YTHDF1 were comparable between groups. Knock-down of METTL3 upregulated 121 genes associated with KRAS signaling pathway and inflammatory responses among 296 genes tested in vitro HK2 cell model.

Conclusions: Kidney tissue expression levels of RNA methyltransferase METTL3 are increased significantly both in the IRI-induced mice AKI model and UIRI-induced AKI-to-CKD transition model. METTL3 might play an important role in the AKI development and AKI-to-CKD transition.

Fig 1.


A
B
MEETTL3 density of total area(%)
P = 0.011
P = 0.038
0
5
10
15
Sham
UIRI