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The role of podocyte-specific NOX5 in chronic kidney disease

Mi Ju Park¹, **Donghyeong Lee**¹, Eun Soo Lee², Seung Seob Son¹, Jeong Suk Kang³, Ji Hye Lee⁴, Hee Seoul Jeong¹, Choon Hee Chung², Eun Young Lee³

¹Department of Medicine and BK21 FOUR Project, Soonchunhyang University, Korea, Republic of

²Department of Internal Medicine, Yonsei University Wonju College of Medicine, Korea, Republic of

³Department of Internal Medicine-Nephrology, Soonchunhyang University Cheonan Hospital, Korea, Republic of

⁴Department of Pathology, Soonchunhyang University Cheonan Hospital, Korea, Republic of

Objectives: NADPH oxidase (NOX) is a major source of reactive oxygen species (ROS) that accelerates the development of diabetic kidney disease and chronic kidney disease. Among them, the most recently revealed role of NOX5 is receiving great attention in the kidneys. However, the role of NOX5 in chronic kidney disease is not well known yet. Therefore, this study tried to investigate the relationship between NOX5 and chronic kidney disease and the possibility of NOX5 as a treatment target for chronic kidney disease.

Methods: We used podocyte-specific NOX5 tg (NOX5 tg) mouse to induce chronic kidney disease with 0.2% adenine diet for 2 weeks. Kidney function and structure were examined by urine albumin/creatinine ratio (ACR), blood urea nitrogen, periodic acid-Schiff, Masson's trichrome, and immunohistochemical stainings. And *in vitro* studies were conducted after generating podocytes genetically overexpressing NOX5. Cytoskeleton of podocytes was investigated by phalloidin staining. The influence of ROS to podocytes was also analyzed using 2',7'-dichlorofluorescein diacetate (DCF-DA).

Results: NOX5 expression was markedly increased in renal glomerular podocytes in NOX5 tg mouse induced with CKD. Also, the expression of urinary NOX5 was even more upsurged when NOX5 tg mouse was fed with adenine diet. And we confirmed an increase of ACR in adenine-induced NOX5 tg mouse, compared with adenine-induced WT mouse. In addition, podocyte cytoskeletal rearrangement was induced by ROS in podocytes by NOX5 overexpression *in vitro*.

Conclusions: NOX5 can accelerate adenine-induced kidney injury, such as podocyte damage, and ROS production by NOX5-induced podocyte cytoskeleton rearrangement. Based on evidence that NOX5 can accelerate adenine-induced kidney injury, this study showed the possibility of NOX5 as a treatment target for chronic kidney disease.