

Roles of Transcription Factor NFAT5 in Renal Tubular Cells for Sodium Homeostasis and During the Progression of Renal Injury and Chronic Inflammation

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Summary

Nuclear factor of activated T-cells 5, NFAT5, is a transcription factor, which is activated by hyperosmolality and induces osmoprotective genes, resulting in cell survival even in extremely high osmolality conditions such as renal inner medulla. NFAT5 is a member of the NFAT family. Whereas NFAT1 to 4 are regulated by calcineurin, NFAT5 is not.

NFAT5 has been suggested to regulate urine concentration. However, *in vivo* studies have so far performed less because suitable gene-engineered animals have not been generated. NFAT5 is expressed ubiquitously and its homozygous deletion results in embryonic lethal. Recent studies suggest the involvement of NFAT5 in various diseases such as arthritis and atherosclerosis. However, the role of NFAT5 in the progression of chronic kidney disease has not been investigated yet.

In the present study, we generated renal tubule-specific conditional NFAT5 knockout (KO) mice. The NFAT5 KO mice exhibited polyuria and less urinary sodium excretion. Systolic blood pressure in NFAT5 KO mice tended to be increased compared with that in control mice. To investigate the involvement of NFAT5 in renal tubules in chronic kidney disease, the mice were subjected to unilateral urethral obstruction (UUO). UUO induced TUNEL positive cells and the expression of cleaved-caspase 3 protein in the kidney tissue in control mice, indicating that apoptosis was induced by UUO. Tubular deletion of NFAT5 promoted apoptosis more than that in control mice.

In conclusion, NFAT5 in renal tubular cells has a crucial role in the urine concentration mechanism. NFAT5 might have a protective role against the progression of chronic kidney disease. Further investigations to elucidate the roles of NFAT5 in the kidney are ongoing.