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Blood Pressure Regulation via Renal Mg^{2+} Transporters

Yosuke Funato, Hiroaki Miki

Department of Cellular Regulation, Research Institute for Microbial Diseases, Osaka University

Summary

In this study, we focused on TRPM6, which is involved in renal magnesium reabsorption. Our previous studies have clarified that mice with renal-specific knockout of *TRPM6*, gene encoding Mg^{2+}-permeable channel involved in renal magnesium reabsorption, showed no blood pressure elevation at the start of the active period, indicating that the circadian blood pressure variation was almost completely disappeared in this mice. First, we confirmed the expression of TRPM6 in mice, and found that TRPM6 is strongly expressed in intestine, kidney, and lung, which is consistent with the previous report. We also confirmed that TRPM6 in the kidney was localized at the apical membrane of distal convoluted tubule, where the final step of magnesium reabsorption occurs. Elemental analyses revealed that renal-specific knockout of *TRPM6* decreased the blood magnesium level to the similar level of renal-specific *CNNM2* knockout mice. Magnesium level of urine was elevated in renal-specific *TRPM6* knockout mice, confirming the importance of *TRPM6* in renal magnesium reabsorption. We also analyzed the circadian variation of locomotor activity and hormones. The locomotor activity and blood AVP level of renal-specific *TRPM6* knockout mice were similar to that of control mice, elevated at active (night) period. On the other hand, the plasma renin activity in renal-specific *TRPM6* knockout mice did not raise at active period as control mice did. Collectively, the renin secretion defect might explain the disappearance of circadian blood pressure variation in this knockout mice, and further analyses may clarify the detailed mechanism of this phenotype.