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Regulation of Circadian Blood Pressure Variation via Magnesium Transporter

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Summary

TRPM6 is a Mg^{2+} permeable channel which localizes at the apical membrane of the renal distal convoluted tubule. It is known to be important for the organismal Mg^{2+} homeostasis, by participating in magnesium reabsorption through this distal convoluted tubule cells. Our previous research revealed that TRPM6 is also involved in circadian blood pressure variation; renal specific knockout of *Trpm6* in mice not just show defective renal magnesium reabsorption as reported, but also almost completely blunted the circadian blood pressure variation. However, the circadian variation of the locomotor activity was not altered, and thus further study was awaited.

In this study, we analyzed this mouse strain to explore the mechanism behind this phenomenon. It is known that distal convoluted tubule, where TRPM6 expresses, is adjacent to macula densa, a region known to regulate renin secretion from juxtaglomerular cells. By immunofluorescence microscopy, we also found that distal convoluted cells are also at the proximity of juxtaglomerular cells. Renin is known to raise blood pressure, and as like the blood pressure, the blood renin content is also known to show circadian variation with sharp rise during the active period. Thus we analyzed the blood renin content of renal specific *Trpm6* knockout mice, and found that it did not elevate during the active period, which is very similar to the results of blood pressure measurement.

We also performed experiments using renal slice culture, and found that renin secretion by adrenergic agonist treatment was impaired by renal specific *Trpm6* knockout. Thus, it can be assumed that blood pressure variation was lost in renal specific *Trpm6* knockout mice was due to the defective adrenergic receptor activation, and further detailed analyses may clarify the overall molecular mechanism of this phenotype.