No. 1432

Mg^{2+} Transporter MagEx2 and Hypertension

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Summary

Salt sensitive hypertension is associated with an increased risk of cardiovascular events, but the precise mechanisms underlying this disease are still largely unknown. Recent large-scale meta-analyses of genome-wide association studies (GWAS) identified several genes associated with blood pressure variation, and MagEx2 is the common gene identified in many independent studies.

MagEx2 belongs to the MagEx family, and we have previously shown that MagEx can stimulate Mg^{2+} efflux and plays an important role for the magnesium absorption from the intestine. Since MagEx2 can stimulate Mg^{2+} efflux as MagEx and it is highly expressed in distal convoluted tubule cells that are important for magnesium reabsorption, we hypothesized that MagEx2 might be involved in magnesium reabsorption as well as blood pressure regulation.

To address these issues, we generated MagEx2-knockout mice. Since homozygotes are embryonic lethal, experiments were performed with heterozygotes and kidney-specific knockout mice. Magnesium reabsorption was impaired in both heterozygotes and kidney-specific knockout mice, and blood pressure was also significantly lower in these mice. However, the expression and phosphorylation (activation) level of NCC, a transporter which is expressed in distal convoluted tubule and important for renal salt reabsorption/blood pressure regulation, was not so significantly altered. Transcriptome analyses revealed that expression level of several genes are significantly altered in MagEx2-knockout mice kidney. Further detailed analyses of these genes might reveal a novel mechanism of blood pressure regulation via MagEx2.