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The Molecular Diagnosis of Salt Sensitive Hypertension Using G-Protein-Coupled Receptor Kinase Type 4 (GRK4) Polymorphisms

Hironobu Sanada, Jyunichi Yatabe, Sanae Midorikawa, Minoru Yoneda,
Shigeatsu Hashimoto, Tsuyoshi Watanabe

Third Department of Internal Medicine, Fukushima Medical University School of Medicine

Summary

G protein-coupled receptor kinase type 4 (GRK4) is important in the pathogenesis of essential hypertension (Proc Natl Acad Sci 2002; 99: 3872). Because activating variants of GRK4 impair the transduction of the renal D1 dopamine receptor and sodium handling, we evaluated the association of GRK4 single nucleotide polymorphisms (SNPs) in salt sensitive (SS) and salt resistant (SR) subjects whose 24-hour ambulatory mean blood pressures (MBP) were measured. The subjects were observed for 7 days on normal sodium (153 mmol/day) diet which was changed to low (51 mmol), high (340 mmol), and normal sodium (153 mmol) that lasted 5 days for each level of sodium intake. Thirty-five SS (MBP from 104 ± 1 to 116 ± 1 mmHg) and 48 SR (MBP from 108 ± 2 to 110 ± 1 mmHg) subjects were studied; sodium excretion in response to the high sodium intake was greater in SR than in SS subjects, resulting in a greater cumulative sodium retention (121 mmol) and weight gain (1.28 kg) in SS than in SR subjects. High sodium intake decreased plasma renin and aldosterone levels and increased urinary dopamine similarly in SS and SR subjects. A genetic model based on GRK4-R65L, GRK4-A142V, and GRK4-A486V was 94.4% predictive of SS hypertension. We did not detect any differences in allele frequencies of variants of ACE, AGT, AT_1R, PAI-I, CYP11β2, D_1R, GNβ3, and ADD genes between SS and SR subjects. Thus, SNPs of GRK4 are important in the pathogenesis of salt-sensitive hypertension and may be useful in the diagnosis of this subset of hypertension.