

Identification and functional analysis of the susceptible genes for salt sensitivity

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It is well known that the restriction of salt intake helps prevent hypertension in some cases. This leads to the hypothesis that the salt sensitivity, which is not homogenous among individuals according to their genetic backgrounds, plays a key role in the pathogenesis of hypertension. To reduce the cardiovascular mortality, it is effective to use the appropriate therapy that adapts to one's genetic disposition. In the present study, we carried out case-control studies to identify the genes responsible for salt sensitive hypertension.

The participants were recruited from two studies with informed consent for genetic analysis. One is Handai Study which consists of the outpatients of Osaka University Hospital, and another is Ohasama Study, a large cohort study in a rural community of Iwate prefecture. In addition to usual physical findings and biochemical measurements, plasma renin activity and aldosterone concentration were measured in Handai Study, and ambulatory blood pressure monitoring for 24 hour (24hr ABPM), home blood pressure measurement, quantification of asymptomatic cerebral ischemia using MRI and atherosclerotic change in carotid artery were examined in Ohasama Study. The following gene polymorphisms were examined as candidates for salt sensitivity: CYP11B2 (aldosterone synthase)/Lys173Arg, alpha-adducin/Gly460Trp and GNB3 (G protein beta 3 subunit)/C825T.

None of the polymorphisms were associated with the presence of hypertension, with casual and home blood pressure and with mean of 24hr ABPM. Even though several alleles that were reported as genetic risk increasing the prevalence of hypertension in Caucasian population were frequently observed in Japanese, these alleles did not increase the risk for hypertension in this study. On the other hand, total cholesterol and plasma potassium level was significantly associated with GNB3/C825T genotype. Though the causal relationship was unclarified, the truncated protein (G beta 3-s) obtained from GNB3 polymorphism might be involved in the regulation of intracellular potassium or in the expression of LDL receptor.

Our results suggested that gene susceptibility for salt sensitive hypertension of Japanese should be examined using Japanese populations and obtaining certain and various phenotypes is a key for the success of post human genome project.