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EFFECT OF NEDD4L GENE FIVE COMMON POLYMORPHISMS ON HYPERTENSION-RELATED PHENOTYPES IN HAN CHINESE HYPERTENSION PATIENTS

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[1]Lijuan Sheng, [2]Pingjin Gao. *[1]1. Shanghai Jiao Tong University 2. Shanghai Institute of Hypertension; [1]Institute of Health Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences; [2]Shanghai Institute of Hypertension*

Objectives Hypertension is a complex disorder; part is due to genetic determinants. Mounting evidence has suggested that NEDD4L plays a pivotal role in maintaining Na^+ balance, extracellular fluid volume and long term blood pressure control. We therefore regarded NEDD4L as a hypertension-susceptibility gene and genotyped its 5 common intronic polymorphisms to assess their association with hypertension-related phenotypes including Na^+, K^+ in serum, and plasma renin activity (PRA).

Methods A total of 1537 individuals were recruited and they were of Han Chinese descent including 669 patients with essential hypertension, 658 normal individuals and 210 patients with primary aldosteronism. The medical records were collected from Shanghai Ruijin Hospital containing the serum and urinary electrolytes and PRA and generally they were city-dwellers. DNA was extracted from whole blood and genotyping was carried out by allele discrimination method. Data were analysed using the Kruskal-Wallis Test, single-locus and haplotype analyses by SAS programme and SimHap software.

Results The serum sodium concentration between normal and hypertensive patients was statistically different $p<0.0001$) and it was statistically different between control and patients with primary aldosteronism as well $p<0.0001$). The five studied polymorphisms met Hardy-Weinberg equilibrium in the population ($p>0.05$). Single-locus analysis suggested that rs10503020 was associated with serum Na^+ concentration and PRA ($p=0.034$ and 0.043, respectively) under additive model in essential hypertension patients. But in normal group, Na^+ concentration was not related with the SNP rs10503020 under the add model. Patients with rs10503020 C allele had higher levels of PRA than those with TT genotypes (CC+CT: 3.57 vsTT: 2.96 ng/ml/h) and were more sensitive to postural change ($p=0.147$). Moreover, in hypertensive group, rs4149601 was associated with plasma aldosterone concentration in the additive model ($p=0.032$).

Conclusions Although both cases' serum Na^+ concentration was significantly different between control and case, only in hypertensive group was it associated with rs10503020. Our results demonstrated that rs10503020 of NEDD4L gene might influence sodium re-absorption in kidney and plasma rennin activity to some extent in hypertensive people in Han Chinese.