Effects of NR3C2 Genetic Polymorphisms on the Antihypertensive Response to Enalapril in Patients with Essential Hypertension

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Purpose
Renin-angiotensin-aldosterone system (RAAS) is the major factor for modulation of blood pressure and involves in the pharmacological effects of several antihypertensive drugs. Many genetic polymorphisms have been found to be associated with the blood pressure response of several antihypertensive drugs. Aldosterone in the downstream of RAAS exerts its major effects by binding to the Mineralocorticoid receptor (MR). Our objective was to investigate the possible impact of NR3C2 polymorphisms on the antihypertensive response of enalapril.

Methods
279 patients were enrolled and administrated enalapril 10mg once a day for two weeks to explore the association of the antihypertensive response to enalapril with NR3C2 genetic polymorphisms. Two NR3C2 tagSNPs (rs5522 and rs2070950) were selected and determined by the MassARRAY assay.

Results
The frequencies of the two minor alleles (rs5522 and rs2070950) were 15% and 24.5% respectively. After 2 weeks of treatment, the reductions in diastolic blood pressure (DBP) were significantly greater in AA genotype carriers compared with AG+GG genotype carriers for the rs5522 polymorphism (P=0.009), and the reductions in DBP were greater in GG genotype carriers compared with GC+CC genotype carriers for the rs2070950 polymorphism, with marginal significance (P=0.065). Rs5522 is still a significant predictor of DBP reduction, adjusted age, BMI, basic blood pressure, sex, WHR and rs2070950 genotype by stepwise multiple linear regression analysis (P=0.003).

Conclusion
NR3C2 rs5522 may be a determinant of the blood pressure response to enalapril treatment in essential hypertensive patients.