Stromelysin-1 (MMP-3) Gene 5A/6A Promoter Polymorphism Is Associated With Blood Pressure in a Community Population

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Background: Vascular remodelling of large and small arteries contributes to the development of hypertension. Stromelysin-1, a member of the matrix metalloproteinase (MMP) family may contribute to arterial remodelling. The expression of stromelysin-1 gene is partly regulated by a common polymorphism in the promoter region of either five or six consecutive adenine bases (5A/6A) that alter transcription factor binding.

Methods: A case-control study of 111 randomly selected community members (553 males and 558 females), aged 27-77 years, who were assessed for conventional cardiovascular risk factors and the stromelysin-1 5A-1171/6A genotype. Mean common carotid intima-media wall thickness (IMT) and presence of plaque was determined by carotid ultrasound.

Results: The frequency of the stromelysin-1-1171/SA allele was 0.45. Univariate analysis demonstrated an association between the stromelysin-1 5A-1171/6A genotype and blood pressure in the whole population. Multivariate analysis showed an independent association between the stromelysin-1 genotype and systolic and diastolic blood pressure (both P<0.005) in the whole sample. When the population was split by smoking status, an independent association with systolic blood pressure (P<0.0001) and diastolic blood pressure (P=0.006) was present only in smokers. Subjects who smoked and carried the 5A/SA genotype had a higher mean systolic (+6.0 mmHg) and diastolic (+2.5 mmHg) blood pressure compared to 5A/6A and 6A/6A carriers. The association between the stromelysin-1 genotypes and blood pressure was recessive with the effect only seen with the 5A/SA genotype. Multivariate analysis in the whole population showed there was no association with mean IMT (P=0.42) or the likelihood of carotid plaque formation (P=0.08).

Conclusions: In this large randomly selected, cross-sectional population, the 5A/SA variant in the stromelysin-1 gene promoter was independently associated with increased blood pressure in the whole population and in smokers but was not associated with either increased carotid IMT or plaque formation.

Pulse Pressure and Interactions Between Polymorphisms in the Angiotensin II Type 1 Receptor and Uncoupling Protein 1 Genes in Hypertensive Hong Kong Chinese

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Background: Hypertension and obesity are strongly inter-related and have multifactorial genetic and environmental components. The angiotensin II type 1 receptor (AT1R) is involved in the regulation of blood pressure and polymorphisms in this gene have been implicated in the development of hypertension. The uncoupling protein 1 (UCP1) is solely expressed in brown adipose tissue and genetic polymorphisms affecting this may be associated with obesity. The present study was performed to assess the contribution of polymorphisms of these two genes on blood pressure or obesity parameters in a family study.

Methods: We studied members of 96 families with a hypertensive proband, including 282 siblings, of which 133 were hypertensive and 144 were obese. Blood pressure, pulse pressure, body mass index (BMI) and waist:hip ratio (WHR) were recorded for each sibling. The AT1R gene A1166C polymorphism and the UCP1 gene A-3826G polymorphism were identified with polymerase chain reaction based RFLP protocols. A multi-locus mixed linear model for quantitative trait locus (QTL) analysis was applied to identify whether these genetic polymorphism loci were related to blood pressure, pulse pressure or body weight.

Results: No significant association was found between the AT1R and UCP1 gene polymorphisms and systolic or diastolic blood pressure. Age and the BMI:WHR ratio were strongly related to the systolic blood pressure (p<0.001), diastolic blood pressure (p=0.0001) and pulse pressure (p=0.0001) and pulse pressure and body mass index (BMI) and waist:hip ratio (WHR) were recorded for each sibling. The AT1R gene A1166C polymorphism and the UCP1 gene A-3826G polymorphism were identified with polymerase chain reaction based RFLP protocols. A multi-locus mixed linear model for quantitative trait locus (QTL) analysis was applied to identify whether these genetic polymorphism loci were related to blood pressure, pulse pressure or body weight.

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Modulatory Effect of Inflammation on Blood Pressure Reduction Following Therapeutic Lifestyle Change via Cardiac Rehabilitation and Exercise Training

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Background: Inflammation promotes the development and progression of atherosclerosis and is associated with several traditional cardiovascular risk factors including hypertension, diabetes, and dyslipidemia. We evaluated the impact of inflammation on improvement in risk factors following 12 weeks of (36 sessions) of therapeutic lifestyle change (TLC) via cardiac rehabilitation and exercise training (CRET) in 635 patients (mean age 64±10.7 years) 4-6 weeks following a major CHD event.

Methods: Patients were dichotomized based on baseline median hs-CRP (median = 3.2 mg/L) values. At baseline there were no differences in age, gender, systolic and diastolic blood pressure. An interaction between the AT1R genotype and UCP1 genotype suggests these loci may be important in determining abnormal blood pressures in relation to obesity.