



<b>Title</b>	<b>Role of genetic variants in gene encoding lipocalin-2 in the development of elevated blood pressure</b>
<b>Author(s)</b>	<b>Cheung, BMY; Ong, KL; Tso, AWK; Cherny, SS; Sham, PC; Lam, TH; Lam, KSL</b>
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## Role of genetic variants in gene encoding lipocalin-2 in the development of elevated blood pressure

BMY Cheung, KL Ong, AWK Tso, SS Cherny, PC Sham, TH Lam, KSL Lam  
Department of Medicine, The University of Hong Kong, Hong Kong

**Introduction:** Lipocalin-2 is recently recognised as a biomarker of obesity and inflammation, which are both risk factors for hypertension. We therefore investigated the association of common single nucleotide polymorphisms (SNPs) in the gene encoding lipocalin-2 (*LCN2*) with elevated blood pressure in Hong Kong Chinese.

**Methods:** Five tagging SNPs were genotyped in 1936 subjects from the Hong Kong Cardiovascular Risk Factor Prevalence Study-2 (CRISPS-2) with a median follow-up period of 6.4 years. Elevated blood pressure was defined as  $\geq 130/85$  mm Hg or taking anti-hypertensive medication.

**Results:** There were only two haplotypes with frequency of  $>5\%$ , namely AGATC (45.5%) and GGTC (41.2%). Haplotype GGTC was associated with elevated blood pressure at follow-up (OR=1.17 compared to haplotype AGATC,  $P=0.031$  after adjusting for age and sex). Among 1381 subjects without elevated blood pressure at baseline, 321 subjects developed elevated blood pressure at follow-up. Haplotype GGTC was associated with the development of elevated blood pressure at follow-up (OR=1.30 compared to haplotype AGATC,  $P=0.011$  after adjusting for age, sex, systolic blood pressure, and follow-up duration; OR=1.44,  $P=0.0015$  after further adjusting for other covariates). Among subjects not taking anti-hypertensive medication, carriers of the haplotype GGTC had higher systolic blood pressure than non-carriers ( $119.7 \pm 16.4$  mm Hg vs  $117.9 \pm 17.3$  mm Hg,  $P=0.043$ ).

**Conclusion:** Our findings suggest, for the first time, that genetic variants in *LCN2* may affect blood pressure. Further studies on the role of lipocalin-2 in blood pressure regulation are warranted.

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## Association of genetic variants in gene encoding lipocalin-2 with plasma alanine aminotransferase and aspartate aminotransferase

BMY Cheung, KL Ong, A Xu, TH Lam, KSL Lam  
Department of Medicine, The University of Hong Kong, Hong Kong

**Introduction:** Lipocalin-2 is a biomarker for obesity, inflammation and insulin resistance, which are all risks factors for non-alcoholic fatty liver disease (NAFLD). Subjects with NAFLD have elevated circulating levels of lipocalin-2 and liver enzymes such as alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and  $\gamma$ -glutamyl transaminase (GGT). We therefore investigated the relationship of genetic variants in the gene encoding lipocalin-2 (*LCN2*) with plasma ALP, ALT, AST and GGT.

**Methods:** Five tagging single nucleotide polymorphisms (SNPs) were genotyped in 1337 subjects in the Hong Kong Cardiovascular Risk Factor Prevalence Study-2 (CRISPS-2) who had plasma liver enzymes measured.

**Results:** The minor T allele of the SNP rs10987900 was significantly associated with 9.6% (95% CI, 2.7-16.0%) lower plasma ALT level ( $P=0.0069$ ) and 6.2% (95% CI, 1.6-10.6%) lower plasma AST ( $P=0.0092$ ) after adjusting for age and sex. The geometric mean (95% CI) of plasma ALT in subjects with CC, CT and TT genotypes were 21.6 (20.9-22.3), 19.9 (18.4-21.5) and 16.4 (12.2-22.1) U/L respectively and those of plasma AST were 22.9 (22.4-23.4), 21.5 (20.6-22.4) and 20.7 (17.6-24.3) U/L respectively. The association remained significant after excluding regular drinkers ( $P=0.0092$  and 0.0035 for ALT and AST, respectively) and after further adjusting for body mass index, triglycerides, high-density lipoprotein cholesterol, 2-hour glucose level, insulin resistance index, C-reactive protein, fibrinogen, regular drinking and current smoking ( $P=0.022$  and 0.014 respectively).

**Conclusion:** This study provides further evidence for the role of lipocalin-2 in the development of NAFLD.

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