

## The epithelial sodium channel and blood pressure

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The epithelial sodium channel (ENaC) is involved in the long- and short-term regulation of blood pressure (BP) and has been implicated in the Mendelian BP diseases Liddle's syndrome and pseudohypoaldosteronism type 1. The  $\beta$ - and  $\gamma$ -ENaC subunit genes, *SCNN1B* and *SCNN1G* are located on a region of chromosome 16 linked to BP by a number of independent studies, including the Victorian Family Heart Study (VFHS) (Wong *et al.*, 1999; Harrap *et al.*, 2002). The VFHS consists of 767 Caucasian families (2880 healthy subjects) representative of the general Australian population. We investigated the association of *SCNN1B* and *SCNN1G* with SBP in the VFHS. Initially a total of 25 SNPs from each gene were genotyped using an extreme phenotyping approach, utilising unrelated subjects from the upper and lower deciles of the SBP distribution. This identified ten SNPs from with nominal evidence of association to SBP (*SCNN1B*: *rs1004749*, *rs239345*, *rs239346* & *rs3743966*. *SCNN1G*: *rs13331086*, *rs11074553*, *rs4299163*, *rs5740*, *rs4281710* & *rs4470152*). To independently test these findings, we genotyped these SNPs in 1971 relatives from 68 large Utah pedigrees selected for high risk of cardiovascular disease. Generalised estimating equations were used to test for association of the ENaC SNPs and BP while controlling for related observations in families. After adjusting for the covariates age, sex and body mass index, we detected significant association for the *SCNN1B* SNP *rs239345* with SBP and DBP ( $p = 0.03$ ) at baseline and for the *SCNN1G* SNPs *rs13331086* and *rs11074553* with SBP and DBP at 25-year follow up ( $p = 0.005$  and  $p = 0.018$  respectively). Our findings suggest that both the  $\beta$ - and  $\gamma$ -ENaC genes are involved in BP determination in the general population.

Wong ZY, Stebbing M, Ellis JA, Lamantia A, Harrap SB. (1999) *Lancet*, **353**:1222-5.

Harrap SB, Wong ZY, Stebbing M, Lamantia A, Bahlo M. (2002) *Physiological Genomics*, **8**: 99-105.