International Congress Series 1261 (2004) 589–591

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# HumTHO1 and blood pressure. An obstacle for forensic applications?

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Received 28 August 2003; received in revised form 28 August 2003; accepted 8 September 2003

**Abstract.** HumTH01 is reported to be associated with arterial hypertension (HT). As forensic polymorphisms must not reveal information about the personality of the tested individual in Germany, this finding is a potential obstacle for applying this locus to casework. We thus tested whether HumTH01 is associated with myocardial hypertrophy or with increased incidence of blood pressure (BP)-related diseases such as myocardial infarction. As we found no influence, it is argued that the use of TH01 for forensic purposes is legitimate. 

*Keywords:* TH01; Forensic DNA typing; STR; Hypertension; Myocardial hypertrophy

## 1. Introduction

From the legal point of view, it is essential that DNA polymorphisms should not reveal information concerning the phenotype of the person analysed. A recent order of the German Federal Constitutional Court [1] stated that it is "decisive ... (to ensure that a DNA investigation is not in conflict with the civil rights of a citizen) ... that conclusions concerning the personality, like ... diseases ... are not permitted".

However, in clinical studies, a positive association between THO1 alleles 9.3 and 10 and essential hypertension (HT) [2] was reported. The goal of the present study was thus to further evaluate potential consequences from the reported association with hypertension.

## 2. Materials and methods

The case group comprised 172 unrelated cases of unexpected death from blood pressure (BP)-related diseases (myocardial infarction, left heart failure, stroke, aortic rupture) in Halle/Saale, Germany. Control group 1 comprised 124 cases of death from natural causes other than those qualifying for inclusion in the case group. Control group 2 comprised 348

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0531-5131/ 
doi:10.1016/S0531-5131(03)01494-8

healthy babies, representing the average population. In 275 cases, the heart weight was measured. TH01 typing was performed as described [3].

## 3. Results and discussion

Essential HT is a risk factor for several potentially lethal events such as myocardial infarction, spontaneous intracerebral bleeding, etc. A genetic finding associated with substantially increased BP can thus be expected to result in an increased incidence of those events. Moreover, hypertrophy of the left myocardial wall should result, with increased heart weight as morphological equivalent.

Nevertheless, we found no differences in THO1 allelic frequencies between a case group with casualties from HT-related events and two control groups (Fig. 1). Moreover, we failed to demonstrate a correlation between THO1 genotypes and heart weights in 275 autopsy cases. (Table 1). These findings suggest that the association of THO1 with HT be weak and not capable of producing significant increases in HT-related deaths or organ malfunction.

But how could a non-coding polymorphism influence HT?

TH01 is located in intron 01 of the tyrosin hydroxylase gene, the rate limiting enzyme in the synthesis of catecholamines, which are pivotal in the regulation of blood pressure [4]. There are at least two indirect ways TH01 could influence blood pressure: Firstly, an allele could be in close linkage disequilibrium (LD) to a gene variant associated with HT. One fact fostering this possibility is the extremely low rate of spontaneous repeat array mutations of this marker leading to conservation of LD [5]. However, up to now, no such gene variant was identified.

The second possibility would be a functional activity of the THO1 sequence via gene regulation [6]. This possibility is supported by recent in vitro investigations, which proved that THO1 acts as a quantitative genomic effector modulating the activity of the tyrosin hydroxylase gene: The THO1 alleles inhibit transcription, and the inhibition is propor-

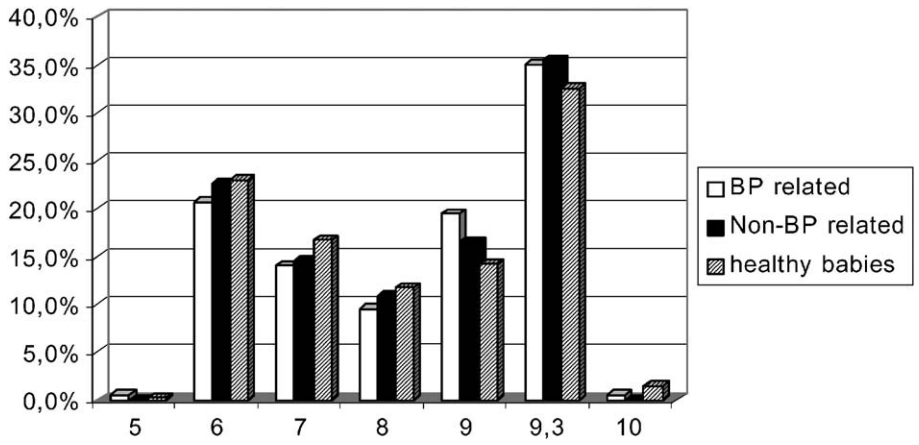


Fig. 1. Allelic frequencies for THO1 in the case group (BP-related causes of death) and two control groups (non-BP-related cause of death and healthy babies).

Table 1
Mean weight of the heart and THO1 alleles 9.3 and 10 in 275 autopsy cases

| Genotype | Heart weight (g) | S.D. |
|---|---|---|
| Without alleles 9.3/10 | 430 | 130 |
| Heterozygous for alleles 9.3/10 | 420 | 115 |
| Homozygous for alleles 9.3/10 | 410 | 120 |

tional to the number of repeats [7]. It is assumed that the effect on transcription is specifically due to the repeat sequence by interaction with factors such as ZNF191 binding to the (TCAT)n repeat, and that other STRs with this repeat motif might have similar effects on other genes. Although it remains to be established whether such STRs influence transcription in vivo, the fact that the regulatory effect might depend on the sequence of the repeat motif is of special interest for forensic DNA profiling: (TCAT) is a rather uncommon motif for forensic STRs. Among the 8 German database systems, only TH01, and of the 13 CODIS loci, only THO1 and TPOX, show this repeat motif.

Nevertheless, the THO1 marker should thus not reveal any substantial "conclusions concerning the personality, ... (or) ...diseases" as demanded by the Federal Constitutional Court of Germany [1]. Based on the current knowledge, we are thus convinced that the use of this useful marker for forensic purposes is legitimate and should not be discontinued. It can nevertheless be expected that the ongoing research in the field of human genetics will reveal undesired associations for some of the polymorphisms used for forensic purposes, and we want to propose a discussion about possible consequences in forensic panels.

## Acknowledgements

The authors would like to thank A. Graul, A. Heide and S. Salostowitz for their excellent technical assistance.

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