

P013 Polymorphism in the pentose phosphate cycle enzymes as a modifier of hyperglycemia toxicity in diabetic nephropathy

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Introduction: We hypothesized that genetic variability in the key enzymes of non-oxidative and oxidative branches of pentose phosphate pathway (transketolase, transaldolase, TKT-like and glucose-6-phosphatedehydrogenase) – a potentially “protective” mechanism in hyperglycemia – can contribute to an interindividual variability in the onset and progression of diabetic nephropathy (DN).

Methods: A total of 12 SNPs with MAF $\geq 10\%$ located in different haplotype blocks were genotyped by means of PCR. Haplotypes were inferred using Bayesian-based algorithm. A total of 434 T2DM subjects were included in the association study (cases were subjects with DN; controls were gender- and age-matched diabetics without DN, ~1:1).

Results: Haplotype distribution of TKT differed significantly between DN vs. non-DN groups ($P < 0.046$, 10 000 permutations). Common haplotype with frequency 0.22 in the whole study population was identified as a risk-haplotype (OR = 2.1). Carrier state of the risk-haplotype was associated with significantly accelerated onset of DN ($P < 0.05$, Kaplan-Meier).

Conclusions: Results suggest that TKT variability might play a role in the individual’s susceptibility to DN. This finding might be an important determinant of the benefit from the treatment with lipid-soluble TKT activator (benfotiamin). Supported by the grant NR 9443-3/2007 from the Ministry of Health of Czech Republic.