

## The Frequencies of Alleles for GSTM1 and GSTT1 Genes in Slovak Population

Šalagovic, J., Kalina, I., Hablová, V., Biroš, E.

Department of Medical Biology, Medical Faculty U.P.J.S. 040 66 Košice, Slovakia



Cancer incidence varies markedly by ethnicity and geographic location. Epidemiological studies suggest that ethnic differences in cancer occurrence can result from differences in inherited susceptibility. The  $\mu$  (GSTM1) and  $\theta$  (GSTT1) members of the glutathione S-transferase multigene family are candidate cancer susceptibility genes because of their ability to regulate the conjugation of carcinogenic compounds to excretable hydrophilic metabolites. The GSTM1 gene is located on chromosome 1p13.3 and GSTT1 gene on chromosome 22q11.2. Individuals who are carriers of homozygous deletions in the GSTM1 or GSTT1 genes may have an impaired ability to metabolically eliminate carcinogenic compounds and may therefore be at increased cancer risk. The frequencies of homozygous GSTM1 and GSTT1 deletion carriers is surprisingly high (i.e., 20-60%) in most human populations and there exist noticeable differences between different ethnic groups. In our study we identified GSTM1 and GSTT1 genotypes in a community-based sample of 248 healthy, unrelated individuals from Slovakia. Our study relied on molecular genetic testing (polymerase chain reaction (PCR)-based method), in contrast to most earlier studies, which were based on phenotypical measurements of enzyme activity. Genotyping is advantageous because it can unequivocally distinguish between GSTM1, GSTT1 and other glutathione transferase gene family members and can reveal the inherited DNA sequence polymorphism that is the basis for a specific lifetime phenotypic trait. Genotype analysis of a large population by PCR is both cost- and labor-intensive. We therefore used the simultaneous amplification of GSTM1 and GSTT1 genomic fragments in the same reaction. We combined in a single PCR reaction two sets of primer pairs previously used for the separate amplification of GSTM1 and GSTT1 genomic fragments and a third pair of compatible primers for the additional amplification of an albumin gene fragment that was used in order to serve as an internal positive control for the success of the amplification reaction.

On the basis of the results from our pooled control samples, we estimate that, in the geographic region of our study (Slovakia), 49.6% of individuals are carriers of the GSTM1 0/0 genotype and 16.9% of individuals are homozygous GSTT1 deletion carriers.

The fact that deletion polymorphisms in GSTM1 or GSTT1 are common implies that the population attributable risk associated with these genotypes may be quite high. A large proportion of cancer in the general population may be explained by genotypes at GSTM1 or GSTT1 because carriers of homozygous deletion genotypes at these loci are so common. Inherited cancer susceptibility may be a stronger determinant of ethnic differences in cancer incidence than is currently appreciated.