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Cytochrome P450 2A6 and GSTM1 gene polymorphism in Thai nasopharyngeal carcinoma

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Nasopharyngeal carcinoma (NPC) remains a serious cancer in southern China and Southeast Asian countries, including Thailand. This cancer is caused by a single factor or a combination of Epstein-Barr virus (EBV), carcinogens and genetic susceptibility. Polymorphism of genes that encode enzymes involved in metabolic activation and detoxification of xenobiotics has been reported to be associated with susceptibility to various cancers. To determine association between cytochrome P450 2A6 (*CYP2A6*) and glutathione S-transferase M1 gene (*GSTM1*) polymorphism and NPC risk in Thais, 78 NPC patients and 145 age-matched healthy controls were examined for *CYP2A6* deletion genotype (**4C/*4C*) and *GSTM1* null genotype (*GSTM1-*) by using PCR-RFLP and PCR assays, respectively. Overall, no association was found between *CYP2A6*4C/*4C* and NPC risk. Interestingly, carriers of at least one **4C* allele or (**1A/*4C* + **1B/*4C* + **4C/*4C*) genotype had a 3-fold increased risk for NPC (95% CI, 1.1-8.4) and males had a 11-fold higher risk for NPC than females. In addition, carriers of at least one **4C* allele had a 5-fold and 9-fold higher risk for NPC of WHO type I than WHO types II and III. Further, the carriers of at least one **4C* allele had a 9-fold higher risk for NPC stage I and II than stage III and IV. When subjects were categorized into 3 groups of age >40, >45 and >50 years, it was found that risk for NPC tended to increase with age for carriers of at least one **4C* allele. For *GSTM1* polymorphism, no statistically significant differences were observed in the frequency of *GSTM1-* between cases and controls. Among NPC patients, a significant association existed between *GSTM1-* and NPC WHO type III ($P<0.05$) with odds ratio (OR) = 2.6 (95% CI = 1.2-6.8), but there was no association with WHO types I and II. When cases and controls were categorized into 3 age groups (>40, >45 and >50

years), the frequencies of *GSTM1-* in groups >45 and >50 years were significantly different from those of controls ($P<0.05$). *GSTM1-* carriers over 45 years had a 2-3-fold higher risk for NPC and the risk increased with age (i.e., OR increased from 2.2 to 3.0 for age groups >45 and >50 years). Carriers of combinations of two-risk genotypes (with at least one of **4C* allele or *GSTM1-*) had a higher risk for NPC compared with those of one-risk genotype. Based on this study, we suggest that *CYP2A6* and *GSTM1* polymorphism may play a key role in NPC development and may be a useful tool for early detection and monitoring of NPC in Thailand.