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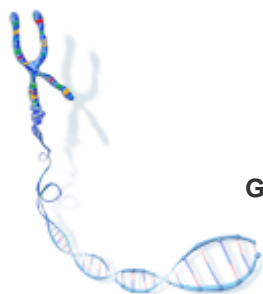
## GSTM1, GSTT1, and the Risk of Squamous Cell Carcinoma of the Head and Neck

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**Gene** *GSTM1*: Polymorphism of this gene results in either production of an enzyme known to play a role in Phase II detoxification of polycyclic aromatic hydrocarbons found in tobacco smoke or no production of enzyme (deletion polymorphism). This gene has been mapped to chromosome 1p13.3.

*GSTT1*: Polymorphism of this gene results either in production of an enzyme known to activate ethylene oxide, epoxybutanes, halomethanes, and methyle bromide or no production of enzyme (deletion polymorphism). It is also involved in Phase II detoxification of polyaromatic hydrocarbons (PAHs) found in tobacco smoke (considered as a minor pathway). This gene has been mapped to chromosome 22q11.2.

### Prevalence of Gene Variants

*GSTM1*: In the United States, case-control studies have reported the deletion genotype varying from 23%-41% for those of African descent; 32%-53% for those of Asian descent, 40%-53% for those of Hispanic descent, and 35%-62% for those of European descent. Several population studies have reported the deletion polymorphism among U.S. Caucasians as ranging from 48%-57%. Other countries have reported varying frequencies of the deletion polymorphism. South American case-control (nonpopulation-based) studies have reported frequencies of 21% for Chileans and 55% for Caucasian Brazilians, 33% for black Brazilians, and 20% for Amazonian Brazilians. Among the French, 46% have been reported to carry the deletion genotype. A large cross-sectional study conducted among Italians reported a frequency of 53%; two studies conducted in Hungary and the Slovak Republic measured frequencies of 44% and 50%, respectively. A population-based study conducted in Finland found a prevalence of 40% for the *GSTM1* deletion genotype. Groups such as Pacific Islanders and Malaysians have a reported frequency of 62%-100%. Other Asian populations have high-reported frequencies of the deletion genotype ranging from 48%-50% for Japanese and 35%-63% for Chinese. A population-based study conducted among Chinese reported a frequency of 51% for the *GSTM1* deletion genotype. Two Korean case-control studies found frequencies of 53% and 56% for the *GSTM1* deletion genotype (1)

*GSTT1*: Studies of *GSTT1* demonstrate that in the United States, the deletion polymorphism of *GSTT1* is less common than the *GSTM1* deletion polymorphism. Among those of European ancestry, 15%-31% have no functional *GSTT1* enzyme. African descendents have frequencies ranging from 22%-29% while those of Hispanic origin carry *GSTT1* deletions of 10%-12%. European studies have reported that the *GSTT1* deletion genotype was present among 21% of Italians and

28% of Slovaks. One South American study found that 19% of both Caucasian and black Brazilians had the deletion genotype compared to 11% of Amazonian Brazilians. Asians have the highest reported *GSTT1* deletion genotype. One study reported 58% of Chinese and 38% of Malaysians have the *GSTT1* null genotype; two case-control studies measured 42% and 46% among Koreans. However, a recent population-based study conducted among Chinese found a prevalence of 46% for the *GSTT1* deletion genotype among their study subjects (1)

#### Disease Burden

Worldwide, squamous cell carcinoma of the head and neck (SCCHN) represents the third most common cancer among men and the fourth most common among women. Tobacco smoking remains the most important risk factor for SCCHN, with 90% of oral cancers and 80% of larynx cancers attributed to this habit. Given the high prevalence of the *GSTM1* and *GSTT1* deletion polymorphisms, the population-attributable risk of disease is extremely high for those who have the deletion genotype and who engage in tobacco smoking.

#### Interactions

Twenty-four studies have been published evaluating *GSTM1*, *GSTT1*, and the risk of SCCHN. The main effect of the gene has been inconsistent, with most studies reporting weak to moderate results. Modest evidence of interaction has been shown with imprecise estimates of effect for risk of SCCHN and *GSTM1* null genotype among studies that have measured dose and duration of tobacco exposure (2-4). For example, after adjustment for age and gender, Sato et al. calculated odds ratios (OR) of 3.1 (1.6, 5.9), 3.9 (1.6, 9.1), and 16.2 (4.3, 61.0) for risk of oral cancer for those with the *GSTM1* deletion genotype and increasing lifetime cigarette dose (4)

Among those studies that have evaluated gene-environment interaction for the *GSTT1* deletion genotype, Olshan et al. reported a suggestive interaction with smoking. For those with the *GSTT1* deletion genotype and who had never smoked (never smokers), the risk of SCCHN was 2.7 (0.5, 12.9) compared to never smokers without the *GSTT1* deletion genotype. Less-than-one-pack-per-day smokers had an OR of 3.7 (0.7, 19.4) while one-pack-per-day-or-greater smokers had an OR of 7.0 (2.2, 22.0) compared to never smokers without the *GSTT1* deletion genotype (3).

#### Laboratory Tests

Individuals with homozygous deletions of either the *GSTM1* locus or the *GSTT1* locus have no enzymatic functional activity of the respective enzyme. This has been confirmed by phenotype assays that have demonstrated 94% or greater concordance between phenotype and genotype. Genotyping methods used in the studies reviewed were consistent with the standard techniques employed for PCR, PCR-restriction fragment length polymorphisms, and multiplex PCR. Internal control primers were stated for all studies.

#### Population Testing

No population testing has been conducted to date, and none are indicated.

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**Web sites** [National Cancer Institute](#)

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