

### Letters to the Editor

## Re: Spitz, M. R., Duphorne, C. M., Detry, M. A., Pillow, P. C., Amos, C. I., Lei, L., de Andrade, M., Gu, X., Hong, W. K., and Wu, X. Dietary Intake of Isothiocyanates: Evidence of a Joint Effect with Glutathione S-Transferase Polymorphisms in Lung Cancer Risk. *Cancer Epidemiol. Biomark. Prev.*, 9: 1017–1020, 2000

### Letter

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Spitz *et al.* (1) have recently described a protective effect of dietary isothiocyanate intake for lung cancer risk in a United States population among current, but not among former, smokers. This protective effect was greater in individuals who were null for both GSTM1<sup>2</sup> and GSTT1 genotypes compared with subjects who had positive alleles for both genes, but there appeared to be no interaction between dietary isothiocyanate intake and GSTM1 genotype alone. London *et al.* (2) have recently shown a protective effect of a high serum isothiocyanate level for lung cancer risk, primarily among GSTM1-null individuals, in a Chinese population.

Isothiocyanates, which have been shown to inhibit tumorigenesis in animal models, are non-nutrient compounds found in cruciferous vegetables. GST-catalyzed conjugation of glutathione with isothiocyanates promotes the elimination of these compounds (3). Among individuals who are genetically deficient with respect to the GST enzymes, elimination of isothiocyanates is likely to be less rapid, which may enhance their chemopreventive effect. This could represent an important example of a gene-environment interaction in human carcinogenesis.

Using data from a multicenter study of lung cancer among nonsmokers (4), we have examined associations between GSTM1 genotypes, cruciferous vegetable intake and lung cancer risk. GST genotyping data were available for

122 lung cancer cases and 123 controls. Subjects recruited at nine different centers throughout Europe and South America were included in the analysis. The majority of lung cancer cases (86.1%) and controls (71.5%) were female. Among cases, age ranged from 18 to 92 years with a mean of 64 years, whereas in controls, these figures were 23–85 years and 59 years, respectively. Age, sex, and center were adjusted for in the analysis. Cruciferous vegetable intake (including broccoli, cabbage, and cauliflower) was measured using a food frequency questionnaire, and consumption was classified as follows: low = less than one portion per month ( $n = 105$ ), medium = between one portion per month and one portion per week ( $n = 90$ ), and high = greater than one portion per week ( $n = 50$ ).

In this population, GSTM1 null was found to be a risk factor for lung cancer (OR, 1.53; 95% CI, 0.87–2.71), which is in agreement with previous findings (5). Overall, a high consumption of cruciferous vegetables appeared to decrease lung cancer risk in this population (OR, 0.64; 95% CI, 0.25–1.67; Table 1). The protective effect of cruciferous vegetable consumption was observed in both GSTM1-positive and -null individuals, although a weak dose-response relationship was apparent only in GSTM1-null individuals (Table 1).

Our data support the finding of Spitz *et al.* that isothiocyanates appear to reduce lung cancer risk. However, whereas Spitz *et al.* found a protective effect among current smokers only, we found this among nonsmokers. Also in our study, there was dose-response relationship between cruciferous vegetable intake and lung cancer risk among GSTM1-null individuals but not among GSTM1 wild-type individuals. These findings support the hypothesis that isothiocyanates may be more important in lung cancer prevention among those individuals who can eliminate these compounds less rapidly, although the strength of our findings are limited by the sample size of the study. Much larger studies will be required to accurately measure the modest effects of genes, such as *GSTM1*, and identify the extent of gene-environment interactions.

*Table 1* Lung cancer risk associated with cruciferous vegetable consumption among nonsmokers, stratified by *GSTM1* genotype

	Cases/ controls	Cruciferous vegetable consumption			P for trend
		OR (95% CI) <sup>a</sup>			
		Low	Medium	High	
All individuals	122/123	1	0.58 (0.26, 1.32)	0.64 (0.25, 1.67)	0.35
GSTM1-positive	57/67	1	0.28 (0.08, 1.04)	0.65 (0.16, 2.66)	0.57
GSTM1-null	62/53	1	0.68 (0.20, 2.29)	0.27 (0.06, 1.33)	0.12

<sup>a</sup>ORs and 95% CIs were adjusted for age (four categories), sex, and center.

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<sup>2</sup>The abbreviations used are: GST, glutathione S-transferase; CI, confidence interval; OR, odds ratio.

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