Letter to the Editor

NAT2 and Bladder Cancer—Response

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Golka and colleagues (1) critically refer to our observation that NAT2 genotype had no impact on bladder cancer risk (2). We were able to demonstrate in our case–control study nested in the European Prospective Investigation into Cancer and Nutrition (EPIC) that occupational exposure to aromatic amines and polycyclic aromatic amines was associated with an increased bladder cancer risk. On the basis of the comprehensive genotyping of N-acetyltransferase 2 (NAT2), we observed that NAT2 slow acetylation was not itself associated with bladder cancer risk. Notably, our main effect of 1.02 [95% confidence interval (CI), 0.81–1.29] is clearly in line with the OR of 1.02 (95% CI, 0.87–1.19) for a tagging single-nucleotide polymorphism that the authors reported from a pooled analysis of their own studies (3).

We fully recognize that EPIC is a population-based cohort with a low prevalence of rare occupations known to entail a bladder cancer risk. We also mentioned in the article that the metabolism of aromatic amines and the genetic variation of enzymes active in these pathways are more complex than can be captured by a deduced slow or fast acetylator phenotype. We cannot exclude the presence of interactions of N-acetylation with rare exposures to particular aromatic amines. Unfortunately, even very large studies have a limited statistical power to go further into details, i.e., refining the N-acetylation status, finding an association with other polymorphic enzymes, and performing accurate assessment of exposure to (rare) arylmonoamines or arylamines. Overall, however, our results do not provide evidence for a strong interaction with occupational exposure.

Golka et al. (1) addressed the decreased bladder cancer risk of slow acetylators in Chinese benzidine-exposed workers (4, 5), whereas studies in German chemical workers showed an increased risk. They attributed this opposite effect to ethnic differences in NAT2 minor allele frequencies (6). However, the decreased risk in benzidine workers may also be explained by differences in the metabolism of arylamines and arylamines (4, 7). We will continue exploring the role of NAT2 in the German cohort study UroScreen in chemical workers with more detailed exposure information about aromatic amines (8).

Genetic testing for the polymorphic gene NAT2 was introduced for purposes of compensation or preventive activities among workers with exposure to aromatic amines, but has been criticized because of ethical questions and insufficient scientific evidence (9). Golka et al. (1) considered our conclusion that testing workers for NAT2 would be inappropriate as an overinterpretation. We still consider it premature to test chemical workers for genetic predisposition not only due to uncertain evidence on the excess risk but especially facing the very low-positive predictive value of NAT2 slow acetylation and other biomarkers in bladder cancer due to the low incidence of this disease (8, 10).

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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References
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