

## NAT2 and Bladder Cancer—Letter

Klaus Golka, Meinolf Blaszkewicz, Silvia Selinski, Jan G. Hengstler, and Hermann M. Bolt

The study of Pesch and colleagues (1) investigated the impact of occupational exposure on bladder cancer risk and its modulation by the polymorphic N-acetyltransferase 2 (NAT2), based on a follow-up of the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, recruited within 1991 to 2000. With regard to interpretation of the results, we have the following comments.

The study investigated 52 at-risk occupations ever performed in 754 bladder cancer cases and 833 controls and did not reveal significantly elevated occupational bladder cancer risks stratified for gender. This may be due to dilution effects by low-level and/or short-term exposures and few observations. However, the results were adjusted for age and region as well as for multiple testing also for infrequent occupations. At present, the coherence of aromatic amine exposures and bladder cancer risk can be seen only in groups of persons or specific areas with higher present or past occupational exposures to aromatic amines. Such a recently detected industrial hotspot is the use of carcinogenic azo dyes in sprays for metal crack testing (2).

The authors address the rapid NAT2 genotype as a bladder cancer risk factor in occupationally exposed per-

sons. This assignment is based on two studies in Chinese benzidine production and use facilities. But it contrasts with results obtained in Caucasian populations, where slow acetylators, when exposed to aromatic amines, are at the higher risk (3).

On the basis of their study, the authors concluded that the NAT2 genotype had no impact on bladder cancer risk. In Europe, the production of most carcinogenic aromatic amines, such as benzidine, was stopped in the 1960s and early 1970s, mostly due to legal regulations. From 1991 to 1993, we conducted a hospital-based study in the county of Leverkusen, a hotspot area of human bladder cancer and of former manufacture of carcinogenic aromatic amines (4). Of note, 55% of the 196 phenotyped bladder cancer patients comprised slow acetylators at a normal percentage (55%). However, the portion of slow acetylators was higher (62%–71%) in subgroups with specific histories of occupational exposure.

It also seems that the "slow" NAT2 genotypes comprise combinations of different "slow" haplotypes with different resulting metabolizing capacities. In this context, we could recently show that the frequent "ultra-slow" NAT2\*6A was associated with an elevated bladder cancer risk, based on 1,712 bladder cancer cases and 2,020 controls (5).

In essence, we regard the final statement of the authors (1) that "testing for NAT2 would be inappropriate in occupational settings" as an overinterpretation.

**Disclosure of Potential Conflicts of Interest**

No potential conflicts of interest were disclosed.

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**Authors' Affiliation:** Leibniz Research Centre for Working Environment and Human Factors (IfADO), Dortmund, Germany

**Corresponding Author:** Klaus Golka, Leibniz Research Centre for Working Environment and Human Factors (IfADO), Ardeystrasse 67, 44139 Dortmund, Germany. Phone: 49-231-1084-344; Fax: 49-231-1084-343; E-mail: golka@ifado.de

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