Polymorphisms in manganese superoxide dismutase and catalase genes: functional study in Hong Kong Chinese asthma patients.

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We read with interest the paper by Mak et al. (1) on asthma in a Hong Kong Chinese population. They reported a protective effect of the catalase (*CAT*) –262 T allele in non-smoking asthma patients. This result is of importance, as it suggests for the first time a potential role of the *CAT* –262 polymorphism in the etiology of asthma.

At variance with previous publications was the lack of association of erythrocyte catalase activity with the *CAT* –262 polymorphism within controls and cases. In a cohort of 196 coal miners, we observed lower erythrocyte catalase activities in miners heterozygous and in those homozygous for the *CAT* –262 T allele, heterozygotes having an intermediate activity (2). Although the difference was not statistically significant, a 28 percent decrease in catalase activity was observed in the non-smoker T carrier controls by Mak et al. (1), similar to the 31 and 33 percent of decrease reported by us (2), and by Ahn et al. (3) in 18 women from a population-based case-control study respectively. As Mak et al. (1) observed a decrease in catalase activity related to *CAT* –262 polymorphism in non-smokers only, we stratified on smoking status in our coal miner cohort. We found again a significant decrease in catalase activity with the *CAT* –262 T allele in current and in ex- or non-smokers (see figure), as we found previously in miners with current high and low exposure to coal dust (2), which demonstrates the consistency of the association. The lack of significance of the association in the study by Mak et al. (1) may be due to a low statistical power as 28 subjects were heterozygous and only one was homozygous for the *CAT* –262 T allele out of the 308 Chinese controls.

It is interesting to note that Mak et al (1) observed a protective effect of the *CAT* –262 T allele in non-smoking asthma patients only. Regardless of the disease, an oxidant-rich environment has been found to increase risk only in subjects with the low-activity catalase *CAT* –262 T allele (4). Factors previously found to be protective, such as an antioxidant-rich dietary environment or a low level of circulating proinflammatory cytokines, seemed to be beneficial only in subjects with the high catalase activity CC genotype (5). Similar to the

oxidant-rich environment in our occupational study, asthma may generate reactive oxygen species, and catalase activity significantly increases in asthma patients compared to controls (1). As catalase is involved in the first response to oxidative stimuli, the increase in its activity may be interpreted as a compensatory response to the changes in the oxidant/antioxidant imbalance occuring in asthmatics. In the study of Mak et al. (1), the level of the oxidant state related to asthma may partly mask the *a priori* deleterious effect of the *CAT* –262 T allele.

Further, the *CAT* –262 T allele frequency in this Chinese population (1) was five times lower than that observed in Caucasians (mean 26 percent [20-56] from 7 studies), and was similar to the frequency observed in 40 African Americans (6 percent) by Zhou et al. (6). The differences in reported *CAT* –262 T allele frequency between studies indicates significant variation between populations, and could also partly explain the *a priori* deleterious effect of the *CAT* –262 T allele, as patterns of linkage disequilibrium across populations were different.

In summary, these results highlight the complexity of the potential role of the *CAT* –262 polymorphism in the etiology of oxidant-related diseases.

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Figure. Catalase activity according to smoking status and to *CAT* –262 genotype

Box plots show the median (bar), the first and third quartile (box), and the first and last decile (fences) for each category. Numbers of miners in each group are shown below each bar.