Correspondence re: Zheng et al., Haplotype of Two Variants in p16 (CDKN2/MTS-1/INK4a) Exon 3 and Risk of Squamous Cell Carcinoma of the Head and Neck: A Case-Control Study.

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Letter

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Zheng et al. (1) have conducted a case-control study to determine the role of two polymorphisms in exon 3 of the CDKN2A gene in squamous cell carcinoma of head and neck. The two polymorphisms 500 C→G and 540 C→T are located in the 3’ untranslated region of the CDKN2A gene and are not part of the coding sequence. Recent studies provide sufficient evidence for the role of the 3’ UTR of mRNA in regulation of gene expression (2). The 3’ UTR of the CDKN2A gene is common to two transcripts that encode p16INK4a and p14ARF cell cycle regulators. The effect of these two polymorphisms on the expression of these two transcripts, if any, remains unknown. The prevalence of one of these polymorphisms 500 C→G has been shown to increase with increasing familial risk of melanoma (3). Our studies on metastatic melanoma showed association of both these polymorphisms with decreased disease-free survival and association of the 500 C→G polymorphism with reduced p53 expression (4). In the same study and in subsequent studies (4–6), we also showed the linkage disequilibrium between the 500 C→G polymorphism and 74 C→A polymorphism in intron 1 of the CDKN2B, which does not involve 540 C→T as misquoted by Zheng et al. (1). In our subsequent study on primary melanoma, we found overrepresentation of the 540 C→T polymorphism compared with healthy controls (5) and also an association with low-grade vertical growth phase melanomas (7). In our continued study on the role of these polymorphisms, we have extensively screened bladder cancer cases and found an association of these polymorphisms with tumour stage and survival.

The method used for the study of both these polymorphisms simultaneously and, consequently haplotype analysis, was described by us in our initial study of sporadic primary melanoma (8), and it has been used in all our above mentioned studies (4–8). Our primer pair and SSCP conditions for the amplification of exon 3 and detection of polymorphisms were copied by Zheng et al. (1). We are happy to know that primer pair and SSCP conditions described by us (8) have functioned well in a study carried out in a different laboratory. However, Zheng et al. (1) have wrongly attributed this primer pair to a study (9) in which exon 3 of CDKN2A was never analyzed and claim to have developed a method, which we have described in our above mentioned studies (4–8). In support of their claim, they refrain from referring to our published method. Moreover, the sequence of the forward primer, located in the intron, is from the reported sequence with GenBank accession no. U12820 and not L27211 (mRNA sequence of p16INK4a transcript of the CDKN2A gene) as claimed by Zheng et al. (1).

References

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