LETTER TO THE EDITOR

Reply: SNPs in ultraconserved elements and familial breast cancer risk

Rongxi Yang¹² and Barbara Burwinkel¹²
¹Helmholtz-University Group Molecular Epidemiology, German Cancer Research Center (DKFZ), Im Neuenheimer Feld 581, 69120 Heidelberg, Germany and ²Department of Gynecology and Obstetrics, Division Molecular Biology of Breast Cancer, University of Heidelberg, 69120 Heidelberg, Germany

To whom correspondence should be addressed. Tel: +49 6221 421461; Fax: +49 6221 421464; Email: r.yang@dkfz.de

Dear Sir,

We thank I.Catucci et al. (in preparation) for performing a replication study on the two ultraconserved element (UCE) variants rs2056116 and rs9572903 by analyzing an Italian study population of familial breast cancer cases. Beforehand, we had analyzed different single-nucleotide polymorphism (SNPs) in UCEs and found the variant rs2056116 to be associated with familial breast cancer risk especially in the (premenopausal) early age group investigating a German study population (1). Catucci et al., however, did not find any association of this variant with familial breast cancer risk especially in the (premenopausal) early age group investigating a German study population (1). Catucci et al., however, did not find any association of this variant with familial breast cancer although the inclusion criteria for the familial BRCA1/2 mutation-negative breast cancer cases were quite similar to ours.

Interestingly, the allele frequencies of this variant were significantly different in the investigated German and Italian study populations. The minor allele frequency (MAF) in German control population is 0.39, whereas the MAF is 0.34 in the Italian control population (P = 0.00007). Remarkably, Ban et al. (2) analyzed this SNP in 938 British trio families (an affected individual and both parents) for an influence on multiple sclerosis risk. Here, the MAF was 0.39 matching the allele frequency from our German study population. Thus, the allele frequency of the investigated Italian study population is significantly different from the so far investigated German and British study populations.

This might be a hint that population-specific factors and/or a different linkage situation with a causative SNP may explain the discrepancy between the two studies. However, as Catucci et al. discussed, also statistical fluctuations might be a quite likely explanation for these observations.

Finally, we completely agree with Catucci et al. that large multicenter studies are necessary to estimate the effect of this variant on breast cancer risk and clarify possible population specific factors.

References


Received December 17, 2008; revised December 17, 2008; accepted December 17, 2008