Author's response to reviews

Title: Low-risk susceptibility alleles in 40 human breast cancer cell lines

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Dear Dr. Kaiser

We have submitted the second revised version of the above-mentioned manuscript. We have specified our responses to the reviewers below. We hope that the manuscript now is acceptable for publication in BMC Cancer. We look forward to your decision.

Yours sincerely,

Mieke Schutte

REVIEWER 1

MAJOR COMMENT

There appears to be a misunderstanding regarding the allelic loss data in Cancer Res 65: 11335; 2005. This paper describes the analysis of gene expression in brain tumors by microarrays. The reviewers quote of this paper refers to the genes that are differentially expressed in the tumors, related to the 1p and 19q allelic losses. Of the identified genes, 210 were located on chromosome 1p and 19q. Of these, 136 associated with loss of 1p, 25 with loss of 19p, and 49 with loss of both 1p and 19q. However, these 210 genes represent only 8.5% of all 1p and 19q genes that are present on the microarrays. Thus, the expression level of 8.5% of all genes in these regions of allelic loss is affected by the deletion of one gene copy. We hope that this clarifies the issue.
Yet, the point is well taken that we have not been clear in our manuscript. We therefore have performed a comparison of expression levels according the genotype groups with and without allelic loss (Table 3). Although numbers are small for some sample groups, there was no apparent association of gene expression levels and allelic loss status. We are not sure whether this analysis complies with the reviewer’s request. A problem with including allelic losses in the analyses is that it is impossible to deduce whether a cell line had been homozygous or heterozygous for the SNPs. We therefore have opted for a direct comparison between major or minor homozygotes and allelic losses.

MINOR COMMENTS

1. We have changed the P-value in <0.01 and have now also included the error bars in Figure 1a.

2. We have changed Figure 2 drastically. The three-genotype groups are now indicated by three different colors and we have indicated the two samples with the FGFR2 isoform in Figure 2. We also have rewritten the text at page 8, by explaining exon array data and describing the results from each expression analysis separately. The legend of Figure 2 has been changed accordingly.

REVIEWER 2

This reviewer had no further comments.