Reviewer's report

**Title:** Association between novel PLCE1 variants identified in published esophageal cancer genome-wide association studies and risk of squamous cell carcinoma of the head and neck

**Version:** 1 **Date:** 21 February 2011

**Reviewer:** Balraj Mittal

**Reviewer's report:**

The manuscript entitled “Association between novel PLCE1 variants identified in published esophageal cancer genome-wide association studies and risk of squamous cell carcinoma of the head and neck” by Ma et al had observed the association of three potentially functional SNPs (rs2274223A/G selected from previously published genome wide association studies and two SNPs rs3203713A/G and rs11599672T/G selected on the basis of predictive functional value) of PLCE1 in 1,098 SCCHN patients and 1,090 controls in a non-Hispanic white population. None of three SNPs was alone significantly associated with overall risk of SCCHN, their combined effects of risk alleles were found to be associated with risk of SCCHN in a locus-dose effect manner, particularly for non-oropharyngeal tumors. However, manuscript has some limitation enlisted below:

**Major:**

1) Authors should mention the recent Genome wide association (GWA) studies conducted in the head and neck cancer and should discuss the results of replication study of GWA study in Head and Neck cancer in the introduction, if any?

2) Is there any Molecular/functional study on the role of PLCE1 in head and neck carcinogenesis? If yes it should be included in the Introduction and Discussion of the manuscript.

3) The exclusion and inclusion criteria of case and control should be clearly indicated in the material and methods section.

4) Genome wide association study by Abnet et al showed 5 SNPs at locus 10q23 of PLCE1 to be significantly associated with ESCC and GCA including two nonsynonymous variants rs2274223 and rs3765524. However most notable was association with rs2274223. Why authors have not included other SNPs of PLCE1 from GWA study in their study? It will be interesting to replicate the others SNPs as well to look their role in head and neck cancer.

5) What are the criteria of selection of SNPs rs3203713 and rs11599672, which were not explored in the earlier published genome wide association study?
6) None of the three PLCE1 SNPs selected was found to be associated with overall risk of Head and neck cancer either at genotype or allelic level. However when subjects were trichotomized according to risk alleles, subjects carrying 3-6 alleles were at increased risk of SCCHN. What could be possible reason of the discrepancy?

7) Authors should also mention the P value at least of the significant results in the text and tables.

8) Author should apply multiple testing corrections like Bonferroni’s correction in the sub group analyses to avoid the false positive associations.

Minor

Show the gel picture of restriction digestions of PCR product

Author should correct the grammatical and spelling errors throughout the manuscript.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

None