Reviewer’s report

Title: Loss of heterozygosity: what is it good for?

Version: 1  Date: 12 March 2015

Reviewer: XIAOYANG RUAN

Reviewer’s report:

Major Issues
The paper tries to provide insight into a topic (the mechanism and consequence of LOH) with somewhat inappropriate sample set. Comparing to other types of cancer, ovarian cancer (OC) has a relatively more complex genetic origin, confounding environmental factor, and histological subtypes with very different prognosis. Genetically, there are familial breast and ovarian cancer that is mostly attributable to autosomal dominant BRCA1/2 mutation, HNPCC (Hereditary Non-Polyposis Colorectal Cancer) related OC that is caused by mismatch repair deficiency, and sporadic cases. Environmentally, virus infection plays an important role in OC. The paper did not aware of this and used samples with mixed histological types without clearly defined the genetic background. This is disturbing in that the observations described in the paper might be for different diseases.

Minor Issues
Only part of the issues were listed
Page 7: “the variant was not called in the matched normal sample or identified as a germline alteration in another tumour/normal pair”. Not clear.
Page 7: “A selection of variants which met the above criteria …”. Please give a proportion and explain briefly the selection criteria.
Page 7: “Affymetrix SNP Mapping array data was obtained for the sequenced cases”. Give a total number here.
Page 7: “The Cancer Genome Atlas Affymetrix SNP6 data were downloaded from the Data Portal”. Problematic sentence. Also, where the Affymetrix 500k data from? The author needs to describe the source of sample more clearly. Are all the wet lab samples from TCGA?

Page 8: “thus excluding regions of allelic imbalance where at least one copy of both alleles was present”. -- where at least one copy of both alleles was present – can be removed.

Page 8: “A candidate TSG screen in ovarian cancer”. This section is very long. So sub-titles will be helpful for readers. The content is not organized efficiently.

Page 9: “A targeted mutation screen was conducted on 86 ovarian cancer cases including high-grade serous and endometrioid, low-grade endometrioid, clear cell
and mucinous subtypes.”. Should be “on the 86 ovarian cancer cases…”. Also, add a total number to the “Ovarian tumour cohort” section on page 6.

Page 9: “The classic two-hit hypothesis would suggest that driver genes should have”. “would suggest … should” sounds very redundant.

Supp table 1: the table can be more efficient

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests