Reviewer's report

Title: Integrated Sequence And Expression Analysis Of Ovarian Cancer Structural Variants Underscores The Importance Of Gene-Fusion Regulation

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Reviewer: zhigang wang

Reviewer's report:

The manuscript was well written. The approach that integrated DNA sequencing and transcriptional profiling analysis in TCGA data from six ovarian cancer patient samples was advanced. They detected a large number of SVs genome-wide at base-pair level resolution, and found only a very small proportion of SVs had the potential to form gene-fusions and detected at the transcriptional level. The Remarkable observation of this study is that only the somatically derived gene fusions, none of the germline derived gene fusions were detectable on the RNA level. This finding suggests the existence of a regulatory mechanism to suppress germline SVs segregating in natural populations. Such mechanisms may be lost or less effective in development of cancer. They concluded their results indicate gene fusions and other SVs are the important factors in the onset and progression of ovarian cancer. They believe the importance of the regulated expression of these variants in determining their ultimate biological and clinical significance. The integrated genomic approach and unique observation in this study will attract attentions from many scientists. It may be appropriate to publish on journal BMC Medical Genomics.

Minor comments:

The authors should be careful for the limitation of the genomic data from a small set of tumors in this study to draw a conclusion, and SVs found in this study may be basically the scar of genomic instability and not be the “drivers” in tumor development and progression.

The author should be aware of at least two of the five cases in this study carrying BRCA2 mutations. It is unclear for BRCA status of P1 in the TCGA data. BRCA1 or BRCA2 mutations are the drivers of 30% of the high grade serous ovarian cancer. These mutations result in deep deficiency of homologous recombination repair with high genetic instability. Large amount of SVs and unique patterns of SVs distribution in tumor genome may be associated with the deficiency. The authors should compare SVs in tumors carrying mutated BRCA to those with wild-type BRCA.

In page 14 last paragraph, is change zero to capital O correct when the gene region RP1-2705.3 became fusion gene RP1-27O5.3-ZNF643? Why did repeat 1p34.2-1p35.1 deletion?

In page 18 first line of conclusion, the first sentence “more important
factors.....than previously envisioned" was probably over-stated. This study didn’t show any recurrent fusion gene(s) with potential functional impact in multiple tumor cases.

Recommendation: Minor revision

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

No