Reviewer’s report

Title: Integrative genomic analyses of APOBEC-mutational signature, expression and germline deletion of APOBEC3 genes, and immunogenicity in multiple cancer types

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Reviewer: Yu-Sun Chang

Reviewer’s report:

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Attn: (MGNM-D-19-00194) Integrative genomic analyses of APOBEC-mutation signature, expression and germline deletion of APOBEC3 genes, and immunogenicity in multiple cancer types by Guo et al.

"Integrative genomic analyses of APOBEC-mutation signature, expression and germline deletion of APOBEC3 genes, and immunogenicity in multiple cancer types" by Guo et al. analyzed the 10 cancer types with APOBEC mutational signatures in TCGA samples, and correlated the inter-relationship of APOBEC3A and 3B isomers, mutational signatures, APOBEC3A/B genotypes, neoantigen loads and tumor infiltrated lymphocytes.

Their analyses reported the following results:

1. The isoform uc011aoc transcribed from APOBEC3A/B germline deletion was associated with APOBEC mutational signature only in breast cancer.

2. APOBEC3A/B deletion genotype associated with mutational signature, neoantigen load and CD8+ in TILs in breast cancer.

Overall comments:

This study has performed bioinformatics analyses of gene expression and APOBEC3 mutation signatures in 10 cancer types in TCGA datasets regarding APOBEC3 genes or genotypes. This type of analysis is no longer novel. However, the detailed investigation of the isoform uc011aoc transcribed from APOBEC3A/B germline deletion is new.

Comments:
The expression levels or the reads from the RNAseq data of isoform uc011aoc seem to be very low (Additional figure 1). Although the analysis indicated that the isoform uc011aoc expression level is significantly correlated with the deletion genotype in breast cancer, distribution of genotypes in samples should be presented. In addition, it would be helpful if the sample sizes in the analysis in all genotypes or two types (non-carrier and HE/HO deletion) can be presented. Even more significant if the expression of isoform uc011aoc can be verified by quantitative RT-PCR. This should be considered as the limitation of the study.

The isoform uc011aoc shares promoter with APOBEC3A. Is there a correlation between level of A3A and the isoform?

Minor comment:
Authors may consider to apply Forest Plot to demonstrate the difference the differential role of the isomers in various cancers with APOBEC3A genotyping.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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