Reviewer’s report

Title: CVE: an R package for interactive variant prioritisation in precision oncology

Version: 0 Date: 30 Nov 2016

Reviewer: Lizhong Ding

Reviewer's report:

The authors develop a R package Cancer Variant Explorer (CVE) that prioritises variants to identify drivers, resistance mechanisms and druggability. The tool is helpful for analyzing the cancer sequencing results to identify functionally important variant and druggable targets. However, the manuscript is not well structured or explained in detail, especially when it comes to the database sources (except for TCGA), algorithms, and their usages, which thereby produce obstacle to quickly understanding. Hence, the manuscript needs to be restructured and give more detailed explanations. The spelling and grammar issues are serious. In conclusion, the manuscript needs major revision.

Page 1 line 37: "examplar" should be "example".

Page 2 line 24: the term "variant prioritisation" is used without prior clear definition and example. To be helpful, the author need to provide a paragraph of review of the definition, example, general process, and background knowledge of variant prioritisation.

Page 5 line 6: Please explain why you are interested in BRAF-wt/RAS-wt patients? If the patients are BRAF-wt/RAS-wt, how can you prioritise putative driver variants in 93 BRAF-wt/RAS-wt melanomas, which is mentioned in page 5 line 18.

Page 6 line 16: "Running CVE with the WGCNA melanoma extension enables the exploration of" lack a space between "WGCNA" and "melanoma".

Page 6 line 27: "we a derived melanoma-specific gene interaction" lacks the verb.

Page 6 line 29: "RNAseq data" should be "RNA-seq data"

Page 9 line 54: "chose" should be "choose"

Page 11 line 50: "Shiny-based prioritisation tools the CVE has the potential to be at the forefront of these developments." To make a new tool outstanding, the new tool, here CVE, is always compared to several old leading tools in the aspects of running results. Please do the comparisons.
The Bioconductor Reference Manual lacks examples for most of the commands/functions. The authors need to write a detailed manual to guide the users one step by one step.

**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.

No

**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.

Not relevant to this manuscript

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

Needs some language corrections before being published

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