Reviewer’s report

Title: Genome sequencing analysis of blood cells identifies germline haplotypes strongly associated with drug resistance in osteosarcoma patients

Version: 1 Date: 02 May 2018

Reviewer: Edwin Choy

Reviewer's report:

In response to my comments, the authors appear to have a fundamental disagreement with my analysis of validated data. I again assert that if you look for an association between haplotypes and any phenotype, be it chemoresponsiveness, you will be able to generate candidate genes even if they were randomly permuted, especially at the significance level of p < 0.05. The authors assert that they identified 5 SNPs associated with both tumor necrosis and overall survival, and this is unlikely to have resulted by random chance. I do not think this assertion is statistically valid. The fact that these SNPs were technically validated to be accurately measured or that these SNPs involve genes with plausible biologic function, does not convincingly argue that they are non-random. But I would welcome a statistics reviewer to analyze this report and prove me wrong. I agree with the authors assertion that their findings should be validated on an independent cohort of osteosarcoma patients before it becomes clinically meaningful. I assert that their findings should be validated on an independent cohort in order to be publishable.

If the publisher can have this manuscript re-reviewed by an independent genomic statistician and show that I am wrong in my assertion that these findings are not statistically robust, then I am willing to allow for publication.

Otherwise, this manuscript is well written and compelling to read.

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

No

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.

No

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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