Reviewer’s report

Title: Variation of mutant allele frequency in NRAS Q61 mutated melanomas

Version: 0 Date: 02 May 2017

Reviewer: Helen Rizos

Reviewer's report:

The main conclusion of this study is that NRAS mutant allele frequency is heterogenous in melanoma and only 30% of cases had significantly increased NRAS mutant allele frequency. The most important concern with the data is that there is no validation that the heterogenous NRAS allele frequency is simply not a result of variable tumour cell content. Although the tumour content is noted as being >80%, there is no independent validation of this.

Considering the fact that mutation specific NRAS antibodies are now available, I think it is essential that a subset of the tumour samples are rescreened to validate the genotyping data with IHC data of mutant NRAS and melanoma-markers. This will ensure that the genotyping data matches the IHC data, and not simply a result of low tumour content.

The allele frequencies derived from the TCGA dataset should also be presented as in Figure 2 (potentially as supplementary) for direct comparison with data generated in this work.

It is not clear where the 104 NRAS Q61 mutated melanomas come from here (page 9, line 7)?

Quality of Figure 1 is not high enough for easy review

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 am able to assess the statistics

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

Acceptable

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