Reviewer’s report

Title: Germline and somatic mutations in patients with multiple primary melanomas: a next generation sequencing study

Version: 0 Date: 20 Mar 2019

Reviewer: Daniela Massi

Reviewer’s report:

In this study, Casula and colleagues evaluated germline DNA specimens from 102 patients with multiple primary melanoma (MPM) using a next-generation sequencing (NGS)-based approach and a melanoma-specific multiple-gene panel. Among MPM patients, 5 cases presented a history of at least 4 MPMs, whose primary melanomas (N=28) were collected and assessed for somatic mutations by NGS analysis. Although CDKN2A was confirmed as the most prevalently mutated gene at germline level, several additional variants were reported in this series of MPM patients. As expected, BRAF was the most frequently mutated gene at somatic level among the above-described subset of melanomas.

The experimental plan was appropriately designed and well conducted in a satisfactorily large collection of MPM patients. The study provides good mutation profiles (at germline and somatic levels) for such a subgroup of melanoma patients.

Minor criticism

In Methods, authors should better specify the criteria used for defining as pathogenic the identified sequence variants.

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.

Yes

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 am able to assess the statistics

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

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organisation that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

None

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal