Reviewer’s report

Title: Expanding the spectrum of A20 haploinsufficiency in two Chinese families: cases report

Version: 1 Date: 05 Mar 2019

Reviewer: Lara Bossini-Castillo

Reviewer's report:

This manuscript describes two novel coding heterozygous mutations in the TNFAIP3 gene that lead to a recently described autoinflammatory disease (A20 haploinsufficiency) in two unrelated Chinese families. The results of this project interestingly widen the number of mutations and clinical manifestations associated to this disorder.

However, information about the sequencing methods is absolutely and surprisingly missing. Therefore, there are several major concerns regarding the sequencing methods and quality controls applied in this study:

1) What was the WES platform used?
2) What was the sequencing coverage?
3) How were the sequencing libraries generated?
4) What sequence read quality control pipeline was applied?
5) What the genome mapping software, parameters, genome build applied?
6) What sample type was genomic DNA isolated from? What protocol was applied?
7) How were the causal mutations prioritized? what coding mutation database or protein prediction software was used? How many mutations were found per individual? what were the functional classifications of these mutations per individual?

Additionally, patients with the same mutation have very different clinical manifestations. Have the authors checked the existence of additional mutations in the same same or genes in the same pathway that may have an additive effect on the phenotype of the most severely affected individuals? Further discussion and justification about this topic must be added and explored in the discussion section.

In Figure 3 no coordinates at all are shown and the names of the individuals are not concordant with the ones used through the rest of the manuscript.
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.

Unable to assess

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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