Reviewer’s report

Title: A novel deletion mutation in KMT2A identified in a child with ID/DD and blood eosinophilia

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Reviewer: Cristina Gervasini

Reviewer's report:

To The Authors

The manuscript by Zhang and colleagues reports on one patient affected by intellectual disability, developmental delay and blood eosinophilia found carrier of KMT2A mutation.

The clinical presentation of the proband is sufficiently detailed, as the molecular test.

The discussion is superficial: the genotype-phenotype correlation is presented unclear and difficult to read.

Several inaccuracies are present.

There are criticisms which should be addressed in order to improve the manuscript and further support the discussion.

-A more detailed discussion about the KMT2A mutation in patients with WDSTS phenotype and in patients without a clear WDSTS phenotype should be reported.

In the Background section the authors should describe that different phenotypes associated to KMT2A mutations have also been reported. In addition, the effect of somatic and germline KMT2A mutations should be discussed separately.

-As a general comment, the genotype-phenotype correlation can be better developed. An effort is requested in order to comment the relationship of KMT2A mutations and the corresponding phenotypes, taking into account the peculiar hematological phenotype. Do the Authors investigate additional possible causes of this clinical sign other than KMT2A mutation?

-I think that the 5 categories presented in Table 1 and discussed in the last paragraph of the Case report section ("To analysis the relation between phenotypes of the child and genotypes of the KMT2A gene, we systematically reviewed related literatures and etc etc." ) is very difficult to read. The Authors should rewrite this part presenting the phenotype associated to KMT2A mutations taking into account the phenotype of their proband. For example, a comment on the presence/absence of the WDSTS clinical signs in the proband should be added. In any case, in Table 1 (if maintained) the references are to be added.
A more detailed comment is requested to discuss the genic localization of the described mutation. At our knowledge, this is the KMT2A earlier truncating mutation so far described (Figure 3). Its localization could afflict the mRNA and/or protein stability and then the effect should be further discussed.

-The comment of the last paragraph of the Discussion and conclusion section "When we compared whether genotypes and phenotype were related, by a large amount of literature, etc etc" should be rewrite to give a final but simply message to the readers.

-Figure 3: the figure represents the KMT2A protein structure, but the mutations are reported in a mixed form: there are mutations as nucleotide changes and other as protein changes: please homogenize the form of the described mutations

-Figure 3: in the figure are not present all the mutations previously described: for example, the 27 novel additional KMT2A mutations reported in the recent paper by Baer et al. 2018 should be added

Additional minor revisions:

-Abstract:

--background the sentence "Lysine methyltransferase 2A (KMT2A) plays an important role in the early brain development 3 and hematopoiesis by regulating histone H3 lysine 4 (H3K4) methyltransferase activity." should be rewrote.

--Case report: "p:25Rfs" is in an incorrect form, please follow the guidelines for correct nomenclature at HGVS site (http://varnomen.hgvs.org/)

-Case presentation: "p:25RfsX55" is in an incorrect form, please follow the guidelines for correct nomenclature at HGVS site (http://varnomen.hgvs.org/)

-Case presentation: in the sentence "To analysis the relation between phenotypes of the child and genotypes of the KMT2A gene, we systematically reviewed 2 related literatures and several major genetic databases, such as HGMD, Development, and OMIM (Figure 3)." The reference "figure 3" is improper

-Discussion : The sentence "The KMT2A gene is one of the H3K4 methyltransferases" is improper: the gene is not an enzyme, please change the sentence

-Figure 3: p:25Rfs and several additional mutations are reported in incorrect form (e.g. c.2126-2127delCT should be c.2126_2127delCT), please follow the guidelines for correct nomenclature at HGVS site (http://varnomen.hgvs.org/)
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.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

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