Reviewer's report

Title: IKZF1 Genetic variants rs4132601 and rs11978267 and Acute Lymphoblastic Leukemia Risk in Tunisian children: a case-control study

Version: 3 Date: 07 Aug 2019

Reviewer: Tri Indah Winarni

Reviewer's report:

Association of IKZF1 gene polymorphisms rs4132601 T/G and rs11978267 A/G with Acute Lymphoblastic Leukemia in a Tunisian paediatric cohort

Reviewer Comments: "green indicate revision"

1. Title: term "association" seems not represent your research design (case-control). Case control study usually is done to seek the risk (Odd Ratio) not association study design, consider your conclusion. Please revise your title and incorporate your aim of study throughout your manuscript.

2. Abstract conclusion: Please revise with more assertive words such as "IKZF1 gene polymorphisms rs4132601 T/G and rs11978267 A/G are the risk factor of ALL in a Tunisian paediatric cohort"

3. How to write human gene name: please using italic style for human gene name (IKZF1 gene), revise it

4. All abbreviation should be spell out in the first appearance. Example: Hardy Weinberg Equilibrium (HWE), in the following appearance you can use abbreviation instead

5. Background:

a. "....genetic etiology dominates in younger age due to lower exposure environmental factors compared to adult". How can you so sure about the less exposure in younger age? How about if they live in very bad environment? Cancer in younger age usually due to germline/inherited genetic susceptibility (risk factor)

b. "The heritable susceptibility to ALL is proved So proven"
c. IKAROS is a potential regulator of lymphocyte and differentiation (17), and immune system development. Please be aware of punctuation in scientific article, review throughout your manuscript. See also in your Method subtitle Subjects: ...cytochemical reactions (myeloperoxidase form ALM and esterase for ALL). (space) Immunophenotyping

2.2. SNP Genotyping (enter into new paragraph) Total genomic DNA was...

6. Grammar/syntax error: this study has already been done a while ago. Please read carefully especially your method and result, and revise accordingly. Example: ...we have collected we had collected; ...ALL classification is (was) made; The guardian of both patients and controls of all participants/subjects are (were) informed; Data is was performing...; Total genomic DNA was isolated in (??) from...; Immunophenotyping is done Immunophenotyping was done....

7. SNP Genotyping: "genotyping of both rs4132601 and rs1197867 were missed for 3 and 17 respectively". I do not get you idea. What are going to say? Are those from cases and control or what? Did they finally excluded?

8. Association Study:...minor allele frequencies were at the limit of significance (P=0.086). I do not think we can say limit of significance, we should say not significantly associated.

9. Table 1. Note: bold types are indicates significant association $p > 0.05$ ($p$ value < 0.05 considered as significant association was stated in your statistical analysis)

10. There is discrepancy between abstract and result (haplotype analysis) of GA haplotype analysis values ($p$ values, OR and 95%CI). Which one is correct? Be careful with number

11. Page 10 line 5: ..... leukemia (MLL). Typo?? review throughout your manuscript.
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.

Not relevant to this manuscript

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

Needs some language corrections before being published

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 organization 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.

I declare that I have no competing interests

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