Author’s response to reviews

Title: The three CYBA variants (rs4673, rs1049254 and rs1049255) are benign: new evidence from a patient with CGD

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Version: 1 Date: 12 Oct 2017

Author’s response to reviews:

Dear Colleagues,

Many thanks for your decision letter dated on Sep 13. We hereby resubmit our manuscript entitled “The three CYBA variants (rs4673, rs1049254 and rs1049255) are benign: new evidence from a patient with CGD” (MGTC-D-17-00023R1) for consideration for publication in BMC Medical Genetics.

The questions raised by you have been dealt with as follows. The changes in the manuscript were marked blue.
Reviewer 1:

1. We modified the title according to your advice.

2. We agree with your point---The CYBA variants alluded to in the manuscript are SNPs and are not associated with CGD. We want to provide more evidence to prove it in our study.

3. Yes, we did the detection of NADPH oxidase component proteins by Flow to confirm whether the patient has CGD or not.

4. As you said, we just did CYBB gene sequencing at first. However, the mutation (c.141+5G>C) was missed at first because of the negligence of the experimenter. So, we did CYBA gene sequencing and found the three variants. Because these variants are not associated with CGD, we checked the CYBB sequencing data again, and c.141+5G>C was found. The variants in CYBA are an accidental discovery. We think the results are helpful for understanding the variants in CYBA. So, we report it here.

5. It is a good idea to test individually for p22phox and gp91phox. As soon as we got the letter from editor, we contacted the patient’s parents. Regrettably, we couldn't get the patient’s blood because of the patient’s personal reason until now. By the way, it is the reason why we resubmit the manuscript until now.

   The patient’s father has the three variants in CYBA and normal b558 estimation. So, we think the decreased b558 expression in the patient can reflect gp91phox expression.

6. The SI of the father is the same with healthy control. We added it in the manuscript.

7. We screened 50 healthy controls according to your advices. No c.141+5G>C in CYBB was found.

8. Because the patient have defected neutrophil respiratory burst function and decreased gp91phox protein expression, and no other mutation in CYBB was found, we think c.141+5G>C is pathogenic.
9. We checked the errors of grammar and syntax by English native speaker.

Reviewer 2:
We wrote a few comments on the variants in CYBA in the manuscript according to your advices.

Thank you all for your comments again. These advices give us a lot of help and make us improve.

Best Regards,

Xiaochuan Wang