Author’s response to reviews

Title: Whole exome sequencing reveals a stop-gain mutation of PKD2 in an autosomal dominant polycystic kidney disease family complicated with aortic dissection

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Point-by-point Responses

Thank the editor and reviewers for these precious comments concerning my manuscript entitled "Whole exome sequencing reveals a stop-gain mutation of PKD2 in an autosomal dominant polycystic kidney disease family complicated with aortic dissection" (MGTC-D-17-00066R1). These comments are all valuable and very helpful for revising and improving my paper, as well as the important guiding significance to my researches. We have studied comments carefully and have made corrections which we hope meet with approval. Their original critiques are followed by our response.

Q: Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format. Please overwrite this text when adding your comments to the authors.
A: As for the referee’s concern, we have included all comments for the authors in the box rather than uploading it as an attachment.

Q: This is a much better written manuscript with a more sounded discussion. The authors still did not make a compelled case of association between the aortic aneurysms found in the patient with the PKD2 mutation found in the family. Since the aortic aneurysms did not find in the all the affected family members, the suggestion of screening for young ADPKD patients for potential aortic dissection seems to be overstep from the conclusion of their study. The suggestion should be limited to the ADPKD patients with uncontrolled hypertension. Although the study is not novel in the mutation found in PKD2 and aortic dissection in the ADPKD patient, it can bring the discussion of aortic dissection in the ADPKD research.

A: We agree. Based on our findings, the suggestion of screening for young ADPKD patients for potential aortic dissection seems inappropriate. We have corrected it as you suggested. Discussion section, line 17, page 7 and conclusion section, line 15, page 9.

Q: The authors response to my previous comment to specification of variant filtering is incomplete. they state '(minimal allele frequency < 0.01)' but there is no reference or details provided about where such information is obtained from, and how it is relevant to the ethnic origin of the family reported here. They have modified their text to indicated that 'All family members were subjected to enhanced computed tomography ...' does this include the married in individuals II.1 and II.4? If not, they should be explicit about who had imaging.

A: Given a lack of large scale sequencing project in participants of Chinese origin, we referred to all populations from the Exome Sequencing Program and Exome Aggregation Consortium as most studies adopted. “The variants were then filtered using standard methods, focusing on rare (minimal allele frequency < 0.01 in all populations from the Exome Sequencing Program and Exome Aggregation Consortium) and pathogenic (predicted deleterious by SIFT or PolyPhen2) variants.” Methods section, line 17, page 5.
All family members included the individuals II.1 and II.4 in our study. “All family members, including individuals II.1 and II.4, were subjected to enhanced computed tomography and no aortic lesions were found except the proband.” Results section, line 13, page 6.