Author’s response to reviews

Title: A novel TEX11 mutation induces azoospermia: a case report of infertile brothers and literature review

Authors:

yanwei sha (shayanwei928@126.com)
liangkai zheng (lkzheng80@126.com)
zhiyong ji (445118679@qq.com)
Libin Mei (meilibin@sklmg.edu.cn)
lu ding (541907511@qq.com)
xu wang (wangxushiwo516@126.com)
shaobin lin (991690296@qq.com)
xiaoyu yang (yxy1921@163.com)
ping li (saarc2001@sina.com)

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Replies to Reviewer 1

Reviewers' comments: Reviewer #1: Interesting paper. Good idea, nice results. A case report, in fact. However, manuscript has to be improved a little bit experimentally and grammatically.

Major points: 1. Control group is needed for evaluation of sequencing in fertile men (at least 100). It is recommended, because authors have found novel mutation in TEX11 gene, that was not observed by other authors. Thus, sequencing of a quite control group should be done, to find, if this mutation may be present not only in azoospermia.

Response: Thanks for your suggestion. Unfortunately, it’s very difficult (cost and limited time for revision) for us to do sequencing evaluation on at least 100 fertile men. The novel mutation in this study was defined based on the published human genome database and NCBI database.

2. What about bioethical written consent from fertile man (men?), which biopsy was used? What was the primary reason for possessing the material from him, if he was fertile? It has to be supplemented and cleared, undoubtedly.

Response: Thanks for your suggestion. I have clarified this in the revision: As a control of normal testicular histology, testicular sections from two fertile men who died from car accident and their body was donated by their family member were obtained from the Pathology Department of our hospital. The written consent was obtained from their family member.

Minor points: 1. English is terrible. It should be edited and corrected by certified native speaker. It will allow to avoid strange descriptions, as: protein expression or race when talking about ethnicity/geography.
Text should be corrected to have a better reading flow and be less chaotic. Response: The revision has been edited by Medjaden Bioscience Limited. A lot of changes have been made.

2. Authors should pay attention on the fact that human genes are written using capitals and italic (TEX11), while for other species only first letter is capital, followed by small ones (i.e. Tex11). The same rule for proteins, but no italic, just straight text. It has to be clear in the manuscript, what literature data concern what species. Response: We have corrected all of them in the whole manuscript.

3. Introduction: some part of text that was in Discussion (lines: 235-288) should be in Introduction. It should be a compilation with the introduction fragment 76-121, finally shorter and less chaotic that is in a present form. Response: Thank you so much for your suggestion. We have changed it.

4. Discussion needs strong rewriting. The proper discussion for results obtained by authors begins from the line 289. Response: The Discussion has been revised.

5. Authors should include more references (marked in the text). Response: We have added some references as requested.

6. Also authors should add more detailed description of procedures and experiments, including providers of buffers and reagents, equipment (i.e., microscope) that was used in the study. Response: Since it is a case report, we didn’t provide detailed description of procedures and experiments. However, we have provided some references for major procedures and experiments. 7. Some parts of Materials and Methods are Results, in fact. So, please, check, if this form of text is appropriate for BMC Med Genet format. If not, then correct the text. Response: Thanks for your suggestion. We have separated Results from Materials and Methods, and added Results as a new section.

8. Seminal analyses should be done according to WHO guidelines. Similarly, karyotyping should be done as described in ISCN. Why there is no such information in the manuscript? Please, clarify this. Response: All experiments were performed according to standardized guidelines, we have clarified in the revision.

Replies to Reviewer 2

Reviewer #2: In this study, The Whole-exome sequencing was performed to study the genetic causes of male infertility, and one novel homozygote mutations in TEX11 gene (W856C) was identified in two brothers with azoospermia but not their mother. The molecular and Histological data are cogent, however, a number of points need clarifying and certain statements require further justification. There are given below:

point 1 The Molecular model of the mutated protein and the pathogenicity of variant need to be assessed by the bioinformatics software and also it is also preferable to have some functional experiments. Response: Thanks for your valuable suggestion. Since it’s a case report, we didn’t perform molecular structure analysis by bioinformatics software and the functional experiments for TEX11 mutation, which will be carried out in a research paper.

point 2 The genetic status of the father must be studied. Response: Since TEX11 is a X-linked gene, we didn’t examine the genetic status of the father.

point 3 The localization of the reported mutation. After comparison of the electropherogram present in the Fig.1 and the GenBank accession number, NM_031276, i can say that the name of mutation (2568G→T, in exon 29, GenBank accession number, NM_031276) is wrong. It should be named (2653G→T, in exon 29, GenBank accession number, NM_031276). Response: Thank you for your correction. We have corrected in the revision.