Author’s response to reviews

Title: Rubinstein-Taybi syndrome in a Saudi boy with distinct features and variants in both the CREBBP and EP300 genes: A case report

Authors:

Mohammad Al-Qattan (moqattan@hotmail.com)
Abdulaziz Jarman (ajarman@kfshrc.edu.sa)
Atif Rafique (drafiq_2@yahoo.com)
Zuhair Al-Hassnan (zhassnan@kfshrc.edu.sa)
Heba Al-Qattan (heba.qattan96@gmail.com)

Version: 2 Date: 09 Nov 2018

Author’s response to reviews:

Re: MGTC-D-18-00379R1

Rubinstein-Taybi syndrome in a Saudi boy with distinct features and variants in both the CREBBP and EP300 genes: A case report

Dear Editor,

Thank you for considering our manuscript. We have carried out the revisions as suggested by the reviewers (changes are highlighted in red).

Santasree Banerjee (Reviewer 1): Comments to the Author:

In this study, the authors performed a genetic molecular study for Rubinstein-Taybi syndrome in a Saudi boy with distinct features and variants in both the CREBBP and EP300 genes: A case report.
Major Points:

1. In this study, please illustrate the clinical details in more comprehensive and detailed way.
   Response: done; see lines 96 and 106

2. In this study, please describe the methodology for identifying the mutation? Please give us the detailed process and quality control system for identifying the candidate variants.
   Response: done; see lines 111-119 and the new Table 2

3. The variant has been written according to the HGVS nomenclature rules? Please confirm it.
   Response: yes

4. There are some typos and grammar mistakes in the text and need some editorial improvement.
   Response: done

5. Please, delete irrelevant "general" phrases and sentences.
   Response: done; see lines 83-85 and the new Table 1. Also see lines 148-158.

6. List up and explain all the abbreviation used in this manuscript.
   Response: done; see lines 183-206

7. Overall written English need to improve.
   Response: The paper was reviewed for written English
Katrina Fontana (Reviewer 2): Dear Editor,

I have revised this case report and it presents new and important information about Rubinstein-Taybi syndrome. However, some issues must be evaluated before considering for publication, as follow:

1) I suggest including in the "Background" information about the main CREBBP and EP300 genes variants that are already known to be associated with the Rubinstein-Taybi syndrome. The authors should make a brief genotype/phenotype correlation.
Response: done; see lines 83-85 and the new Table 1; and also lines 172-175

2) I suggest including in the "Mutational Analysis" a short description of the molecular methods used for the study of CREBBP and EP300 gene variants.
Response: done; see lines 111-119.

Jennifer Below (Reviewer 3): The authors present a case report with notable clinical characteristics of a child with RSTS and describe a likely causal mutation in CREBBP as well as a possibly benign mutation in EP300. The author suggest that some of the phenotypes observed may be due to interacting effects of the two observed variants. The paper is clear and concise and is generally well written (there is a minor typo on page 5, where the authors say 'evaluation' when I think the might have meant 'evolution').
Response: The typo was corrected. See line 127.

I have few comments, which I believe would strengthen this case report.

1) it would be nice to see a table comparing features of RSTS from other published reported cases to this new case
Response: see the new Table 1
2) the methods used to genotype the EP300 and CREBBP variants is completely absent- results and quality control measures from sanger sequencing should be shown (or taqman genotyping, or whatever methods the authors used). It would also be important for the reader to know exactly what portion of the genome was interrogated- for example comparisons are made to other cranio-facial abnormalities, but it is not explicitly clear to the readers whether or the the authors checked genes known to cause those cranio-facial abnormalities for mutations in this proband

Response: done; see lines 111-119 and the new Table 2.

Thank you

M M AL-Qattan