Author's response to reviews

Title: Variation in DNAH1 may contribute to Primary Ciliary Dyskinesia

Authors:

Faiqa Imtiaz (fahmad@kfshrc.edu.sa)
Rabab Allam (RAllam@kfshrc.edu.sa)
Khushnooda Ramzan (kramzan@kfshrc.edu.sa)
Moeenaldeen Al-Sayed (moeen@kfshrc.edu.sa)

Version: 2
Date: 10 February 2015

Author's response to reviews: see over
Author’s response to reviews

Title: Expanding the clinical phenotype of a mutation in DNAH1 causing Primary Ciliary Dyskinesia

Authors: Faiqa Imtiaz (fahmad@kfshrc.edu.sa); Rabab Allam (RAllam@kfshrc.edu.sa); Khushnooda Ramzan (kramzan@kfshrc.edu.sa); Moeenaldeen Al-Sayed (moeen@kfshrc.edu.sa)

Version: 3

Date: 10 February 2014

Reviewer’s report

Title: Expanding the clinical phenotype of a mutation in DNAH1 causing Primary Ciliary Dyskinesia

Version: 3

Date: 2 December 2014

Reviewer: Pierre Ray

Reviewer’s report: I acknowledge the efforts made by the authors to answer the comments I made in my previous reviews unfortunately they failed to even acknowledge my most important request: “The conclusions should however be turned down throughout the manuscript. The authors should indicate that a yet uncharacterized gene could be involved but that the identified mutation may be responsible for PCD and that mutations in DNAH1 may induce PCD.”

Authors: We have modified all text in the manuscript to concur with the Reviewer’s statement as above and have rephrased the Conclusion of the manuscript as follows:

In summary, we have identified PCD patients from the same family with a missense variation that segregates with the disease phenotype in the DNAH1 gene. In addition to adding DNAH1 as a gene that may be involved in giving rise to PCD, the clinical diagnosis and the subsequent genetic findings have translated into an overall positive and beneficial outcome for the index patient and family and will be of benefit for future preventative and counseling measures in the future.

Reviewer: I think this message was quite clear. It has in no way been taken into consideration so I feel it is almost an insult to my reviewing to submit again this manuscript with, as title: “Expanding the clinical phenotype of a mutation in DNAH1 causing Primary Ciliary Dyskinesia” and as conclusion to the abstract: “DNAH1 represents a novel PCD specific causing gene and its identification adds to the growing list of genes involved in this clinically and genetically heterogeneous disorder.”

Authors: We have modified the title as instructed to “Variation in DNAH1 may contribute to Primary Ciliary Dyskinesia”.
We have modified the conclusion of the abstract to: “Molecular variation in DNAH1 may play a role in PCD and its potential contribution should be considered in patients where all known genes are excluded.”

Reviewer: Again with the data presented here the author’s conclusion remains highly speculative. The author can only conclude that DNAH1 MIGHT represent a novel PCD gene. The authors have not brought any functional validation that the identified variant is indeed pathological.

Authors: The following has been added to the Discussion:

“In addition, the authors cannot exclude the probability that although this variant was the only one found and may play a role in PCD, it is possible that a pathogenic causal variant may be located in an uncharacterized gene or in a known gene that may have missed by the constraints of the methodology used in this study. Further investigation including functional analysis is necessary to determine the effect of this variant on the protein and to explore the presence of SNPs or molecular variants working in parallel with the p.Lys1154Gln variant causing the expanded phenotype seen in the patient described here.”

Reviewer: Furthermore, as I mentioned previously the authors may have well missed the real causal variant located in an uncharacterized gene or in a known gene that might not have been covered by whole exome sequencing.

Authors: The authors believe this is addressed in the section above.

Reviewer: These caveats must be discussed and the authors have to modify the title, the abstract and the remaining of the manuscript to indicate that the identified mutation MIGHT be involved in PCD but that their analysis was in no way exhaustive and that they cannot exclude the possibility of having missed the real causal variant.

Authors: We have modified all sections of the manuscript and we believe that the overall message and statements have been “turned down” as the respected Reviewer suggested.
Reviewer's report

Title: Expanding the clinical phenotype of a mutation in DNAH1 causing Primary Ciliary Dyskinesia

Version: 3

Date: 7 December 2014

Reviewer: Muhammad Tariq

Reviewer's report: Comments are addressed.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician