Author’s response to reviews

Title: Molecular diagnosis in recessive pediatric neurogenetic disease can help reduce disease recurrence in families

Authors:

Mahmoud Issa (myissa2002@hotmail.com)
Zinayida Schlachetzki (z.schlachetzki@gmail.com)
Valentina Stanley (vstanley@ucsd.edu)
Renee George (reeegeorge@gmail.com)
Jennifer McEvoy-Venneri (jmcevoyvenneri@ucsd.edu)
Denice Belandres (dbelandres@ucsd.edu)
Hasnaa Elbendary (hasnaa_mohamed24@yahoo.com)
Khaled Gaber (krgaber@gmail.com)
Ahmed Nabil (ahmadnabil248@yahoo.com)
Mohamed Abdel-Hamid (mohamadnrc@hotmail.com)
Maha Zaki (dr_mahazaki@yahoo.com)
Joseph Gleeson (jogleeson@ucsd.edu)

Version: 3 Date: 14 Apr 2020

Author’s response to reviews:

MGNM-D-19-00222R2 April 14, 2020
Response to Editorial Comments
Molecular diagnosis in recessive pediatric neurogenetic disease can help reduce disease recurrence in families

Editor Comments

1. Ethics approval

Thank you for your response. However, we ask that you please include a statement in the “Ethics approval and consent to participate” section of your Declarations confirming that your study was submitted to and approved by a local ethics committee in Egypt. Please also ensure that the full name of the ethics committee is included in this statement.
Response. Done. We think there is some confusion because we previously had two separate “Ethical” sections in the manuscript, the first was in the Methods section and the section was after the Funding section (page 22), and I think that the Editorial Office may have only seen the short one on page 22. We have now merged these two sections into a single Ethical Approval and Consent to Participate on page 22 now that reads:

“The University of California San Diego Human Research Protection Program (HRPP) IRB approved recruitment of subjects for NGS and return of research results to the referring physician and family under protocol #140028 entitled “The Genetics of Childhood Neurological Diseases” with Dr. Gleeson as PI. All subjects or their parents or legal guardians signed a consent in their fluent language, and additionally an assent was signed by mentally capable underaged individuals in the form of a childhood assent if between the ages of 7-12, and an adolescent assent if between the ages of 13-16 years of age. The study was submitted to and approved by the Egyptian National Research Centre Medical Research Ethical Committee (MREC) serving as the local ethics committee in Egypt. The Egyptian National Research Centre Medical Research Ethical Committee (MREC) IRB approved the study for confirmation of research results, fetal genotyping and genetic counseling for families from the Clinical Genetics Department with Dr. Zaki as PI. The Egyptian National Research Centre Medical Research Ethical Committee (MREC) IRB approved the study for the Department of Prenatal Diagnosis and Fetal Medicine with Dr. Gaber as PI for amniocentesis, genetic testing, and eTOP. The IRBs were independent from the investigators and sponsors, and were from the same institute and country in which the study took place. Appropriate ethical committee approval was included for both countries.”

If anything further is lacking, please let us know.

2. Consent to Participate

Thank you for your response. However, we ask that you please include a statement in your “Ethical approval and consent to participate” section, clarifying whether informed consent to participate, written or verbal, was obtained from all of the participants in the study and clearly state this in your manuscript. Please note that in the case of minors, which refers to individuals younger than the age of 16, consent to participate must be obtained from their parents or legal guardians. As such, we ask that in your “Ethics approval and consent to participate” section, to clarify whether informed consent to participate, written or verbal, was obtained from the parents or legal guardians of any participant under the age of 16 and clearly state this in your manuscript. If consent was verbal, please state the reason and whether the ethics committee approved this procedure. If the need for consent was waived by an IRB or is deemed unnecessary according to national regulations, please clearly state this, including the name of the IRB or a reference to the relevant legislation.

Response. Done. We now state in the Ethical Approval and Consent to Participate section “All subjects or their parents or legal guardians signed a consent in their fluent language. Additionally an assent was signed by mentally capable underaged individuals in the form of a childhood assent if between the ages of 7-12, and an adolescent assent if between the ages of 13-16 years of age.” No verbal consent or assent was obtained. If further clarification is needed, please provide required language so that it can be incorporated into the Ethical Approval and Consent to Participate section.
3. Consent for publication

Thank you for your response. However, we ask that, in your “Consent for publication” section, you clarify whether WRITTEN informed consent for publication of clinical details and/or clinical images was obtained from all of the participants. Please note that in the case of minors, which refers to individuals younger than the age of 18, consent for publication must be obtained from their parents or legal guardians. As such, we ask that in your “Consent for publication” section, to please clarify whether written informed consent for publication of clinical details and/or clinical images was obtained from the parents or legal guardians of any participant under the age of 18.

Response. Done. We have now edited the Consent for publication section to read “Written consent for publication of identifying images or other personal or clinical details of participants that compromise anonymity was documented in the consent form. Written consent to publish images of a minor under the age of 18 was obtained from their parents or legal guardians.”

4. Authors’ contributions

Please consider the list of authors as it currently stands with reference to our guidelines regarding qualification for authorship (http://www.biomedcentral.com/submissions/editorial-policies#authorship).

Currently, the contributions of authors VS and HME does not automatically qualify them for authorship. In the section “Authors’ contributions”, please provide further clarifications on their contributions, and see our guidelines for authorship below.

An 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study. Authors are expected to fulfil the criteria below (adapted from McNutt et al., Proceedings of the National Academy of Sciences, Feb 2018, 201715374; DOI: 10.1073/pnas.1715374115; licensed under CC BY 4.0):

Each author is expected to have made substantial contributions to the conception OR design of the work; OR the acquisition, analysis, OR interpretation of data; OR the creation of new software used in the work; OR have drafted the work or substantively revised it

AND to have approved the submitted version (and any substantially modified version that involves the author's contribution to the study);

AND to have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

Please note that acquisition of funding, collection of data or general supervision of the research group, alone, does not usually justify authorship. You may acknowledge individuals who assist in the acquisition of funding or of data or supervise the research group in the Acknowledgments section of your manuscript.
If you wish to amend the list of authors, please use the standardised form which you and your co-authors must complete. The authorship change form can be found at the following link: https://resource-cms.springernature.com/springer-cms/rest/v1/content/7454878/data/v5
All instructions can be found on the form, please treat the 'current authorship' section as the original authorship. Please return the form within 14 days by email to the Editorial Office with all author signatures (including those newly added/removed).

Response. We appreciate your careful attention to this matter. We have now amended the Author Contribution section to clarify the roles of VS and HME to qualify them for authorship. The new section read “MYI, HME and VS interpreted whole exome sequence data, screened families for entry criteria, and collected data for supplementary tables.”

5. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Should you wish to respond to these revision requests, please put your responses to the reviewers’/editors’ comments in the Response to Reviewers box in Editorial Manager. Please do not upload a separate letter.

Response. Done