Author’s response to reviews

Title: A missense founder mutation in VLDLR is associated with Dysequilibrium Syndrome without the quadrupedal locomotion

Authors:

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Author's response to reviews: see over
Dear Editor,
We wish to thank you and the two reviewers for taking the time to improve our manuscript. We have accepted and carried out all the changes suggested by both reviewers. Here is a point-by-point response to the comments of the two reviewers:

Referee 1
Minor essential revisions.

1) abstract, results section: change “This is the first homozygous reported missense mutation” to “This is the first reported homozygous missense mutation”.
   Our Response: The suggested change has been carried out.

2) Page 5, paragraph 1. Missing opening brackets “heights (5-25%)”.
   Our Response: We added the missing brackets

3) abstract, methods section: as written, readers would expect that massively parallel sequencing was performed in both cases. This should be edited to reflect the two approaches. It would be clearer to say something like “SNP mapping and candidate gene sequencing in one consanguineous Omani family from the United Arab Emirates with cerebellar hypoplasia, moderate mental retardation, delayed ambulation and truncal ataxia was used to identify the mutation. In a second unrelated consanguineous Omani family, massively parallel exonic sequencing was used”.
   Our Response: The suggested change has been carried out.

Referee 2

Minor Essential Revisions
General:
1. VLDLR should be italicized throughout the manuscript when it refers to the gene, including in the title.
   Our Response: The suggested change has been carried out. All the VLDLR have been checked and italicized where we refer to the gene.

2. Remove # sign in front of OMIM designations throughout.
   Our Response: The # sign has been removed as suggested.

3. Check the manuscript for several instances of the use of the term ‘affected’ that is not followed by individual or person and add the latter.
   Our Response: This has been checked and changed as suggested.
4. To be consistent Family should always be capitalized.  
Our Response: Changed as suggested.

5. Growth parameters should be referred to as 10th centile vs 10%.  
Our Response: Changed as suggested.
6. ‘Figure’ should always be capitalized in the text.  
Our Response: Changed as suggested.

Title Page:  
7. Title: ‘…without the quadrupedal…’ should be ‘without quadrupedal…’.  
Our Response: Changed as suggested.

8. ‘Correspondance authors’ should read ‘Corresponding author’.  
Our Response: Changed as suggested.

Abstract  
9. ‘We combined SNP mapping with massive parallel exonic sequencing (and candidate gene analysis)….’, bracket phrase should be included as this approach was also used.  
Our Response: This statement has been changed as suggested by referee 1.

Background  
Our Response: Changed as suggested.

Materials and Methods  
11. DNA methodologies: the word ‘candidate’ has a space in it.  
Our Response: Changed as suggested.

Our Response: missing brackets added.

13. Last paragraph of Family 2, last sentence, ‘consistent, strikingly similar’ – just use one of the terms.  
Our Response: Changed as suggested (the word consistent has been deleted)

Discussion and Conclusion:  
14. End of paragraph 1, remove ‘this’ …..in (this) Arabian peninsula.  
16. Paragraph 2, second sentence should read: ‘Affected individuals demonstrate significant truncal ataxia and either learn to walk…..  
17. Paragraph 2, forth sentence: ‘….complex interaction between environmental actors and the cerebellar malformation and not the type of causative mutation…..’  
18. Add ‘inferior’ to ‘…portion of the cerebellar vermis…. in fifth sentence.
19. Last paragraph, last sentence should read: ‘The affected individuals in our two families….., suggesting that it should be possible to provide targeted testing for this mutation in patients…’

20. Conclusions: need comma after ‘VLDLR type, and….’

Our Response: All the above suggested changes have been carried out.

Figure Legends:

21. Define gray symbol as possibly affected status.

Our Response: the gray symbol has been defined as suggested

We hope that you will find the manuscript is now acceptable for publication in BMC Medical Genetics.

Looking forward to hearing from you