Reviewer's report

Title: Prune Belly Syndrome in Surviving Males can be caused by Hemizygous Missense Mutations in the X-linked Filamin A Gene

Version: 0 Date: 26 Aug 2019

Reviewer: Kirsten Y. Renkema

Reviewer's report:

Iqbal and coworkers report on the identification of hemizygous FLNA gene variants in male Prune Belly Syndrome (PBS) patients who survive into adulthood. The evidence shown for a causal relationship between PBS and FLNA gene variants includes 1) the identification of overlapping FLNA gene variants in two half-brothers with PBS by whole exome sequencing, 2) the identification of two additional PBS patients with FLNA gene variants, 3) functional characterization of the variants that shows enhanced binding of FLNA to ITGβ1. I recommend a more in depth discussion on genotype-phenotype correlation by connecting what is known from patients described previously to the results of the current study.

Minor comments

1. Discussion: Please, elaborate more on whether you see a clear genotype-phenotype correlation between FLNA variants and the different related phenotypes. How could the diversity in phenotypes related to FLNA variants be explained? The discussion section contains a lot of information on patients previously described. How does this information connect to your findings specifically? Please, connect the literature to you own findings in male PBS patients who survive into adulthood.

2. Page 8, line 9: 'Not only does our work add to the population of surviving males with (...)'.
What is meant here? What does the work add exactly? Please, clarify.

3. Methods: Page 4, line 20: please add units (e.g. degrees Celsius) to indicated 37 and 65.

4. Methods: Page 4, line 42: explain how the normal pediatric PBS-unaffected individuals were recruited for bladder tissue isolation.

5. Page 6, line 60: the authors indicated Figure 3. Please, be more precise on the contents of Figure 3A and/or 3B?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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