Reviewer’s report

Title: A novel study of Copy Number Variations in Hirschsprung disease using Multiple Ligation-dependent Probe Amplification (MLPA) technique.

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Reviewer: Eli Hatchwell

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Title: A study of Copy Number Variations in Hirschsprung disease using the Multiple Ligation-dependent Probe Amplification (MLPA) technique.

I have now been convinced that this paper will be of interest to those in the field and should therefore be published. I still feel that that this paper does not necessarily inhabit the correct side of the line between research and diagnostics, and feel strongly that, in the future, such studies will not be worthy of publication. As mentioned before, a complete analysis of gene mutations should, by default, imply CNV analysis as well as basic sequencing. That is why MRC-Holland is a successful company (because diagnostic labs use their kits, knowing that sequencing alone is insufficient to exclude causative mutations).

As for the writing, I am surprised that, despite being asked to have a native speaker review the use of English in the original manuscript, there are still many errors in this resubmitted manuscript. These will need to be corrected before publication! I do not have time to list these exhaustively but here are some examples:

Page 2, ABSTRACT/Background, 4th sentence: “In order to eliminate the misdetection of CNVs…” needs rephrasing. As it stands, it suggests that CNVs are routinely detected, whereas the opposite is true.

Page 2, ABSTRACT/Conclusions, 2nd sentence: “…further analyzes…” should be “…further analyses…”

Page 3, BACKGROUND, 1st sentence: “…neural crest cells migration…” should be “…neural crest cell migration…”

Page 4, last sentence: “…are not the adequate…” should be “…are not adequate…”

Page 5, middle of page: The authors use the terms heterozygosis and homozygosis. I think that sentence needs to be changed and the terms ‘heterozygous’ and ‘homozygous’ used instead (with the appropriate sentence structure).
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests