Reviewer's report

**Title:** Novel MLPA procedure using self-designed probes allows comprehensive analysis for CNVs of the genes involved in Hirschsprung disease

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**Reviewer:** Alessio Pini Prato

**Reviewer's report:**

This is an interesting paper regarding search for CNVs of four genes in a wide series of Hirschsprung patients with MLPA technique. A similar paper was recently published by the Authors on BMC Medical Genetics and found no CNVs for other genes involved in the pathogenesis of the disease including Ret proto-oncogene.

This paper is well written, well-designed and clear.

However, I have some concerns:

1 - Was Ethical Committee approval obtained by the Authors?
2 - Authors should provided detailed demographic informations including male to female ratio and associated anomalies in this series of patients. In particular, associated anomalies are mandatory for a proper interpretation of the results.
3 - Given that only 1 deletion in GFRalpha1 gene was identified over 4 screened genes in 208 patients, I assume that CNVs are of marginal importance in Hirschsprung’s pathogenesis. This should be properly addressed in the discussion section.
4 - I'd like to know if the Authors looked for the GFRalpha1 deletion in the parents of the patients. In the discussion section there is a misleading statement on this regard (not stated in the results) that should be clarified
5 - It would be of interest to the reader to know the exact phenotype of the patient with the GFRalpha1 deletion (renal anomalies?).

Anyway, this paper could be suitable for publication on the Journal provided the above concerns are addressed properly.

**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