Reviewer's report

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

**Version:** 1  **Date:** 7 May 2009

**Reviewer:** Sarah H Elsea

**Reviewer's report:**

Major:
The authors describe results of an MLPA study of copy number variations in Hirschsprung disease. This is a straight-forward paper and discussion illustrating that CNVs in 4 commonly associated genes appear not to involve CNVs. My concern here about the conclusions from the authors is the sample source. The authors indicate the patients have the disorder, but they never indicate if these patients have a known mutation that is causative of the disorder or if they are idiopathic cases. If the cases are all idiopathic, then this should be indicated. If, however, the cases all have mutations in a known Hirschsprung gene, then these are not the cases to evaluate for CNVs. This needs to be clarified.

2. Regarding the patient samples indicated with the mutations near the MLPA probes, it seems these patients should have been screened previously for mutations in these genes, or they are not idiopathic cases. In fact, it seems possible the 2 mutations detected could actually be causative. For the first patient, the "mutation" is indicated P953L, but DNA, not protein should be written in the text--or both. The second patient has a 2 bp deletion, which would result in a frameshift.

Minor:
1. page 4, lines 5-6. Sentence is not clear.
2. Would recommend a primary English speaker review the details of the text for clarity.

**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.