Reviewer’s report

Title: Application of targeted multi-gene panel testing for the diagnosis of inherited peripheral neuropathy provides a high diagnostic yield with unexpected phenotype-genotype variability

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Reviewer: Byung-Ok Choi

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Re: MS ID: 1588559471684757

Title: Application of targeted multi-gene panel testing for the diagnosis of inherited peripheral neuropathy provides a high diagnostic yield with unexpected phenotype-genotype variability

In this manuscript the authors generated targeted gene panel for inherited peripheral neuropathy (IPN), which is genetically heterogeneous. For this investigation, they designed a targeted NGS panel assay including 56 genes, and validated the panel with 448 patients with different types of clinically-suspected IPN. Overall the study was well organized. However, there are several points to enhance the manuscript before the publication.

Major points:

1. The authors identified 1830 variants and classified into four categories, however, some classification lacks the logical explanation. Especially, description on the class 1 (benign) and class 2 (likely benign) is needed. Since the entire novel variants were not experimentally proven, more detailed description might enhance other clinician’s understanding.

2. The authors detected copy number variations in PMP22 gene from 3 patients (2 duplication and 1 deletion). Since they also mentioned that PMP22 duplication is prescreened, the effectiveness in the detection of PMP22 duplication through the gene panel is questionable. Because the duplication is critical in the diagnosis of CMT, they need to demonstrate the effectiveness using previously confirmed CMT1A patients.

3. Interestingly, the authors also found multiple genetic causes. Considering that the genetic cause of IPN is more than 70, there is high probability of the patients with multiple genetic causes. So more detailed description on the clinical feature of the patients might enhance the readers’ knowledge on the genotype-phenotype correlation in IPN.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

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