Response to Reviewer's Comments

Reviewer(s)' Comments to Author:
Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: The author described a case of DOCK8 immunodeficiency syndrome with large deletion. The author claimed initial WES did not detect the deletion. The DOCK8 deletion was finally confirmed by MLPA. This case highlighted the important of using the right method to detect the clinically meaningful mutation. However, some revision is required. Major issue: 1. The author stated they detected the large deletion of DOCK8 by "copy number variation (CNV) analysis of NGS data". However, the kit they used is actually Multiplex Ligation Probe Amplification (MLPA) not NGS. MLPA is generally not classified as NGS. Therefore, I recommended the author to use the term "MLPA" in the whole manuscript. 2. To see is to believe. Please provide the MLAP result that indicated the DOCK8 deletion. Minor issue: 1. The author only described they use "Agilent SureSelect Human All Exon platform" for WES. This is a exome capture kit for WES library. It will be better to provide more detail information about the analysis pipeline (mapping, annotation, variant calling and variant filtration). Actually it is possible to detect large deletion in WES using specific CNV analysis software. But the MLPA remains the gold standard for DNA copy number determination.

1. The author stated they detected the large deletion of DOCK8 by "copy number variation (CNV) analysis of NGS data". However, the kit they used is actually Multiplex Ligation Probe Amplification (MLPA) not NGS. MLPA is generally not classified as NGS. Therefore, I recommended the author to use the term "MLPA" in the whole manuscript.

Reply:

I thank the reviewer for the comments. This is a valid concern raised by the reviewer. The specific gene testing for DOCK-8 was done by a lab outside the country (Biosciencia laboratory, 55218 Ingelheim, Germany), this lab serves as a reference lab for our hospital. As stated in the report (supplementary file 3), the deletion was first detected by analyzing the NGS data followed by a confirmation by MLPA.

If the reviewer and the editor agree, I prefer to keep the discussion focused on the CNV analysis in general. However, I have added details on the MLPA in the manuscript in in

the case and discussion.

2. To see is to believe. Please provide the MLAP result that indicated the DOCK8 deletion

Reply:

I thank the reviewer for the comments. I have obtained the final results for the NGS data analysis and MLPA (supplementary file 3). The data, which consist of the copy number variation analysis results, have been added to this manuscript as Supplementary file 2

3. The author only described they use "Agilent SureSelect Human All Exon platform" for WES. This is a exome capture kit for WES library. It will be better to provide more detail information about the analysis pipeline (mapping, annotation, variant calling and variant filtration)

Reply:

I thank the reviewer for the comments. The whole exome sequences (WES) analysis pipeline is now outlined in Supplementary file 1

Reviewer #2:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: This very well conducted case report reflects the challenges of PID diagnosis, and the role of targeted gene testing with CNV analysis that ultimately might detect deletions that can be missed by WES. The manuscript is very concise, and for enriching the report, some figures illustrating the genetic tests would be valuable.

Reply:
I thank the reviewer for the comments. As requested, a paragraph regarding Multiplex Ligation Probe Amplification (MLPA) and a figure outlining the process, (figure 3) have now been added to the manuscript.