Reviewer's report

Title: Exome sequencing circumvents missing clinical data and identifies a BSCL2 mutation in congenital lipodystrophy.

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Reviewer: Massimiliano Rossi

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Minor Essential Revisions

The question posed by this article is well defined and interesting. It concerns the role of NGS in the diagnosis of a multiple congenital abnormalities/intellectual disability (MCA/ID) syndrome (Berardinelli-Seip Congenital Lipodystrophy/BSCL due to mutations in the BSCL2 gene) in the presence of limited available clinical data.

Indeed whole exome sequencing (WES) is a powerful, effective and attractive diagnostic tool especially for disorders which are relatively clinically homogeneous but genetically heterogeneous.

However, in the Conclusion, the authors state that WES can be used to even replace clinical investigations. This is questionable: even if a molecular diagnosis is made, a careful clinical assessment is still essential, in order to characterize the degree of clinical severity especially in conditions characterized by a possible intra/interfamilial variability (such as BSCL2 mutations).

Lines 136/137: “increased ALT/GPT ratio (49 U/L)”: please clarify

Figures should be numbered in sequence according to the citations in the text (currently they appear in the text in the following order: 1A; 2; suppl 1A; suppl 1B; 1B; 1C, suppl 1C).

Level of interest: An article of importance in its field

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