Author's response to reviews

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

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Reviewer 1

1. We have in general rewritten the manuscripts so that it now state that exome sequencing in this case was used in priori to a complete clinical investigation of the patients. It should now be clear that WES was used to complement and accelerate, but not completely replace, a thorough clinical assessment.

2. A list of the identified homozygous variants is now presented in Supplementary Table 1 (row 118).

3. We now state that the BSCL2 variant was considered the most likely candidate due to primarily its compatibility with the available clinical presentation (row 163-165).

4. We added a sentence describing targeted NGS with a reference to Rhem HL et al (row 118-119).

5. We added the ‘per base’ coverage obtained in our experiment to the Results section (row 118-119).

Reviewer 2

1. In general we now state that WES is used to complement and accelerate, but not completely replace, a thorough clinical assessment.

2. The entrance, “increased ALT/GPT ratio (49 U/L)”, is an error by our side;
ALT/GPT ratio should have been ALT (GPT) and is the same as ALT. This value (49 U/L) was measured one year prior to the now only presented value (64 U/L) (row 138-139).

3. We removed the first reference to figure 2, as the pictures were retrieved in the clinical re-evaluation of the patients described later in the paper. This should put the Figures more in order according to citations (row 62).