Reviewer’s report

Title: Clinical course, mutations and its functional characteristics of infantile-onset Pompe disease in Thailand

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Reviewer: Luisa Politano

Reviewer's report:

The AA report the results concerning molecular diagnosis, follow-up and response to the ERT treatment in a Group of 12 Thailand patients with infantile-onset Pompe disease (IOPD), aged between 15 days and 8 months.

All patients presented the classical disease appearance at birth characterised by hypertrophic cardiomyopathy and generalised muscle weakness. The GAA assay showed levels of the enzyme less than 1%. Interestingly, the molecular analysis showed five novel variants, validated by transfection analysis in COS-7 cells. These novel mutations were located in both N-terminal beta-sheet domain and in the catalytic domain. Furthermore two hotspot regions were identified, respectively in exons 14 an 5, Accounting for the 62% of all mutations.

The manuscript is very interesting as it provide new acquisition in the field of molecular variants causing IOPD in Asia. An adding value is the possibility to limit the analysis to the these two exons, as first approach sparing cost and time and speeding up the diagnosis times.

Only 3/12 (25%) of the patients - sharing different mutations - received ERT therapy, at 4 weeks, 6 and 11 months respectively. Rather than the type of mutations, the different results seem to be related to the start time, earliness of treatment, so I would suggest to the authors not to emphasize in the abstract and conclusions the sentence " These data can be useful.........................and provide additional information of the genotype/phenotype correlation and prediction of long-term response to enzyme replacement therapy...." for the reasons just mentioned (small number of treated patients and the different mutations).

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess
Are the conclusions drawn adequately supported by the data shown?
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Yes

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Needs some language corrections before being published

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