Reviewer’s report

Title: Molecular characterization of β-thalassemia intermedia in the West Bank, Palestine

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Reviewer: Valentina Brancaleoni

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The paper by Faraon et al. reports the molecular characterization of intermedia thalassemia in Palestine. The work expand the knowledge about genotypes/phenotype correlation in TI.

In some cases in the result section some paragraph are not clear (see below), since the reader have to suppose some facts that are explained in the discussion section. But I would like to understand the results immediately, and not reading the discussion. Please, try to be more clear.

It is not clear to me why it is not possible to have a TM patient older than 30 years… With the correct follow up and treatment the life expectation of TM (or better transfusion dependent) thalassemic patient is now greatly increased.

You report that 'most of patients were results of consanguineous marriages'. Please, report also how many homozygotes (% or number) are from consanguineous marriages in the section 'b-thalassemia genotypes'.

Table 2: please check carefully table formatting, since in the provided file is not clear. It lost the line definition, since for space issue the text goes sometimes down. In some case, I did not couple correctly beta and alpha genotype.

What do you mean with (1:0:0) in the column of alpha thal? Please add a caption to explain this.

Beta A: is it the normal beta allele? I did not understand at a first glance. I suggest to use instead 'wt' (wildtype) is more comprehensible to the largest majority of readers.

Page 11 line 41: (talking about group III): which patient had the occasional transfusion? The one with the coinheritance of alpha 3.7 deletion? Which patient did never show splenomegaly? Always the one with 3.7 deletion? If yes, I should state it more clearly to the reader and not only let to the reader's interpretation.

Otherwise, I did not understand correctly, so please specify in both of cases.

Page 11, line 46: the 'patient' homozygous for c.-151C>T, we can say that it is a silent case, since Hb is almost normal, he/she never transfused and I think there are no other symptoms. I think you detect it only for HbF % and HbA2 level. I should state this fact.

Page 12 line 26: the correct spelling is 'fourth' not forth
Page 12 line 39: You referred to the wrong table, did you mean table 3?

Page 12 line from 26 to 41: which was the patient who have a better phenotype? The one with also alpha mutation? Please, explain more clearly this issue to the reader (as above).

Page 14 line 51: I think this sentence is not useful, you refer to table 5 in the discussion; so you can avoid it.

Although the authors are aware of the existence of other genetic modifiers influencing thalassemia phenotype, they did not clearly discuss the results citing the possible influence of other loci (BCL11A and HMIP loci) as other determinants of HbF production. I would suggest to analyze this loci in their patients if it would possible and to add to the paper. Since I understand that it is not always possible, I kindly suggest to address this issue and to insert it in the discussion section. i.e. page 21 line 14: which major QTL?

**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.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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