Reviewer's report

Title: Characterization of the Papillon-Lefevre Syndrome in Mexicans.

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Reviewer: Muhammad Tariq

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This study by Romero-Quintana et al., performed screening of CTSC gene in 9 Mexican families and identified same novel mutation in all families.

Major Concerns:

1) Authors report here 20 patients and analyzed 9 of them. This creates confusion for readers by mentioning 9 patients in abstract and 20 patients at end of introduction section. I would suggest being consistent with patients number. If remaining 11 patients are not available then there is no reason to mention 20 patients in this study. Also authors should make clear in text that 9 patients belong to seven different cases/families.

2) Authors presented the clinical features in much detail in text. Authors should summarize these features in a table form.

3) Authors investigated 7 families having in total 9 patients and all patients interestingly having same disease-causing mutation 203C/T (7 homozygous and 2 heterozygous). This apparently suggests a founder mutation and potentially a common ancestral haplotype among these Mexican families. I would suggest to analyze few STR markers around CTSC gene in these families. This would generate real message of this study.

4) Authors presented “Cases 2P and 4P are found compound heterozygous for mutations 203T/G and 458C/T”, although 458C/T is a neutral polymorphism. How authors argue for disease causation in these 2 patients?

5) Most sections of the methods are written in much detail. Authors should shorten these sections (with proper references).

6) Results are mostly repeated in “Discussion”. Discussion should be more compact and meaningful.

7) Can authors explain how 203T/G is loss of function mutation?

8) Did authors check splice junctions of CTSC gene for mutations in these patients? If yes then they should mention in manuscript that coding and splice junctions of gene were screened in patients.

9) Number of controls (n=8) for the SSCP analysis is not sufficient.

Minor revisions:

1) Since this study does not contain a large patient cohort, I would suggest to modify the title of the paper like “identification of novel mutation in CTSC gene
causing PLS in Mexican patients” or Mutational analysis of CTSC gene in nine Mexican patients with PLS.

2) Gene name should be italics throughout the manuscript.

3) Author affiliations should be in English for general readers.

4) DNA isolation method should go first and then PCR-SSCP/Sequencing.

5) 5’ and 3’ ends of primer sequences are not shown.

6) Mutations at protein and nucleotide should be represented according to standard format http://www.hgvs.org/mutnomen/.

7) Did the authors look at disease gene mutation databases to see if the presumed pathogenic change or changes have been described previously?

8) Did the authors look at bioinformatics tools (PANTHER, Polyphen-2, SIFT etc) whether mutation in CTSC is predicted deleterious or benign?

9) Previously how many CTSC mutations are known causing PLS? Here authors should cite Human gene mutation database (HGMD) for quick reference to have number of mutations in this gene.

10) Make sure that reference section is written on journal format.

11) Manuscript should be reviewed by expert in language.

Level of interest: An article of limited interest

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.