Reviewer's report

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

Version: 1 Date: 30 July 2012

Reviewer: Muhammad Naeem

Reviewer's report:

Major Concern:
Cases 2P and 4P were found to be compound heterozygous for mutation 203 and 458 (T/G and C/T) and no other causal mutation has been identified in these cases? The 458 (T/G) mutation is defined as a polymorphism (symptomless mutation) in the previous literature (Ref 50 in this manuscript; Allende et al 2006; Human Mutation) and (Ref 49 in this manuscript; Lefèvre et al; 200; Journal of Investigative Dermatology). In these studies this 458 (T/G) conservative mutation was reported as a polymorphism along with other causal mutations in the affected individuals. Moreover, there were normal controls identified with this mutation in homozygous state and the mutation was present in high frequency in normal population. Allende et al 2006 had thus suggested that not all mutations in Papillon-Lefèvre Syndrome should be considered as a cause of disease, whether case studies or general population screening is performed.

The study by Hart et al 2000 (Ref 48 in this manuscript) was the only one that documented 458T>G variation as a causal mutation in heterozygous state with 199-222del. However, I am not sure about the control data, if any available for this mutation in study by Hart et al?

Discretionary Revisions

1= Study to determine founder effect for 203T>G mutation will add interest in this manuscript.

Minor Essential Revisions

Check following lines/words

Page 3

1= Para 1: 2nd last line: “Among others conditions”

2= Para 2: line 1: more than 60 mutations have been reported; (there are 77 mutations reported so far according to hgmd)

3= Para 3: revision of sentences (CTSC, also known as ------to ----- monomers) as to be more clarified/simple for general readership

4= Para 3: “The enzyme has been involved on the cleavage”

Page 4

5= Para 2 (last line): “such severe periodontitis”
Para 3 (last line): mention as “of nine PLS patients”

Page 5

Cell isolation: “LPS”-free (full for abbreviation once)

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**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