Reviewer's report

Title: Telomere shortening may be associated with human keloids

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Reviewer: Shirley Russell

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Major Compulsory Revisions

1. The authors need to include more information in Table 1 about the keloid and normal tissue. In addition to the age and gender of the subjects, they should include, as was done in their previous publication (Reference 3), the age of the keloid scar. While the age of the donor may be important, the age of the scar is likely to give a better indication of the relative number of cell divisions the fibroblasts have undergone, and would be helpful in drawing conclusions about the basis of shortened telomeres. In addition, the authors should indicate which if any of the tissues and cultures used here were used in the previously published study.

2. The authors need to provide justification for including Figure 3 in which the values for the normal and keloid strains at 48 and 72 hours are almost identical to findings included in Figure 4 of their 2009 publication in Mol Cell Biochem (reference 3 of the current manuscript). Interestingly in the previous publication keloid fibroblasts did not show increased ROS at 96 hours although the description of findings in the results says that they did. In the current figure, the keloid fibroblasts show increased ROS at 96 hours although the authors indicate that the increase is not statistically significant.

3. Again regarding reference 3, the authors had previously shown elevated ROS in both keloid and hypertrophic scars. However, in the current manuscript where they suggest that the shortened telomeres may be due to increased ROS, they provide no information about telomere length in hypertrophic scars. Including such data, if available, might strengthen the association between oxidative stress and shortened telomeres in this system.

4. The authors indicated that decreased telomere lengths were significantly correlated with ROS levels in normal relative to keloid fibroblasts. A figure showing the correlation for individual strains would be helpful in visually assessing the correlation.

5. While Figure 1 indicated a statistically significant average telomere shortening when comparing 20 controls to 20 keloid samples, Figure 2 shows only one normal strain and 3 keloids. It would be useful to show more of the normal samples to get a better sense of the consistency of the difference in the different tissues.

6. The authors hypothesize that telomerase might be less active in keloid than in normal samples. However, while they indicate no hTERT (RNA?) expression in
keloid fibroblasts, they do not indicate whether there is expression in normal tissue although hTERT RNA was measured in the normal skin specimens. Findings from both tissues should be presented even though data are not shown.

Minor Essential Revisions

1. The writing of the manuscript needs to be improved including correction of small grammatical and spelling errors. For example, the description of telomerase findings are confusing, as is the discussion of telomerase activity versus hTERT RNA expression and the role that oxidative stress might play in telomerase activity.

Discretionary Revisions

1. The manuscript would be enhanced if the authors provided discussion relevant to if and how telomere shortening might contribute to keloid pathogenesis and the eventual termination of keloid growth.

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

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.

Declaration of competing interests:

I declare that I have no competing interests.