Author's response to reviews

Title: Morphometric characteristics of basal cell carcinoma peritumoral stroma varies among basal cell carcinoma subtypes.

Authors:

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Author's response to reviews: see over
Dear Editor,

Thank you for the recent reviews of our manuscript. We have addressed the comments of the reviewers below. The changes to the manuscript are highlighted in red in the revised version. We hope that you will agree that the manuscript has been substantially improved by these revisions and will now be acceptable for publication in your journal.

With Kind Regards,

Chris

Reviewer’s report#1
Reviewer: J Andrew Carlson
Responses to Comments to Authors

1. RESPONSE: We wish to thank the reviewer for his additional insight and perspective on the unique characteristics of basal cell carcinoma in comparison to other malignancies. We have incorporated the reviewer’s points into the introduction and discussion (pp. 4, 11).

2. Are the methods appropriate and well described?
No. Ostensibly tumor and stroma diameters/radii are being measured on BCC typed as either superficial, nodular and infiltrative. The criteria that is used for these classifications is not given; no accounting for transitional (combined) BCC types tumors is made; and the character and make up of peritumoral stroma or host response to BCC are ignored. RESPONSE: Tumour subtype classification was based on the criteria described in Crowson; this point has been added to the Methods section (p. 7). Additionally, at the request of the other reviewer we have added illustrations of the three subtypes of basal cell carcinoma discussed in this study.

For example, biopsy site changes can induce an infiltrative-like BCC pattern in proven nodular pattern BCC (4), which would confound results as its not authentic infiltrative BCC. Or, wound healing is suspected to induce regression in biopsied BCC (5). RESPONSE: We did not include any cases with prior biopsies. This point has been added to the Methods section (with reference to the studies mentioned by the reviewer). Do to a lack of recognized classification schemes for basal cell carcinoma stroma, we did not attempt to sub classify stroma types. These points have also been added to the Methods section (p. 6). It is not true that the host response was ignored, as we did collect data in the presence or absence of a marked host immune response.

3. Are the data sound?
No, because the lack of and poor definitions of variables measured and samples studied. One really does not know exactly what the measurements taken represent. RESPONSE: Please see response to points one and two above.

4. Does the manuscript adhere to the relevant standards for reporting and data
deposition?  
No. See above comments. RESPONSE: Please see response to points one and two above.

5. Are the discussion and conclusions well balanced and adequately supported by the data?  
No. See above comments. RESPONSE: Please see response to points one and two above.

6. Are limitations of the work clearly stated?  
NO. RESPONSE: We agree that this was a weakness in our original submission. Additional discussion on this point has been added to the discussion.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?  
No, See comments below. RESPONSE: Please see response to points one and two above.

8. Do the title and abstract accurately convey what has been found?  
NO. RESPONSE: The title has been revised to better reflect the main findings of the study.

9. Is the writing acceptable?  
Yes.

Reviewer's report#2  
Reviewer: Olivier Piot  
Responses to Comments to Authors

1. The results seem to depend highly on the selection of the ROI. This selection is performed manually according some arbitrary rules (ex. stroma divided by 2 when it is between 2 separate tumour nests). Can the authors comment this point? In addition, it would be worthy to present histological sections of the different BCC subtypes and to illustrate the ROIs selection. For pathologists, the morphological characteristics of BCC subtypes are certainly well known, but for non-experts it is far to be obvious. RESPONSE: These points are explained in the methods section (pp. 6, 7). See also the response to Reviewer 1, question 2. A new figure has been added to illustrate an example of each of the basal cell carcinoma subtypes discussed in our study.

2. The use of the different statistical methods should be more clearly presented. The statistical relevancy of results presented in Table 2 relies on a KW test (with p-values as presented) or rather on a chi-squared test?. In Table 2, why the comparison between the subtypes is carried out between the set of the 3
classes, and not between 2 classes as in Table 1? 

RESPONSE: This has been corrected in Table 2.

3. The results on immune reaction and elastosis (Table 2) are not compared, nor even discussed, with the results on the morphometric characteristics (Table 1). These results appear as separate studies without any link. Can the authors comment this point? The authors should study the link/correlation between the morphometric results and the presence of immune reaction or elastosis. 

RESPONSE: This is an interesting point. We have added this analysis to the Results and Discussion section (pp. 8, 9).