Reviewer’s report

Title: Cancer associated fibroblasts (CAFs) are activated in cutaneous basal cell carcinoma and in the peritumoural skin.

Version: 0 Date: 14 Oct 2016

Reviewer: Magnaldo Thierry

Reviewer’s report:

The study by Omland and colleagues aims at characterizing the gene expression profile of (dermal) fibroblasts activated in the presence of basal cell carcinoma human cancer. The paper is mainly descriptive; the study is based on NG RNA sequencing experiments from either healthy skin (buttock), « non involved peritumoral skin » or tumoral lesions. From a technical point of view, it is not clear whether RNAs were extracted from laser micro dissected skin/tumor sections. It is not clear either which type of BCCs were included in the study. It is not mentioned if RNA were extracted from dermis, epidermis, or both. This should be precised as well as the method(s) applied to differentiate epidermal and dermal gene expressions.

I would be suprised that fibroblasts are impacted in the same way by the different types of BCC. The type(s) of BCCs included in the study should then be precised; unless all BCCs are from same type, the sample seems rather small to conclude on statistical significiance of results. Also, analyses of non photo exposed buttock skin are not systematically presented, but it is not explained why? To me this is an essential control.

A table mentioning the age of patients, the number of BCCs, the ethnic origin, the pigmentation characteristics, the history of sun exposure, the familial history, should be presented. Table 1 mentions only 9 BCCs, without any additional details.

In general, even for a descriptive study, at least more clinical and technical informations should be presented to support authors conclusions.

The paper is missing functional analyses. The methodology is difficult to follow and may even be confusing for the reader.
Other points:

M&M

p6L1: this is just an example what means « frozen skin material was thawed in RNA later () and minced…

also, P6 L24: what means Microm HM560 cryostat cut 10 microm that were mounted on slides?

the manuscript should be carefully edited.

p6 L14-L16, does this mean that previously obtained data were pooled with the present series of experiments? if this is the case, statistical analyses are seriously flawed.

Results

P9, L 23-28, what is the meaning of this sentence?

P9, L 36; references quoted correspond to reviews; please refer to the original papers if this applies.

Figure 1, involved (tumoral skin) seems more heterogeneous than other samples in terms of mRNAs accumulation (not « overexpression », not « transcription »); could this be due to sample heterogeneity?; this should be clarified in view of IF or IHC results that do not clearly support authors' conclusions.

Still in figure 1, the P4H panel only shows 17 samples, not 18 as mentioned in the text. Figures, text, and legends changes are required.

Figure 2, and corresponding results, (P9 L61), FAPa is not detected by RT-Q-PCR (figure 1); in the text it is said « staining of the peritumoral skin also revealed FAP a … »; please clarify; positive staining in the absence of mRNA is quite confusing.

Microphotographs should be more carefully chosen. For instance, PDGFR labeling in buttock is not acceptable, but many other panels are not well chosen when not out of focus. Presentation of results should then be reconsidered.

Figure 3, most results indicate that accumulation of screened mRNA is superior in peritumoral skin than in the tumor skin. What does this mean? Statistics are only showed when significant. For instance in the CXCL12 panel, the comparison between « B » and « T » is not performed.
Idem for CCL18 and CCL22, the comparison between « P » and « T » is not shown; as a reader I understand that differences are not significant; however this might also mean that yields of RNA extraction may differ according to the body site as mentioned somewhere in the manuscript. This point should be carefully addressed.

Figure 4
Conclusions drawn from a single field of immunofluorescence should be avoided. Even if the authors think that these results are representative, a more objective presentation, including statistical analysis of results, should be presented. None of the IF IHC micrographs include scale bars. Magnification values are poorly informative in a scientific paper.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I recommend additional statistical review

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