Reviewer’s report

Title: Remodeling of extracellular matrix by normal and tumor-associated fibroblasts promotes cervical cancer progression

Version: 2
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Reviewer: Ines Lohse

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In the manuscript by Fullar et al evaluate the effects of patient-derived normal and tumor-associated fibroblast on growth and migration of the patient-derived cervix cancer cell line CSCC7. The conclusions are that migration and invasion of cervical cancer cells requires remodeling of the tumor-associated stroma.

The data presented by Fullar et al strongly supports previous evidence demonstrating the importance of tumor-associated fibroblast for tumor cell invasion and remodeling of the tumor microenvironment. I do, however, believe that the presentation of the manuscript does not do the data justice. Poor writing makes it very hard to follow the flow of the manuscript.

The manuscript must undergo serious editing prior to possible publication.

Major Compulsory Revisions

1. The manuscript would benefit from a spellcheck and major editing by a native English speaker. Missing punctuation and grammatical discrepancies make it hard to follow the story.

2. Page 5, line 101: “Growth signals generated by the tumorous extracellular matrix…” Please change this sentence. The extracellular matrix doesn’t generate growth signals but rather contains signalling molecules deposited by CAFs and tumor cells. This sentence is rather confusing.

3. Page 7, line 152: Please describe CSCC7 cells better, what markers do they express? How was purity and stability of the line evaluated?

4. Page 7, line 152: How was purity of the NF and TF line evaluated? How many passages were used for this experiment? Please comment on culture conditions (Oxygen concentration). What is the rationale for the medium change at passage 3? Were the NF established from areas adjacent to the tumor or cancer-free areas?

5. Figures 3, 4, 5 and 6 are described twice (page 12, line 272 and page 15, line 330; page 12, line 280 and page 15, line 337; page 13, line 302 and page 15, line 349; page 14, line 312 and page 16, line 355). It makes the second part feel very repetitive, especially since they message is similar. While I appreciate that the authors intent to discuss the TF/NF and tumor cells separately, I would make more sense for the reader to merge these sections.

6. Page 16, line 369: How were tumor cells identified in this experiment? It can’t
be excluded that these cells are fibroblasts or immune cells.

Minor Essential Revisions
1. Page 6, line 126: Please comment on whether Ethics approval was obtained for patient samples used on the TMA.
2. Page 6, line 129: Was the counterstain really H&E? Generally only Eosin is used.
3. Page 7, line 146: The table should be moved to supplementary as there is no benefit from it being part of the main manuscript.
4. Page 9 line: which 2 types of fibroblasts were used?
5. Fig. 3: please add error bars to the growth curves.
6. Fig. 5/6: some of the plots are very blurry and hard to read. Please improve picture quality.
7. Page 19, line 436: Change “indicate” to suggest.
8. Page 27. Line 689: please remove the location (A,B, ect) from the figure title.
10. Page 27. Line 744: please remove the location (A,B, ect) from the figure title.

Discretionary Revisions
1. Page 21, line 469: Is that data part of another manuscript? It would be interesting to include it here.

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.