Reviewer’s report

Title: CTHRC1 Induces Non-small Cell Lung Cancer (NSCLC) Invasion through Upregulating MMP-7/MMP-9

Version: 1 Date: 17 Jul 2017

Reviewer: Barbara Mary Fingleton

Reviewer's report:

This revised manuscript from He et al addresses some but not all the previous reviewer comments. Most responses instead suggest that questions raised will be answered in follow-up studies. While additional experimentation cannot always be done, the authors should at the very least address some of the points raised in the discussion. For example, they should discuss the unusual apparent nuclear localization of CTHCR1, and also the possibility of the driver mutation (e.g. EGFR or k-Ras) in the cell lines or cancers being a critical regulator of the downstream effect of CTHCR1.

Additionally, the authors have taken the unusual step of removing a significant part of the data provided in the initial submission, i.e. the mouse studies. However there are still some sections that retain description or discussion of mouse studies that need to be removed. These include lines 333-347 in the results as well as the corresponding figure sections 3l and 3J. Also in the discussion, lines 565/566 and 575-577 suggests that CTHCR1 causes metastasis, but that has not been established in this manuscript. In this regard, the title of the manuscript should also be changed to remove 'and metastasis'.

Finally, reviewer 3 refers to 'MMP4', which is included as a row in figure 3A.B. There is no matrix metalloproteinase-4 (this name was originally assigned to an already named member of the family and so has been deleted). A protein that has 'MMP4' amongst its many alternative names is interleukin enhancer binding factor-3 (ilf3), but this is completely unrelated to the proteinases implicated in tumor invasion. Therefore the inclusion of "MMP4" in figure 3A.B is misleading and should be removed.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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I recommend additional statistical review

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