Reviewer’s report

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

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Reviewer: Barbara Mary Fingleton

Reviewer's report:

The manuscript by He et al describes very comprehensive studies identifying the function and mechanism of action of CTHRC1 in non-small cell lung cancer metastasis. This is a very data-rich study that uses a variety of approaches to identify genes regulated by CTHRC1 and then test their function in vitro and in vivo, as well as clinical relevance.

The only real problem is the assumption that involvement of MMPs means effects a migration/invasion phenotype. As has been clear for several years now, MMP functions are much broader than this, and in fact effects of MMPs on tumor proliferation or survival are clearer in vivo (e.g. Acuff et al Cancer Res 2006; Liu et al Lung Cancer 2007). It is notable that the authors' migration assays were conducted over periods of time that were long enough for proliferation to play a role in the results seen. Moreover, the experimental metastasis assays employed (tail vein injections) are considered assays of colonization ability (survival and outgrowth) as migration and invasion are not necessarily required for tumor foci formation in the lungs. The authors should address whether proliferation plays a role by immunostaining tumor sections from mice that received the various genetically manipulated cell lines.

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.

No
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

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