Reviewer's report

Title: long non-coding RNA MEG3 inhibits NSCLC cells proliferation and induces apoptosis by affecting p53 expression

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Reviewer: Valentina Profumo

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Major Compulsory Revisions

1) To better understand the functional role of MEG3 in affecting cell proliferation and apoptosis, the authors should perform loss-of-function experiments in normal human bronchial epithelial cells (16BHE) or tumor cells in which MEG3 RNA is expressed at high levels.

2) The authors are also encouraged to discuss why MEG3 is not down-regulated in some NSCLC adenocarcinoma cell lines (e.g., NCI-H358 and NCI-H1299) and tissues. For example, do the authors know whether the different NSCLC cell lines, in which they evaluated the expression levels of MEG3, differ for their ability to proliferate or migrate/invade? Furthermore, for a better understanding of MEG3 expression pattern, it should be also helpful to represent MEG3 qRT-PCR data in all normal and NSCLC tissues (by dividing them into adenocarcinomas and squamous cell carcinomas).

3) The authors claim that MEG3 may regulate NSCLC cell proliferation and apoptosis by activating p53. However, they also found that a p53 target, p21, is not modulated upon MEG3-dependent p53 activation. So, I encourage the authors to evaluate the expression levels of other p53 target genes upon MEG3 over-expression. In addition, do the authors know whether NSCLC cells (SPC-A1), that they used for their experiments, express wild-type p53 protein? This may help understand why p21 is not activated after MEG3-dependent p53 activation in SPC-A1 cells.

Minor Essential Revisions

1) With reference to the text and legends, the authors should invert figure 3C and 3D.

2) The manuscript is nicely written, but some typesetting errors occur in the text (e.g., spaces between words just before references and references often miss).

3) Page 5 (line 6), the authors write “Maternally expressed gene 3 (MEG3), encoding IncRNA...”. I am not sure that “encode” can be used with reference to a long non-coding RNA. The authors are encouraged to check.

4) With reference to pages 6 and 7 (“Cell lines and culture conditions” paragraph), replace “Four NSCLC adenocarcinoma...” with “Six NSCLC adenocarcinoma...”; replace “NCI-358” with “NCI-H358”; mention NCI-H1975 cell line; describe how 16HBE cell line is cultured.
5) Pages 8 (two lines before the end) and 9 (last line), please check “Sigma-Aldrich (country???)”.

6) Legend to table 1, rectify “correlation of the expression of HOTAIR”; add superscript “a” to the title in column 3.

7) Page 14, the authors write “MEG3 was overexpressed in SPC-A1 and A549 cells by transfecting them with pCDNA-MEG3 or empty vector”. That is conceptually incorrect, since I am sure that they did not achieve an over-expression of MEG3 by transfecting cells with empty vector.

Discretionary comments

1) Page 15, the authors write “Eighteen days after injection, the tumors formed in empty vector group were substantially bigger than those in the pCDNA-MEG3 group”. To emphasize the effect of MEG3 up-regulation, I suggest the authors write “Eighteen days after injection, the tumors formed in pCDNA-MEG3 group were substantially smaller than those in the empty vector group”.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests