Reviewer’s report

Title: MEG3 promotes proliferation and inhibits apoptosis in osteoarthritis chondrocytes by miR-361-5p/FOXO1 axis

Version: 2 Date: 10 Oct 2019

Reviewer: Prashant Kumar

Reviewer's report:

This manuscript titled "MEG3 inhibits proliferation and promote apoptosis in osteoarthritis chondrocytes by miR-361-5p/wnt/β-catenin axis" by Wang et al., report that the expression of lncRNA MEG3 and miR-361-5p in OA was significantly decreased and increased respectively than that in normal. Also it was observed by the author that MEG3 was competitively binding with miR-361-5p in OA chondrocytes and might inhibit cell proliferation and promote cell apoptosis via Wnt/β-catenin pathway. Rat model was used in the study to show that MEG3 contributed to the cartilage matrix degradation. Major Comments:1. Figure resolution is very poor. The figures need to re-drawn or re-uploaded with higher resolution2. Similar study has been reported by Chen et al. and Xu et al. (31253047, 29255591). What is the novelty with respect to the published reports?3. MEG3 lncRNA has also been previously reported to restore the cellular processes such as cell proliferation by inhibiting Wnt signaling and at the same time increasing the expression of GSK3B (PMID 29781534). Why have the authors checked specifically the Wnt pathway? Adding this information will help increasing the impact of the study4. The destruction complex formed in Wnt signaling may be checked for its expression with respect to β-catenin expression and observed for a negative correlation in expression after Wnt signaling inhibitor treatment5. MMP-1 and MMP-13 expression have been observed in the mice model. However, it has been mentioned in the introduction to be overexpressed in OA. Their relevance in extracellular matrix dissolution must be discussed in the manuscript6. Clinical significance of the study has not been discussed. The possibilities of using MEG3 or miR-361-5p/Wnt/β-catenin axis as a target for treatment options must be discussed7. In result section authors are claiming the expression of Ki67 and PCNA are high in pCDNA3.1-MEG group. However, in the western blot result (Figure 2E) contradicts the statement8. In result section "The effect of MEG3 on proliferation, apoptosis and cartilage matrix degradation of OA chondrocytes was inhibited by miR-361-5p" authors are claiming the PCNA and Ki67 are low in NA3.1-NC + miR-361-5p mimics group was decreased than that in pCDNA3.1-NC + mimics NC group. However, the western blot images do not support the claim.9. Authors claim that the expression of Wnt/β-catenin is down-regulated in pcDNA3.1-MEG3 + XAV939 group than other groups, but the expression level is similar to the control group (pCDNA3.1-NC) (Figure 4 C). Authors can also include the western blot data of Wnt pathway proteins for OA and normal groups. Minor comments: 1. MEG3 expression or MEG3 lncRNA expression must be noted in the manuscript using constant nomenclature2. In the discussion section ‘EMG3’ is mentioned instead of MEG33. A schematic depicting the results with respect to the expression of molecules and their regulation could be included for better understanding

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?**
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Yes

**Are the conclusions drawn adequately supported by the data shown?**
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No

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Not relevant to this manuscript

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