



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Stem Cells*

**Manuscript NO:** 64620

**Title:** Epigenetic regulation by lncRNAs in osteo-/adipogenic differentiation of mesenchymal stromal cells and the pathogenesis of degenerative bone diseases

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05489967

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Research Scientist

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-02-26

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2021-03-29 16:19

**Reviewer performed review:** 2021-04-05 03:51

**Review time:** 6 Days and 11 Hours

|                           |   |
|---------------------------|---|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |



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| <b>Peer-reviewer<br/>statements</b> | Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous<br>Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No |
|-------------------------------------|---|

### **SPECIFIC COMMENTS TO AUTHORS**

Dear authors, the authors wrote a review about the role long noncoding RNA in controlling epigenetic modification involved in mesenchymal stem cells and bone diseases and the control of their differentiation. They divided the review in few parts summarizing the DNA methylation, and histone methylation. They provide a list of example and references linking the role of lncRNA with the differentiation of MSC into osteoblast and chondrocyte. The figure and the table provide accurate information. I have some comments: - All latin words must be written in italic (via, in vivo, etc) - Them font should be consistent over the manuscript (e.g "As a critical transcription factor for adipogenesis, C/EBP- $\alpha$  was found to be upregulated via the recruitment of the MLL3/4 complex to its promoter, which is guided by the binding of PA1 (a component of the MLL3/4 complex) " - Methylation is important to control gene expression, but the source of methyl donor is more important because deficiency of methyl donor or the alteration expression of enzyme involved in the methyl metabolism (GNMT, BHMT,...). The authors should explain methyl donors but also if lncRNA are involved in altering the expression of enzyme involved in methyl metabolism. - It is true that it is generally accepted that methylation of DNA is associated with gene repression. However, it is not always the case. for example, imprinting of the H19 locus is related with the expression and the non expression of H19 and IGF2 (H19 is mentioned few times over the manuscript). it will be interesting that the authors wrote few sentences about the increase of gene expression because of DNA methylation (H19 loci, PMID: 31914996...). DNA methylation is also involved in the chromatin structure in the nucleus, that regulates genes expression by controlling the location of the genes in the nucleus.



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Sincerely,