

To: ***World Journal of Stem Cells***

Dear Editor and Reviewer,

Thank you very much for having our manuscript entitled “***Adipokine regulates mesenchymal stem cell osteogenic differentiation: a review***” reviewed in a timely and professional manner and for giving us an opportunity to revise the manuscript. At this time, we have re-submitted the revised manuscript through the Submission System again. Our point-by-point responses to the reviewers’ comments are detailed below.

**Reviewers' comments and responses:**

Major point:

The authors in presenting each adipokine should add a reference that indeed reports the fact that, the specific factor that is reviewed for its effects on MSC osteogenic differentiation is also considered an adipokine since it is also produced in the adipose tissue. There are several examples in which this reference is not cited when presenting a specific adipokine, for example interleukins, MCP-1, TGF-beta, Gremlin-1 and others.

**Response:** We have added appropriate references to all adipokines that did not add the corresponding reference at first presentation. (Ref.21, Ref.33, Ref.112, Ref.113)

How the Nampt, Gremlin-1 and Katepsin can be considered adipokines? Please explain better.

**Response:** We have made an explanation for why Nampt, Gremlin-1 and Cathepsin is regarded as an adipokine, and have added appropriate references. (Ref.70, Ref.71, Ref.112, Ref.113, Ref.90, Ref.91)

Minor points:

1) Page 2, in the Introduction: “Adipokine is a factor secreted by adipose tissue and

has multiple functions..." please use the plural Adipokines, because they are a group of proteins

**Response:** We have already corrected this mistake.

2) Page 3 in the paragraph Cytokine and cytokine-like proteins: "...process of the differentiation of various stem cells, such as lipid, osteoblast, chondrogenic, and musculogenic." Please correct musculogenic with myogenic. And at page 4, same paragraph: "Epidemiological studies have reported that patients with osteoporosis have higher circulating chemicals [39], and the knockout of chemerin or its receptor CMKLR1 inhibits lipogenesis..." what are circulating chemicals, it is correct?

**Response:** We have corrected "musculogenic" with "myogenic" and corrected "circulating chemicals" with "circulating chemerin".

3) Page 4 in the paragraph Proteins of the fibrinolytic system: "Vignesh K Rangasami et al. [45] found that micellar-loaded TF silencing nanocoliters based on pluronon could effectively induce higher differentiation of MSCs in osteogenic and lipid-forming media." What are nanocoliters based on pluronon?

**Response:** We have corrected "micellar-loaded TF silencing nanocoliters based on pluronon" with "pluronic micelle-mediated tissue factor silencing".