

Response letter to reviewers.

We appreciate the positive referees' appreciation of our review manuscript. We addressed all referees' concerns, and correspondent changes were made within the manuscript.

Reviewer #1:

Specific Comments to Authors:

-The manuscript, even if in some parts it appears to be a little convoluted, is well written and deals with the role of interleukin 17 in osteogenic differentiation in an in-depth and updated manner.

***Answer:** The manuscript was edited by the Journal's automated manuscript editor, and we also reviewed the entire manuscript; In various sections, we made some changes to avoid long paragraphs, plus some English corrections were made by a highly proficient English speaker. We hope that the modifications made can improve the reading of the manuscript.*

-A weakness of the paper is the conclusion, which is trivial. No mechanistic hypothesis is formulated as to why interleukin 17 can work positively or negatively on bone.

***Answer:** We thank the reviewer for these concerns. According to information of both pro-osteogenic and anti-angiogenic IL-17 function included in the manuscript, we conceptualize a hypothesis that may explain the dual role of IL-17 on osteogenic differentiation and added after the first conclusion statement.*

We focus on NF-kB signaling and its influence on Wnt pathway interaction with IL-17, thus regulating the osteogenic differentiation fate under IL-17 induction.

-By the way, the last sentence is repeated 2 times.

***Answer:** We realized our editing mistake and deleted the related sentence.*

Reviewer #2:

Specific Comments to Authors: The title reflects the main subject of the manuscript and the abstract summarizes and reflects the work described in the manuscript. It is a good review because the authors have consulted a wide and updated bibliography on the subject and have focused on what has been published about the role of IL-17 in osteogenic differentiation, which is a key process in bone repair and regeneration.

Minor concerns:

-Authors must add keywords in the manuscript.

Answer: *We thanks the referee for indicating the missing keywords, and we added them in the manuscript correspondingly*

-On page 13, line 5, the authors misspell Runx2.

Answer: *we corrected the indicated Runx2 misspelled word.*

-Authors repeat this paragraph "Furthermore, a dichotomy of IL-17A roles can result from species-specific characteristics of MSCs and MSC-derived osteoblasts due to the interplay of various microenvironmental issues that condition IL-17A effects or mode of action at the cellular level. Although it is clear that IL-17A profoundly affects osteogenic differentiation, further standardized studies are necessary to unveil how osteogenic differentiation is either positively or negatively regulated and when IL-17 acts as a pro-osteogenic or anti-osteogenic cytokine. Finally, a deep understanding of the precise inflammatory and tissue conditions may help design better therapeutic strategies for IL-17A-associated bone diseases" at the conclusion of the manuscript.

Answer: *We thank the referee for pointed out this editing manuscript mistake, and we deleted the duplicate paragraph.*