Author's response to reviews

Title: (5R)-5-hydroxytriptolide Inhibits Osteoclastogenesis through RANKL/RANK/OPG Signaling Pathway

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Author's response to reviews: see over
Dear Editor,
Thank you for the opportunity to revise our manuscript again. We do appreciate the reviewer’s comment on the manuscript and have discussed it for several times, but we still think the current version of Fig 5 can show the status of osteoclast well, thus we did not replace it. Our reply to the reviewer’s comment is listed below.
Best wishes.

Sincerely yours,
Dongyi He

Reviewer's report:
To the authors
I received the revised manuscript from authors. I think that authors revised their paper carefully; however, I am afraid that I can hardly detect osteoclasts in Figure 5. This figure is essential for evaluating the author's work. We can not call the stained cells in Figure 5 as "osteoclasts".

Reply: Thank you for the comment. Apparently, the reviewer is a real expert on osteoclast and has strict scientific attitude, we really appreciate that. As we known, the criteria of TRAP-positive staining multinuclear cell could be used to determine the osteoclasts and this criteria has been proved by many studies such as Cell Death Dis. 2014,5:e1166; Cell Death Differ. 2004,11 Suppl 1:S97; Exp Cell Res. 2010, 316(19):3254; Bone. 2007, 41(1):77-86; J Cell Physiol. 2008, 214(3):714; J Biol Chem. 2011, 286(27):24458. Therefore, we think it is fine to use this method to determine the osteoclast. In addition, some of researches (J Cell Biochem. 2009, 108(4):947; Cytokine. 2012, 59(2):252) used CD51/61 as a surface marker to determine the osteoclast. However, we believe TRAP-positive cells are at least not inferior to the surface marker CD51/61 because two recent studies by Chiu (Arthritis Res Ther. 2010;12(1):R14) and Petitprez (Int J Lab Hematol. 2015 Feb;37(1):29) suggested that other markers such as CD16 and CD14 are better markers for osteoclast identification. In our opinion, we always believe a good marker should reflect some of the function properties of the cells, thus TRAP is better than CD51/61 because it is somehow show the function change of the cells. We really believe our data are right for the osteoclast. Anyway, the reviewer’s suggestion is always important for us. Thanks again for the comment.