Reviewer's report

Title: Lactobacillus fermentation enhances the inhibitory effect of Hwangryun-haedok-tang on ovariectomy-induced bone loss

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Reviewer: Seong Hwan Kim

Reviewer's report:

Authors suggested the enhancing effect of Lactobacillus fermented HRT (fHRT) on the inhibition of ovariectomy-induced bone loss.

1. In cell-based and in vivo assay, fHRT more strongly inhibited the RANKL-induced formation of TRAP-positive multinucleated osteoclasts compared to HRT. But, authors failed to show the difference between both in mode of action study. Different with the inhibitory activity, c-Fos was strongly inhibited by HRT. c-Fos is one of up-stream regulators of NFATc1. Also, overexpression of NFATc1 did not rescue the inhibitory action of HRT or fHRT. With this result, authors suggested that HRT-BU and fHRT-BU can act as an inhibitor of NFATc1 activity or downstream signaling. This suggestion is not acceptable to elucidate your study. In conclusion, authors showed the phenotypic action of HRT and fHRT, but failed to elucidate the mode of action.

2. In figure 6, no correlation between values and image (G). In figure 6G, fHRT-treated sample is osteopetrotic; cortical bone is thicker and the trabecular bone is denser than the control.

3. Statistical analysis is full required in all graphs.

Further experiments should be done for elucidating the mode of action and authors should re-evaluate the in vivo data to ensure the reality of microCT’s results and its images.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.