Reviewer's report

**Title:** The peroxisome proliferator-activated receptor (PPAR) alpha agonist fenofibrate prevents bone loss, while the PPAR gamma agonist pioglitazone exaggerates bone loss, in ovariectomized rats

**Version:** 1  **Date:** 4 December 2010

**Reviewer:** Hua Zhu (David) Ke

**Reviewer's report:**

This is a well-designed study and the data is well presented. The manuscript is very well organized and clearly written. However the major issue is the interpretation of the data and the conclusion regarding the effects of FENO. The authors concluded that FENO has anabolic effects on bone and prevented bone loss. This reviewer did not see good supporting evidences of the conclusion based on the data presented in this manuscript.

(1) To determine the effect of your testing agents, the most important comparision is between OVX controls and OVX treated with agents. This reviewer did not see any significant differences between OVX rats treated with FENO and OVX controls in parameters listed in Figure 2, Tables 1, 2 and 3. Therefore, this reviewer recommend to revise the conclusion of this manuscript regarding the effects of FENO in OVX rats. FENO has no effect while PIO decreases bone in OVX rats sounds like the correct conclusion according to the data presented.

(2) On the second paragraph of Page 15, the in vivo data did not support the effects of FENO on osteoblast differentiation and maturation, since there was no significant difference between FENO-OVX compared with OVX controls in osteocalcin. The increased osteocalcin level in FENO-OVX group is due to the effect of OVX, not FENO (lines 11-13, page 15). please revise.

(3) The mechanism of action of PIO on bone needs more data to support. While it is clear that PIO induced further bone loss in OVX rats but both osteocalcin and CTx were significantly decreased compared with OVX controls.

(4) Bone histomorphometric analysis of both trabecular and cortical bones for this study will help understand the effects on osteoclast and osteoblast. please consider to include these data in your revised manuscript.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**
no