Reviewer's report

Title: Hyperadiponectinemia enhances osteogenesis through osteoblast formation in mice

Version: 2 Date: 26 July 2010

Reviewer: Urszula Iwaniec

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Mitsui et al. assess the role of circulating adiponectin on bone using transgenic mice overexpressing human full length adiponectin in the liver. The study adds insight into the potential role of adiponectin in bone metabolism.

Major Compulsory Revisions

1. The authors did not measure osteoblastogenesis (the rate of osteoblast formation). Also, osteocalcin levels cannot be used to infer that osteoblastogenesis was higher (page 8, line 5). Figure 3 suggests that osteoblast activity was increased. The increase in MS/BS suggests osteoblast number was increased. Thus, the increase in BFR was likely due to a combination of increased osteoblast activity and increased osteoblast number. However, the authors did not determine the contribution of increased osteoblast production or increased lifespan. Therefore, in the abstract and throughout the text the authors should replace “enhances osteoblastogenesis” with the more accurate “enhances bone formation.”

2. How was mouse adiponectin affected by treatment? Also, please indicate what the normal circulating levels of adiponectin are in the mice.

Minor Essential Revisions

1. Page 4, line 14: Define ALP.

2. Page 4, line 20: Type 1 collagen?

3. Page 5, line 20: Provide additional information about the instrument (e.g., DEXA?).

4. Page 5, line 22: Describe the histology and histomorphometry methods (e.g., how were bones embedded, location and size of sampling site, how trabecular number and osteoid thickness were determined, etc.). Also provide information regarding the fluorochrome labeling schedule and how MS/BS.

5. Page 7: What post-hoc test was used? Were ANOVA assumptions of normality and homogeneity of variance met in each data set? If not, please transform data or use appropriate nonparametric statistics.

6. Results: How did overexpression of the human adiponectin affect mouse
serum adiponectin?

7. Results: Describe the effects of treatment on BMC in the Results. BMC is a true measure of bone mass whereas BMD, by itself, is impossible to interpret.

8. Table 2: Are the values for N.Oc/B.Pm correct? 100+ osteoclasts/mm only accounting for 1% of bone surface seems unlikely.

9. Table 2: Please adjust values to be consistent and reasonable with reference to decimal place. The SDs are often indicated using a different number of significant digits than the means. Also, the unit for MAR is incomplete.

10. Figure 5A: Provide units on Y axis.

11. Page 8, line 5: Change osteoblastogenesis to bone formation here and throughout the manuscript as osteoblastogenesis was not measured.

12. Page 9, line 1: Bone formation rate is not presented in Table 2.

13. Page 9, line 3: Stiations?

14. Page 11, line 14: Change ‘highs’ to ‘high.’

15. Page 11, line 21: Change osteoclastogenesis to osteoclast # or surface as osteoclastogenesis was not measured.

16. Conclusions: Change osteoblast formation and osteoblastogenesis to bone formation.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.