Reviewer’s report

Title: Interleukin-11, a cytokine produced by breast cancer cells, augments osteoclastogenesis by increasing the pool of osteoclast progenitor cells

Version: 1 Date: 19 September 2012

Reviewer: Julie Sterling

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1. Is the question posed by the authors well defined?
The questions are clear but the focus is somewhat lost by the present order of the manuscript. I would switch the order and start with the observation that Breast cancer conditioned media are capable of supporting the development and/or survival of osteoclasts, then the IL-11 neutralizing antibody data, then that IL-11 does not stimulate osteoclastogenesis independently of RANKL or with low doses of RANKL, IL-11 does not affect survival, IL-11 promotes development/survival of osteoclast progenitor cells.

2. Are the methods appropriate and well described?
The authors use the appropriate methods, and they seem to be well-described. However, there are some details in the figures that need to be addressed.

1. While the differences are obvious, there needs to be some quantification of this data. Additionally, the resorption pits need to be highlighted or indicated more clearly to readers that may not be used to looking at these types of figures (I can clearly see the differences). Another option would be to show a higher magnification image.

2. What is the magnification on Figure 2? It would be helpful to show the scale on the figure. Need to show quantification.

3. You need quantification. Images of bone slices need to be clearer.

3. Are the data sound?
Yes, the data seem sound. They have large differences in their assays, and the experiments seem to be done thoroughly.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
The discussion does a very good job at describing the relevance of these studies. I thought it did a better job with the order than the rest of the paper. Once the order of the results is changed there will need to be some minor changes to the discussion (top of page 16) for the order.
6. Are limitations of the work clearly stated?
Acceptable.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
They do a fair job in acknowledging the previous work and discussing the controversies within the IL-11 field. I think they should mention either in the discussion or the introduction the other factors that MDA-MB-231 cells are known to express and that contribute to bone resorption. However, I thought they convincingly show that IL-11 is involved.

8. Do the title and abstract accurately convey what has been found?
The title accurately conveys the study, but it could be re-phrased in a more direct way to make more of an impact. Something along the lines of “Tumor-produced IL-11 increases the osteoclast progenitor pool leading to an increase in osteoclasts and bone resorption.”

The abstract still needs work. The relevance of the study should be more prominent. I would also argue that the authors have not delineated the precise mechanism underlying the role of IL-11 in breast cancer induced osteolysis. They have examined how IL-11 stimulates osteoclast differentiation and bone resorption, but more studies are needed to truly know the precise mechanisms here.

9. Is the writing acceptable?
The manuscript is well-written and very interesting. They have strong data, and some minor changes in how the order the manuscript will help with the impact. Overall, I thought this was an interesting manuscript, and while I have several corrections that need to be addressed, the majority are minor.

Major Revisions: The data in figures 1-3 needs to be quantified.
Minor Revisions: Changing the order of the text and some minor changes to the figures listed above.
Discretionary changes: I suggest a more streamlined title, but the current one is acceptable. Also, I think the abstract could be improved.

**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:**
I declare that I have no competing interests