Reviewer's report

Title: Effects of antibody to receptor activator of nuclear factor kappa-B ligand on inflammation and cartilage degradation in collagen antibody-induced arthritis in mice

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Reviewer: Ulrike Harre

Reviewer's report:

In this article, the authors investigate a putative ameliorating effect of an anti-RANKL antibody on collagen antibody induced arthritis (CAIA). They found no differences in inflammation or cartilage destruction whether CAIA subjected mice received the anti-RANKL antibody or not.

You would expect the anti-RANKL antibody to have no effect on CAIA induced inflammation. However, it is an interesting finding that this antibody also shows no effect regarding cartilage degradation, although the quality of cartilage analysis definitely needs to be improved.

Major Compulsory Revisions:
1. Apparently, the authors have conducted the CAIA experiment only once with 5 to 6 mice per group. This number is too low to draw any conclusions (even for a negative result), especially with the extremely high standard variations of the RA+/Ab- group in Figure 3.
2. In table 1 the authors describe that none of the RA- animals had swollen limbs. Yet in Figure 3, the RA-/Ab+ group develops an arthritis score from day 11 which is contradicting Table 1.
3. The scoring system of Figure 3 is not entirely clear. Did the authors use a cumulative score or did they calculate the mean of all paws?
4. In Figure 2 the authors nicely demonstrate that the antibody against RANKL worked in the RA- mice by investigating the increase of the bone density in the tibia. However, this does not proof for 100% that the antibody also works in a more inflammatory environment. Would it be possible to provide these data also for the RA+ mouse groups?
5. In Figure 4 and 5 it would be nice to have a quantitative analysis of the amount of inflammation and cartilage destruction (for example a semiquantitative scoring system). In addition, HE staining is not the best staining to investigate cartilage destruction. A toluidine blue or safranin o staining would be much more appropriate.
6. In Figure 5E the serum COMP of the RA- mouse groups should be included to show that the CAIA had an effect on the COMP levels.

Minor Essential Revisions:
1. In Figure 4, the labeling on the left side was not readable.

**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.