Reviewer's report

Title: Dickkopf-1 (Dkk-1) in plasma and synovial fluid is inversely correlated with radiographic severity of knee osteoarthritis patients

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Reviewer: Mariput Corr

Reviewer's report:

Dr. Honsawek et al. present their findings on the amount of Dickkopf-1 (DKK) measurable in the plasma and synovial fluid of patients with radiographic knee osteoarthritis and the plasma level of DKK in normal control patients. The manuscript is well presented.

There are several points, which would improve the clarity of the manuscript.

- Major Compulsory Revisions

1. The authors state that their data suggest that low levels of DKK-1 correlate with progressive arthritis. The only data presented are for a single time point in a cross sectional study and cannot be extrapolated to determining progression (conclusion page 13).

2. In the methods on page 5 there is a statement that none of the participants had diabetes or inflammatory disease and later in the same paragraph it reiterates that arthritis, cancer and other chronic diseases were excluded. Were there two stages of exclusion? The controls are described after the exclusion criteria. Were the same exclusion criteria applied?

3. Please clarify if the plasma was drawn at the same time as the synovial fluid aspirate was performed.

4. As there are a limited number of patients in this study Table 1. should be expanded to include the gender, age, and BMI by Kellgren and Lawrence classification. Counting the data points there are 17 K/L 4 and 8 K/L 2 patients. Including the stratification in the table would clarify this point.

5. Figure 1 should be limited to a comparison of the plasma levels between OA patients and controls. Including the synovial fluid data here is redundant with figure 4 and there is no appropriate control.

6. The conclusion drawn from the Pearson correlation in Figure 3 should be tempered. There is a relatively low level of Dkk-1 in all of the synovial fluids and there are two “outliers” in the limited number of patients in the K/L 2 group (n=8). If these two points were excluded then there would be a relatively flat line through the groups. The small number of individuals in the K/L 2 group limits the emphasis that can be placed on interpreting this data.

7. In Figure 4 it is clear that overall the plasma levels correlate with synovial fluid levels, however it is equally clear that this is not uniformly proportional in all individuals. In the cluster of patients with DKK-1 plasma levels around 200pg/ml
a rough estimate of the spread of synovial levels is 25-70 pg/ml. This point should be clarified in the results.

8. The discussion should also include the point that the daily variation of plasma DKK-1 has yet to be fully determined and it is unclear which activities might influence plasma levels (walking, jumping, eating etc). Only a single time point is shown.

9. On page 11 the authors conclude that there are differences in local and systemic production, but no data are provided on the location of synthesis.

Minor Essential Revisions

Page 3 The statement: “More recent studies suggest a potential role for DKK-1 in malignant bone disease and arthritis. “ Should be referenced. The next sentence should be changed to one report and not "Recent studies" as there is only one reference supplied.

Page 12 the sentence “Moreover, the data derived from this study…. Does not make sense.

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

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