Reviewer’s report

Title: Serum and Synovial Fluid Cytokine Profiling in Hip Osteoarthritis: Distinct from Knee Osteoarthritis and Correlated with Pain

Version: 0 Date: 21 Nov 2017

Reviewer: Nicole Cattano

Reviewer’s report:

Thank you for the opportunity to review the manuscript entitled Serum and Cytokine Profiles are Distinct between Patient Cohorts with Hip or Knee Osteoarthritis and Correlate with Hip Pain. The authors should be commended for their hard work in this novel line of research. While the findings of this study are interesting, the manuscript overall is difficult to follow and has some significant clarifications or structuring needed in order to strengthen the quality and understanding of the research study.

Overall - the title is confusing as to what is distinct from each other. Upon initial impression, it is unclear if it distinction between serum and cytokine…or Hip and Knee OA. Consider rephrasing

Keyword - consider selecting words that are not included within the title

Unclear as to why the correlations are only run in Hip OA

Pg 4 introduction - lines 20-23…this sounds like you are describing different phenotypes of OA and later reference little work in this area. There has been significant work in this area and the authors should consider referencing the work of authors such as Driban, Karsdal, Kittleman, & Dell'Isola work. Or distinguishing the difference between their work and what you are referencing.

Pg 5 line 42 - still remains unclear as to why this correlation was only specifically run in the hip cohort

Inclusion criteria for normal seems vague - whey were participants potentially excluded based on their personal and family history. Please clearly state the exclusion criteria

Pg 6 line 25/26 - radiographic evidence of KL grading…does this mean a KL of 1 or above? Please clarify

Clinical assessment of Hip OA cohort---when did the participants complete the clinical outcome measures. And why were these specific outcome measures chosen. Lastly - what is the validity/reliability of these measures.
Serum sample collection - please address when this occurred and whether there was a rest period prior to sample acquisition. There is ample evidence that exists regarding the need for this timeframe for biomarker stabilization/normalization.

Statistical Analysis

Pg 7 line 47 - Given the non-normality, I agree that Mann Whitney Wilcoxon test is appropriate…however it does not compare the means. Please revise

Pg 8 line 9 - multiple correlations are often corrected (as authors indicated) yet the new p value is not indicated/does not seem appropriate or different. Please state here.

Results

Page 9 line 9 - when I start reading this section - it remains unclear what cytokines or markers were investigated and why. As well as what processes or tissues they are indicative of. Please consider outlining more clearly in procedures/methodology.

Page 9 line 18 - it is confusing when you state within subsets of patients within 3 cohorts. Does this not mean hip vs knee vs. normal?

Line 29 - while I think it is a good idea to statistically run these tests for confounding variables - there is not a justification as to why this is built in (in background/introduction). Consider adding language or citations as to why.

Discussion

Page 11 Scatter plot discussion - can you postulate other reasons as to why certain markers may be similar or different based on joint affected and normal?

Please clarify in results and here whether the differences were found in Serum or Synovial fluid for cytokines as they can be assessed in either. Also still wondering if any markers were assessed in both fluids.

Limitations Page 12 line 9 - you just stated that age was not correlated with inflammatory markers yet cannot confirm it with limitations of not knowing normal participants' ages.

Page 12 - when discussing synovial fluid vs. serum markers it may be more valuable to provide these more clearly in the results section and provide references/support for why you are postulating that these differences are existing, and how these findings compare to what others have found with these markers.

Page 13 - please provide references for the validation of previous studies

Need more deliberate limitations & conclusion sections
Seem to have a couple of formatting/missing information for references

Table 2 seems to not add much value to results/interpretation. Consider different way to present data or discuss in text

Figure 3 B consider marking which ones are significantly different

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal

Do you want to get recognition for reviewing this manuscript? Add a record of this review to Publons to track and showcase your reviewing expertise across the world’s journals. Signing up is quick, easy and free!

No