Reviewer’s report

Title: Effects over time of two platelet gel supernatants on growth factor, cytokine and hyaluronan concentrations in normal synovial membrane explants conditioned with lipopolysaccharide.

Version: 2 Date: 4 March 2015

Reviewer: Charles Malemud

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Manuscript for Review: Diana L. Rios et al. Effect over time of two platelet gel supernatants...

1. Is the question posed by the authors well defined? YES. However, in contradiction to the 1st line of the Introduction, synovitis is a common manifestation of osteoarthritis.

2. Are the methods appropriate and well described? YES (no further comments)

3. Are the data sound? NO

3a) Data represent a phenomenon rather than a mechanistic response. That is some measurements go up, some go down and others remain the same.

3b) There is no clear-cut rationale for why reaching or approaching synovial fluid levels for the response to LPS for the various factors that were measured was a chosen as an endpoint. This is most troublesome for why TNF-# levels in the equine synovial fluid was used as one of the barometers of response.

3c) Why was LPS used as the activation step? The use of LPS as a model activator PRP would appear to have little relevance to osteoarthritis.

4) Do the Figures appear to be genuine? YES

5) Relevant standards? YES

6) Discussion and Conclusions (NO) Much of the Discussion recapitulates the Results section. The authors should focus on addressing what the significance of these results mean in mechanistic terms.

7) Limitations? Some limitations are pointed out. Extrapolating results from in vitro explant culture to clinical use of PRP is a major limitation.

8) Acknowledgement of previous work? YES

9) Title and abstract? YES

10) Writing. It was difficult to follow the Results section where the data in the Figures were simply recapped in the text.
Major Compulsory Revisions: The author’s must more clearly provide a clear-cut rationale for choosing the response indicators PDGF-BB, TGF-#1, TNF-#, IL-4, IL-1ra, HA. The points raised in the Discussion regarding IL-1ra should be re-thought. Anti-IL-1 therapy in several osteoarthritis clinical trials had little success, probably because there was sufficient IL-1ra already in the OA synovial fluid or that IL-1ra just doesn’t work well in osteoarthritis in the context of an inflammatory milieu. Page 18: 2nd paragraph, lines 1-2. With respect to reference 14, it is recommended that the conclusion drawn in this sentence be toned down.

Minor: References #9 and #26 are incomplete. Reference #33 is missing the year of publication.