Author’s response to reviews

Title: A multi-chamber tissue culture device for load-dependent parallel evaluation of tendon explants

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Author’s response to reviews:

August 27, 2019

Ciarán Fitzpatrick, PhD
Editor
BMC Musculoskeletal Disorders

RE: Manuscript Submission - Soreide et al.

Dear Dr. Fitzpatrick,
Please find enclosed the second revision of our manuscript entitled “A multi-chamber tissue culture device for load-dependent parallel evaluation of tendon explants” by Endre Soreide and colleagues to be reconsidered for publication in BMC Musculoskeletal Disorders.

We have comprehensively addressed the final comments from the reviewers and included a point by point response in the appendix to this letter.

We reconfirm that this manuscript has not been published elsewhere and is not under consideration by another journal. All authors have approved the manuscript, disclosed any potential conflicts of interest, and agreed with its resubmission to BMC Musculoskeletal Disorders.

On behalf of all authors, we look forward to hearing from you at your earliest convenience.

Sincerely,

Andre van Wijnen

Response to reviewer

GENERAL COMMENTS: This study details a relatively novel tissue sample culturing system to assess the effects of tension on whole tendon samples. The study has been performed in a competent fashion, using state of the art equipment. However, tendons are not subjected to continuous tension strains. Indeed, they thrive under cyclical tension conditions. Hence, the model, though the authors seem to have validated it, is not representative of physiological conditions, and/or pathology. This should be specified.

REQUESTED REVISIONS:
The authors are obviously in love with what they have done, and I share with them much of their enthusiasm. However, the large number of genes selected may introduce a degree of chance in altered expression which does not seem to be accounted for in the statistical analysis. Some of the genes studies are involved in inflammation, which has recently been resurrected as a primum movens of tendinopathy (see https://www.ncbi.nlm.nih.gov/pubmed/28596062 and https://www.ncbi.nlm.nih.gov/pubmed/28002908)

Response to reviewer: We thank you for these remarks. In response of these new comments on our previously revised manuscript, we have now further clarified the rationale and relevance of the gene expression studies. Also, we have added minor revisions throughout the manuscript for clarifications for the reader.

All genes where selected prior to study start to investigate the potentially ongoing processes within tissue while in the explant culture device. A panel of genes were selected to assess in particular extra cellular matrix production/deposition and remodeling/organization, in addition to
inflammation markers known to affect the mentioned biological processes. A bio-statistician was consulted and supervised the analysis of the data to ensure both an accurate, reliable and valid analysis and presentation of the results. Please find additions to the Discussion, page 12, line 6-13.

We agree with the reviewer that the culturing device does not fully represent physiological conditions as it does not apply cyclical tension conditions to the tissue. This has been addressed and clarified in the manuscript, page 14, lines 9-15.