Author’s response to reviews

Title: Regulation of Gene Expression in Human Tendinopathy

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Version: 2 Date: 1 April 2011

Author’s response to reviews:

Dr. Haiko Sprott
BioMed Central

Dear Dr Sprott,

Thank you for your consideration of our manuscript MS:1726195765496362 Regulation of Gene Expression in Human Tendinopathy for publication in BMC Musculoskeletal Research. We thank the reviewers for their time and effort. Below please find our specific comments and changes made to address each of the reviewers concerns. We have also extensively proof read the manuscript and have made a number of minor spelling, grammatical and sentence structure changes.

Reviewer 1

1. Reviewer one pointed that that the statement “nicely aligned collagen fibers” can be ambiguous. We completely agree with the reviewer and have modified the statement to make it less ambiguous.

2. The reviewer also questioned whether age may have had any influence on gene expression. While we tried to control as many variables as possible, all human studies consist of heterogeneous populations. As we mentioned in the results section, as part of the analysis we performed ancova analysis to identify any potential covariates (including, histological disease score, disease duration, steroid use, NSAID use, gender, duration of symptoms and age that might affect the data. Less than 2% of the disease related genes show correlated expression patterns with age suggesting that disease has a significantly stronger effect on expression then age and any changes in gene expression based simply on age are masked by the effects on gene expression due to disease.

Reviewer 2
1. “GeneChip Operating System” was changed to “GeneChip Operating Software”.

2. The reviewer correctly questioned why we have used the non-parametric Wilcoxon test instead of the more powerful paired t-test. The reviewer is absolutely correct in suggesting that we use the paired t-test. While both the Wilcoxon and paired t-test give correlated results, the paired t-test is more acceptable for the type of analysis presented here. We thank the reviewer for pointing this out. In response to this concern, we have performed a paired t-test on the data and have updated the tables and the text where appropriate to reflect this analysis. This changes do not affect any conclusions presented.

3. The reference to the MSigDB has been updated and the collection of genesets used has been clarified

4. The duplicate reference 21 has been eliminated and corrected in the text.

5. Table 3, 5, 6, 7 and 8 have been updated with p values based on a paired t-test and q-values have been added.

Sincerely,

Scott A. Jelinsky