

## ***Inflammation and the continuum model: time to acknowledge the molecular era of tendinopathy.***

Re: - Revisiting the continuum model of tendinopathy pathology: what is its merit in clinical practice and research? BJSM Online First April 2016

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Dear Editor,

The original continuum theory mentioned little concerning inflammatory mechanisms in tendon disease likely due to the lack of scientific studies at that time. Since then we and others have clearly defined a role for inflammatory cells<sup>1</sup> and the subsequent inflammatory/matrix crosstalk involving cytokine regulation<sup>2</sup> in human tendinopathy. It is therefore surprising that the updated continuum model again fails to acknowledge the molecular role that inflammation likely plays in damage events associated with tendinopathy.

We appreciate the term inflammation continues to evoke divergent opinions between clinicians and scientists within the field (Dean et al BJSM). However clear pathological and molecular evidence exists of its dysregulation throughout the spectrum of human tendon disease; while inflammatory change may help to explain the mismatch between pain and macroscopic tendon structure<sup>1</sup>. The use of a quotation from a twitter feed (Fig 1) as evidence that cytokines are biologically inert within the context of tendinopathy seems biased and inappropriate considering the strong evidence base throughout landmark publications in the scientific literature demonstrating a key role of cytokines in musculoskeletal pathologies<sup>4</sup>.

We agree that much remains to be elucidated surrounding inflammatory mechanisms in tendinopathy and in particular where inflammatory mediators sit within the hierarchical pathophysiological mechanisms involved in clinical disease. However, this model has and continues to set precedent within the field and should therefore reflect the growing molecular evidence that modulating inflammatory pathways may provide novel translational therapies to a disease that current treatments are failing our patients.

### References

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3. Dean, B.J., Gettings, P., Dakin, S.G. & Carr, A.J. Are inflammatory cells increased in painful human tendinopathy? A systematic review. *Br J Sports Med* **50**, 216-220 (2016).
4. Schett, G. et al. How Cytokine Networks Fuel Inflammation: Toward a cytokine-based disease taxonomy. *Nature Medicine* **19**, 822-824 (2013)