In vitro inflammatory response to surgical scaffolds for rotator cuff repair

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ABSTRACT

Introduction
Surgical scaffolds are used to augment rotator cuff tendon repairs. Interactions between recruited immune cells and tendon-resident stromal cells influence whether the scaffold is integrated or rejected by the body. The primary aim of this *in vitro* study was to compare the inflammatory response of human monocytes to different surgical scaffolds. The secondary aim was to determine how this monocyte response affects the behavior of human rotator cuff tendon-derived stromal cells *in vitro.*

Materials and methods
Primary human monocytes were cultured on four commercially available scaffolds: LARS ligament (synthetic); GraftJacket (allograft), Permacol (xenograft, cross-linked), and Conexa (xenograft, non-cross-linked). Secreted inflammatory proteins were measured after 1 and 10 days. Foreign body giant cell formation was assessed after 10 days. Proliferation and gene expression of tendon stromal cells were assessed after being grown in a conditioned medium from monocyte-scaffold cultures.

Results
After 10 days, monocytes cultured on the Conexa scaffold secreted the highest levels of the pro-inflammatory markers GM-CSF, IL-8, and IL-10 (fig. 1). After 1 day, tendon stromal cells incubated in conditioned media from Conexa-monocyte cultures expressed lower Collagen Type VI and increased *MMP3* and *MMP6* mRNA (fig. 2). Foreign Body Giant Cell formation was most prominent in monocytes cultured on the Permacol scaffold (fig. 3).

Discussion
In vitro experiments demonstrated that xenograft scaffolds elicited a more pronounced pro-inflammatory response in human monocytes compared to synthetic and allograft scaffolds. Inflammatory cytokines secreted by monocytes in response to xenografts may modulate scaffold integration through paracrine signaling to tendon stromal cells. These findings may help explain the clinical performance of xenograft scaffolds for tendon repair and inform future scaffold design.

Level of evidence
N/A

Abstract summary
In vitro inflammatory response of human monocytes is greater on xenograft scaffolds compared to allograft and synthetic scaffolds.

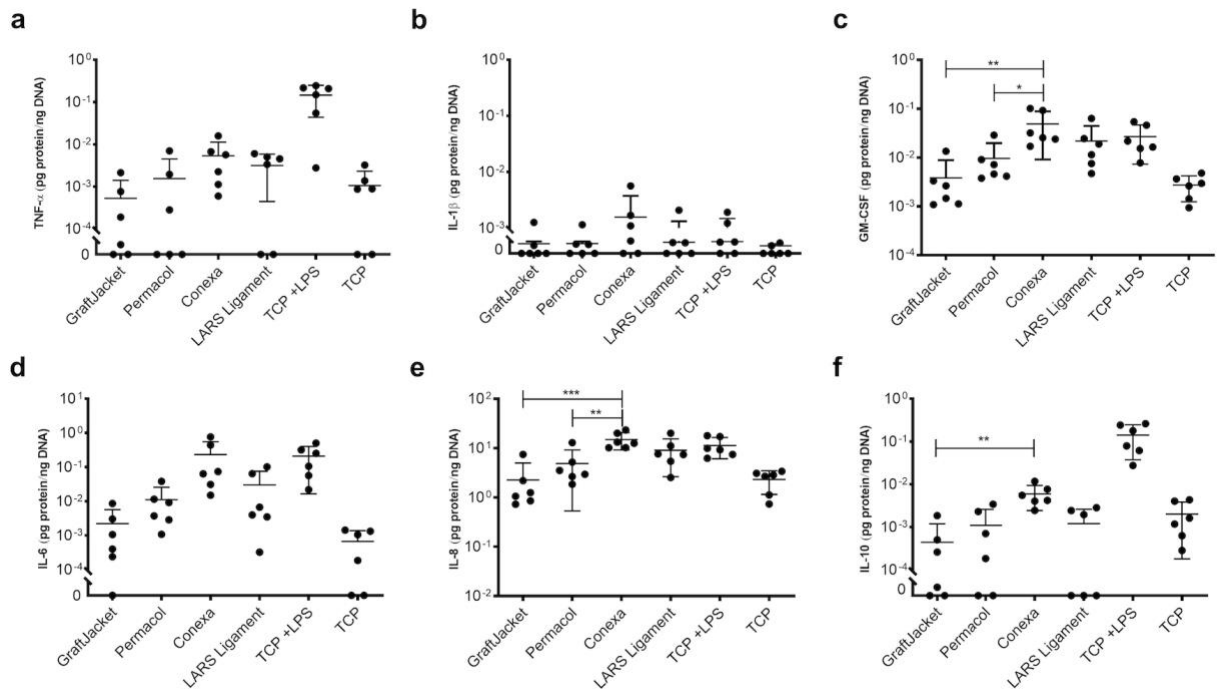

Figure 1. Quantification of monocyte-secreted proteins on scaffolds after 10 days (mean +/- SD). Protein expression was standardized to DNA content (after subtracting any residual DNA content). TNF-α (a), IL-1β (b), GM-CSF (c), IL-6 (d), IL-8 (e), and IL-10 (f). *≤0.05, **≤0.01, and ***≤0.001, ****≤0.0001.

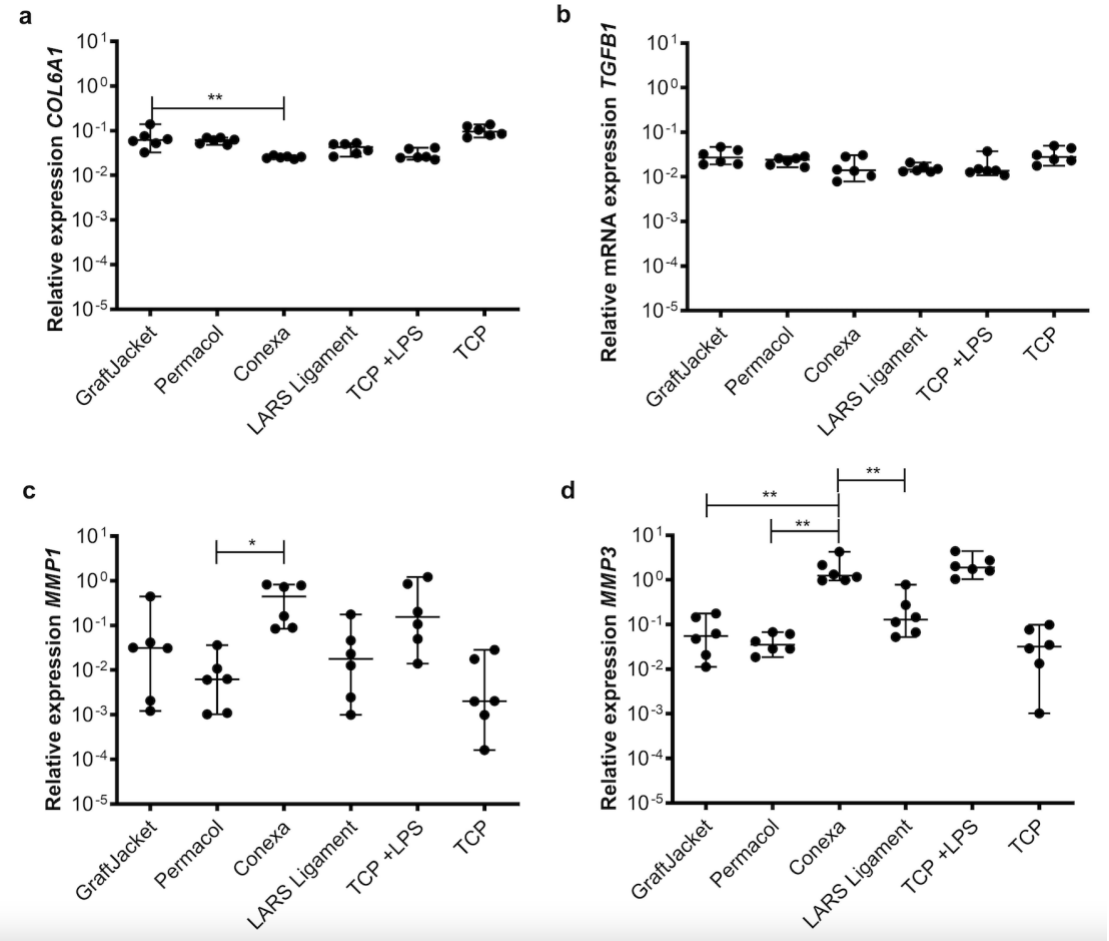

Figure 2. Quantification of tenocyte mRNA relative to *GAPDH* after exposure to day 1 monocyte medium (mean +/- SD). *COL6A1* (a), *TGF-B1* (b), *MMP-1* (c), and *MMP-3* (d). *≤0.05, **≤0.01, and ***≤0.001, ****≤0.0001.

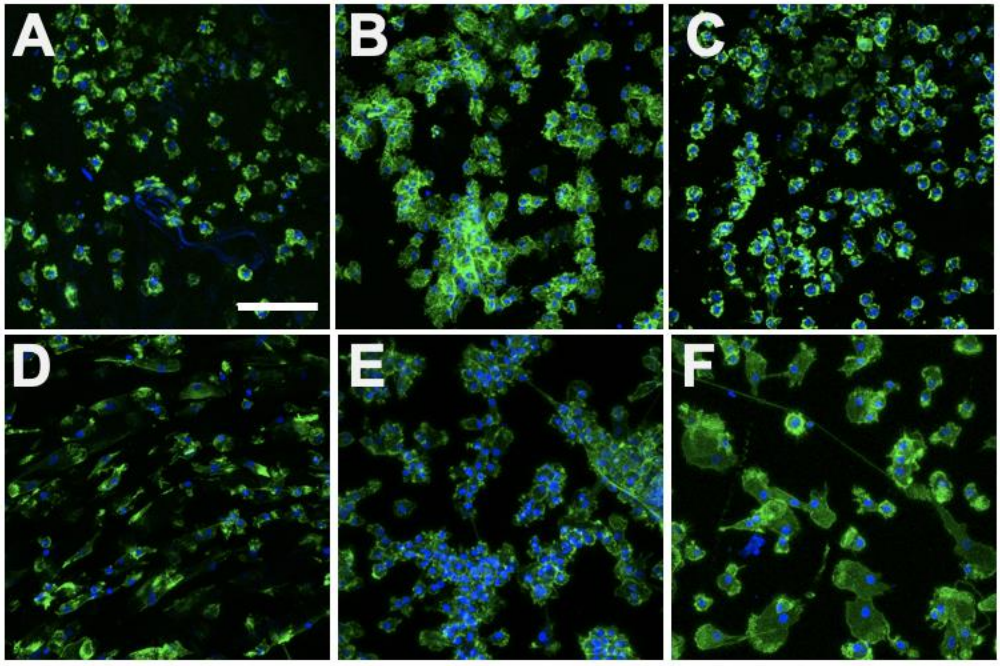

Figure 3. Confocal images of foreign body giant cells forming on scaffolds and controls after 10 days of incubation on scaffolds with Il-4-enriched monocyte media. GraftJacket (A), Permacol (B), Conexa (C), LARS ligament (D), TCP + IL-4 (E), and TCP (F). Images taken at 20X. Scale bar= 100µm. Green stain is actin filaments and blue stain is DAPI.