In vitro inflammatory response to surgical scaffolds for rotator cuff repair

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Introduction

- Surgical scaffolds are used to augment rotator cuff tendon repairs
- Interactions between immune cells and tendon stromal cells influences 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 stromal cells

Methods

- 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

Figure 1

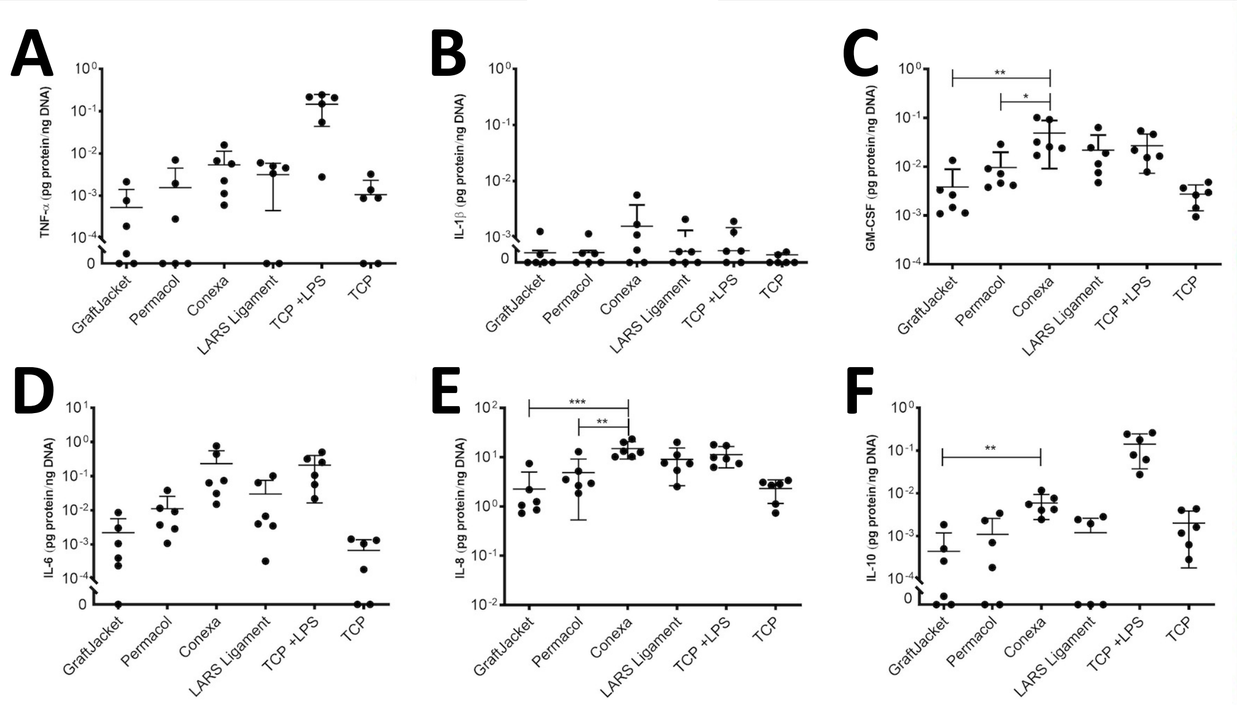
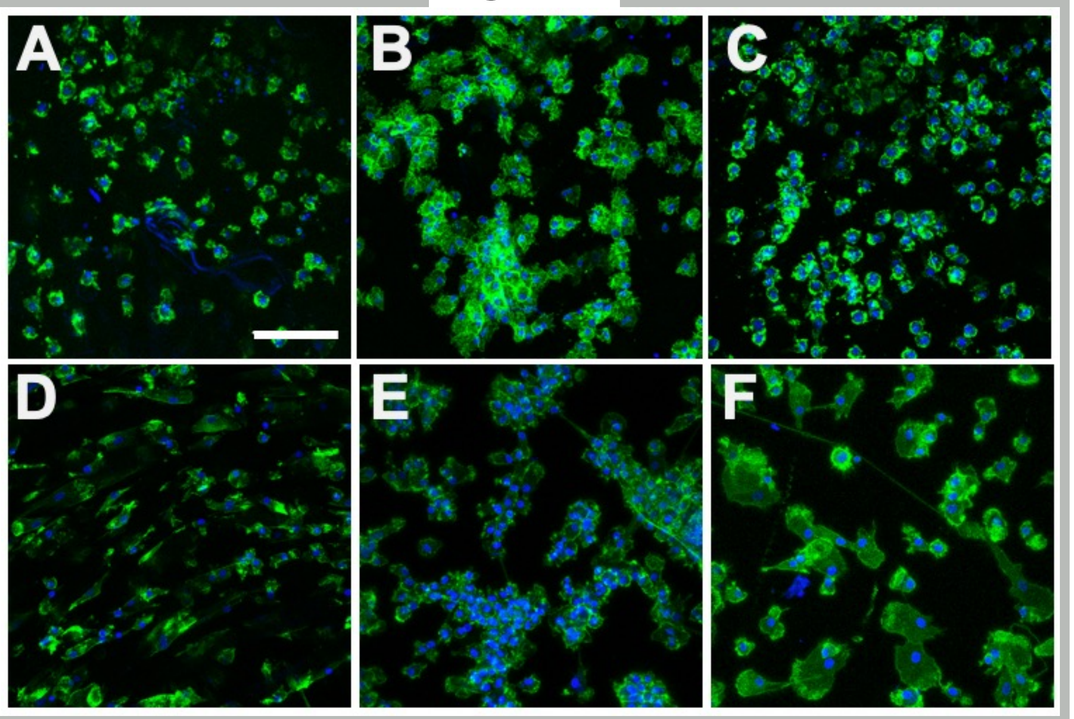


Figure 2



- **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. Confocal images of foreign body giant cells after 10 days in 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=actin filaments, blue=DAPI
- 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)
- Foreign Body Giant Cell formation was most prominent in monocytes cultured on the Permacol scaffold (fig. 2)
- 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 (data not shown)

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

Acknowledgements

- This project was funded by a grant from Tornier, Inc. and the NIHR Musculoskeletal Biomedical Research Unit, Oxford