

## OSTEOIMMUNOLOGY

## Could inhibition of IL-1 and TNF improve healing of meniscal lesions and prevent the development of osteoarthritis?

Tissue degradation resulting from injury to the knee menisci can lead to the development of osteoarthritis. Evidence suggests that cell accumulation at the meniscal lesion is important for repair of the damaged tissue and restoration of joint function. Now, data from Farshid Guilak and colleagues at Duke University, North Carolina, published in *Arthritis Research & Therapy*, increase our understanding of the influence that cytokines might have on this process.

“...strategies to inhibit the local inflammatory cascade may improve meniscal repair...”

“We have discovered that an important factor that prevents meniscal repair is the presence of inflammatory cytokines, such as IL-1 and TNF- $\alpha$ ,” states Amy McNulty, a co-author of the paper. Using *in vitro* scratch-wound assays and meniscal

explant cultures as models of meniscal injury, Guilak and collaborators were able to show that IL-1 and TNF markedly decreased meniscal cell proliferation, but not migration, compared with controls. The suppression of proliferation manifested in reduced cellularity at the wound. Furthermore, extracellular matrix deposition in the wound was less extensive after cytokine treatment, in comparison with controls. A corresponding decrease in the resistance of the wound to shear stress was demonstrated, indicating inhibition of repair.

“We also found increased proliferation of superficial zone cells compared to cells deeper within the tissue, suggesting that the superficial layer of cells plays a crucial role in initiating and modulating the repair process,” explains lead author Katie Riera. Interestingly, the anabolic cytokine transforming growth factor  $\beta$ 1 increased total cell proliferation, but not migration, in comparison with controls; however,

cells below the superficial layer accounted for most of the proliferation observed, and no improvement in wound healing was noted.

“Our study suggests that strategies to inhibit the local inflammatory cascade may improve meniscal repair,” says Guilak. “In particular, the results of this study suggest that increasing meniscal cell proliferation could enhance integrative repair in tissue engineering constructs and meniscal injuries,” he continues. However, further investigation is required to clarify the role of cytokines in meniscal repair and to assess their potential as therapeutic targets.

David Killock

**Original article** Riera, K. M. *et al.* Interleukin-1, tumor necrosis factor- $\alpha$ , and transforming growth factor- $\beta$ 1 and integrative meniscal repair: influence on meniscal cell proliferation and migration. *Arthritis Res. Ther.* **13**, R187 (2011)