

**Control/Tracking Number:** 19-A-795-OARSI

**Activity:** Abstract

**Current Date/Time:** 11/28/2018 3:44:50 PM

## **INTERLEUKIN-17 IS A POTENTIAL CONTRIBUTOR TO THE INFLAMMATORY ENVIRONMENT IN THE OA JOINT**

**Author Block J. Y. Mimpfen**, S. Kluzek, S. G. Dakin, A. J. Price, F. E. Watt, A. J. Carr, S. J. Snelling; Univ. of Oxford, Oxford, United Kingdom

### *Abstract:*

**Purpose:** Osteoarthritis (OA) has been historically viewed as a degenerative disease caused by 'wear and tear', with the loss of articular cartilage as the most important clinical feature. Modern imaging techniques have shown us over the last decade that OA is a multifactorial disorder that affects multiple tissues in the joint, including the subchondral bone and synovium. Synovitis is now increasingly recognised to be involved in OA pathogenesis, with *in vitro* studies showing production and release of pro-inflammatory cytokines (such as interleukin (IL)-6, IL-8, and IL-17, infiltration of mononuclear cells, and increased angiogenesis. This study aimed to establish whether the pro-inflammatory cytokine IL-17 contributes to the inflammatory environment within the OA joint. We hypothesized that IL-17 can contribute to inflammatory cell recruitment to the OA synovium and that IL-17 responsive stromal cell populations within the OA joint can further drive inflammation.

**Methods:** Formalin-fixed paraffin-embedded synovial tissue from injured and early-stage knee OA patients was stained for IL-17 receptor A (IL-17RA) and IL-17 receptor C (IL-17RC) as well as for the macrophage markers CD68 and CD206. Freshly isolated synovium from end-stage knee OA patients was digested for FACS analysis using a macrophage panel. Stromal cells from synovium (synovial fibroblasts) and cartilage (chondrocytes) from end-stage knee OA patients were cultured to passage 3 and assessed for IL-17R mRNA expression by RT-qPCR. In addition, these stromal cells were treated for 24h with 10 ng/ml rh IL-17 and RNA was harvested for RNA-Seq analysis.

**Results:** We detected *IL17RA* and *IL17RC* mRNA in cultured chondrocytes and synovial fibroblasts from end-stage OA patients and showed that IL-17 receptors IL-17RA and IL-17RC are expressed in synovial tissue sections derived from injured and early-stage OA patients. While protein expression of IL-17RA was significantly higher in patients with a high synovitis score compared to a low synovitis score ( $p=0.012$ ), IL-17RC did not show this difference ( $p=0.98$ ). IL-17RA staining showed a trend toward correlation with CD68 ( $p=0.07$ ) and correlated significantly with CD206 staining ( $p=0.004$ ). IL-17RC did not correlated with CD206 ( $p=0.88$ ), but showed a trend towards significance with CD206 ( $p=0.53$ ). FACS data confirmed the presence of CD206+ macrophages in end-stage OA synovium. In cultured synovial fibroblasts and chondrocytes from end-stage OA patients, IL-17 treatment significantly upregulated the mRNA expression of several granulocyte-attracting and -regulating factors such as *CCL2*, *CXCL3*, *CXCL6*, and *CXCL8*.

**Conclusions:** This study shows that IL-17 may contribute to the inflammatory environment in the joint by acting on synovial fibroblasts and chondrocytes to driving mononuclear cell influx. As IL-17 responsive cells are correlated with macrophage populations, IL-17 may be able to further drive inflammation by acting on these inflammatory cells as well as on synovial fibroblasts and chondrocytes.