

**Title: A Novel Regulatory Role of L-Plastin in IL-1 $\beta$ -mediated Inflammation in Human Chondrocytes****Author(s): Andrew Alejo, Nazar Hussein, Fayez Safadi****Affiliation:** Northeast Ohio Medical University

Osteoarthritis (OA) is the most prevalent joint disease worldwide, causing chronic disability in older people. Various factors are associated with its pathogenesis, including aging, obesity, joint instability, and joint inflammation. Several pro-inflammatory mediators such as Interleukin 1 beta (IL-1 $\beta$ ) are able to activate NF- $\kappa$ B signaling cascades. There are two distinct pathways, which can activate the NF- $\kappa$ B signaling cascades. The first one termed canonical pathway is the activation of the IKK $\alpha$ /IKK $\beta$ /IKK $\gamma$ -NEMO complex. The second one, the non-canonical pathway, is the activation of NF- $\kappa$ B-inducing kinase (NIK). L-Plastin (LPL) is an actin-bundling protein essential for actin regulation in multiple cell types. It was reported that LPL protein expression was elevated in rheumatoid arthritis. We hypothesized that LPL might also be a regulator for inflammation in OA. First, we assessed the gene expression/protein levels of LPL in primary human chondrocytes subjected to IL-1 $\beta$  treatment and found that LPL expression increased in the IL-1 $\beta$ -treated chondrocytes compared to controls. Next, we determined role of LPL inhibition by treating TC28 cells with LPL inhibitor post IL-1 $\beta$  treatment. LPL inhibition led to negative modulation of NF- $\kappa$ B signaling cascades in chondrocytes. Also, our data showed that the LPL inhibitor was able to decrease proteoglycan degradation in mouse femoral heads ex vivo organ cultures treated with IL-1 $\beta$  compared to controls. Studies are underway to determine the role of modulating LPL using in vivo studies, which include C57B/6 and LPL $^{-/-}$  mice post-traumatic-induced OA model and determine whether LPL modulates inflammatory osteoarthritis.