activation of canonical and noncanonical NF-kB signalling, and increased the expression of inflammatory cytokines and adhesion molecules, which could be blocked by targeting NIK.

**Conclusions** These findings suggest that in addition to regulating noncanonical signalling, NIK can serve as an amplifier of canonical NF-kB signalling and associated inflammatory responses in EC, which may play a role in development and maintenance of chronic inflammation. Consequently, NIK may be an attractive therapeutic target.

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**LUMICAN: A NOVEL GYCOPROTEIN MEDIATING INFLAMMATION IN OSTEOARTHRITIS**

**Introduction** LUMICAN (LUM) is major extracellular matrix protein which is present in glycoprotein format in adult articular cartilage. Recently, LUM was shown to augment pathogen-associated molecular patterns (PAMPs) activation of the TLR4 signalling cascade. Given that TLR4 is highly associated with inflammation in rheumatic disease, we aim to decipher the LUM role in Osteoarthritis and TLR4 associated inflammation.

**Objectives** To measure LUM in synovial fluid from patients with arthritic conditions and to study the role of LUM on TLR4 activation in osteoarthritis.

**Methods** Synovial fluid (SF) was obtained from knee meniscus tear (n=11), first carpometacarpal (CMC-1) OA (n=11) and knee OA (n=40) patients. LUM glycoprotein levels were analysed by enzyme-linked immunosorbent assay (ELISA). Human monocytes were isolated from healthy individuals and differentiated into M1-like and M2-like macrophages by lipopolysaccharide (LPS) and interleukin-4, respectively. LUM (1 ug/ml) was added either together with macrophage polarization inducers or alone. Primary chondrocytes and OA cartilage explants were stimulated for 24 hour with LUM (1 mg/ml), LPS (10 ng/ml), or a combination of both. Conditioned media was analysed for selected secreted molecules by xMAP technology. Macrophages surface expression markers CD197 and CD206 were analysed by Fluorescence-Activated Cell Sorting (FACS). Cartilage explants were immunofluorescently double stained for collagen type II and X.

**Results** LUM glycoprotein levels were significantly upregulated in knee OA SF vs. controls. In normal articular chondrocytes, LUM combined with LPS caused an upregulated secretion of catabolic markers characteristic of OA such as IL-6, MMP-1, and MMP-13 in comparison to LPS stimulation. LUM alone had no observable effects. A similar response occurred in cartilage explant cultures, with increased MMP-1 secretion levels and marked cartilage degradation with the LPS/LUM combination. Interestingly, LUM stimulation with the polarisation inducer, LPS for M1, and IL-4 for M2 macrophages, upregulated M1 macrophage secretion of TNF-alpha and downregulated IL-10 secretion in M2 macrophages relative to control and LUM alone. FACS results followed the same trend, with increased CD197 expression in LUM/LPS combination vs. LUM alone or control, and downregulation of CD206 expression when LUM/IL-4 combination vs. LUM alone or control.

**Conclusions** Our results suggest an inhibitory role of Smoc2 on mineralization. The inhibitory effects on mineralization are at least partially regulated through interaction with calcium. Moreover, Smoc2 is a regulator of chondrogenic differentiation and cartilage homeostasis by regulating canonical and non-canonical Wnt signalling.

**Disclosure of interest** None declared