Part of a scientific paper discussing the effects of a novel MK2 inhibitor in a model of enthesitis.

**Background:**
Enthesitis or inflammation of tendon/ligament anchorage points is the cardinal lesion in spondyloarthritis (SpA). Through the use of cytokine targeting biologicals and also murine models, several key mediators have been shown to have a role in enthesitis, such as IL-23/17 axis and TNF. We have previously shown that the human enthesis contains myeloid cells capable of IL-23 and TNF production and range of T-cells capable of IL-17A secretion. Attempted inhibition of the p38 MAPK for inflammatory disease in the past has yielded mixed results. The MAPK-associated protein kinase 2 (MK2) is situated downstream of the p38 MAPK, relaying the phosphorylation signal to the nucleus, and is thus a promising target.

**Objectives:**
To determine if a novel MK2 inhibitor (MK2i) could suppress innate and adaptive immune responses in an in vitro human enthesis model.

**Methods:**
Normal spinal process enthesis was obtained from patients undergoing spinal decompression or surgery for scoliosis correction. Following enzymatic digestion, entheseal cells (n=5) were harvested and stimulated either with LPS/IFNγ (Enthesal myeloid cell activator) or anti-CD3 (Enthesal T-cell activator) with and without MK2i (1, 0.1, and 0.01μM) for 24 hours. Supernatant was harvested and protein detected using multiplexing for panels relating to inflammation (IL-1β, IL-6, IL-8, IL-10, IL-17p, IL-17A, IL-17F, IL-23, IL-22, IFNγ, TNF, and IL-18a).

**Results:**
LPS/IFNγ stimulation of entheseal cells, 1μM MK2i significantly attenuated secretion of TNF, IFNγ, IL-6, IL-10, IL-8 and CCL2.

**Conclusion:**
The novel MK2 inhibitor (MK2i) significantly attenuated secretion of pro-inflammatory cytokines in entheseal cells, suggesting its potential therapeutic efficacy in the treatment of enthesitis-related diseases.

**References:**