**Changes in ion channel expression in synovial fibroblasts in an in vitro model of osteoarthritis**

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**Purpose;**

Synovitis is thought to play an important role in the progression of inflammatory osteoarthritis (OA). We hypothesise that paracrine signalling between synovial fibroblasts (FLS) and primary nociceptor neurones may contribute to the development of pain in inflammatory OA. This signalling involves cytokines and may lead to differential expression of ion channels in FLS and/or neurones. FLS ion channel changes in response to cytokine exposure may therefore constitute biomarkers of inflammatory OA and yield pharmacological targets for novel, joint specific, analgesia.

**Methods;**

Synovial fibroblasts were isolated from rat knee joints as described previously by von Banchet et al., 2007. These were treated with vehicle or IL-1β and TNF-α (both 10ng/ml) for 72hr before analysis. 84 ion channel genes were analysed by qPCR in parallel to whole-cell patch-clamp experiments that measured predominant whole-cell currents.

**Results;**

The largest FLS induced change in ion channel mRNA detected (*smallest* p-val) was that for Kcna6 (decreased, p<0.0005, *n=4 treated, 4 control*). In parallel to this, patch-clamp experiments showed there was a decrease in outwardly rectifying whole-cell conductance.

**Conclusion;**

Kcna6 encodes a voltage-gated potassium channel, Kv1.6. To our knowledge this has not been reported previously, in FLS, but it is a widely distributed ion channel and has been previously reported in cardiac fibroblasts. The role of Kv1.6 is well established, where it serves to modulate excitability. Interestingly, motor neurone Kv1.6 are decreased following exposure to sporadic amyotrophic lateral sclerotic cerebrospinal fluid. In other tissues its role is less well established, but our data are entirely consistent with the hypothesis that IL-1β / TNF-α exposure can activate FLS cells by means of decreasing potassium conductance. Our approach to studying ion channels in OA provides further support for the immunometabolic aspects of OA.

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