Introduction: Hyaluronan (HA), the high molecular weight polysaccharide consisting of repeating glucuronic and N-acetylgalactosamine units, is synthesized during joint cavitation (1). HA synthesis persists in the adult joint helping to sustain friction free articulation. Immobilization studies have shown that the removal of mechanical stimuli interferes with joint cavitation (2&3) and so mechanically induced factors are likely to play a major regulatory role in joint morphogenesis. This role of mechanical stimuli in maintaining hyaluronan synthesis in the adult joint is likely to be essential.

Previous work has shown that it is the synovial fibroblasts which synthesize HA within the synovium as high activity of the enzyme uridine diphosphoglucose dehydrogenase (UDPGD), required for precursor saccharides, has already been reported (4). Once synthesized, HA is secreted into the synovial cavity where it combines with the synovial fluid to help lubricate the joint. During osteoarthritis, along with a change in cellular architecture of the synovium, there is a decrease in the UDPGD activity of the synovial fibroblasts leading to a subsequent decrease in HA synthesis (5). This adds to the loss of joint mobility and knee pain associated with osteoarthritis.

Although we understand how HA is synthesized, the stimuli controlling this synthesis remain elusive. We hypothesise that restoration of normal synovial HA concentrations is dependent upon mechanical stimuli and that OA synovial cells can respond to mechanical stimuli. Here we show that after a brief period of mechanical strain, cultured human OA synovial cells can increase and sustain media HA concentrations.

Materials and Methods: Synovium was obtained from patients (both male and female, age range 57-77 years) undergoing total knee joint replacement surgery with the relevant ethical approval and patient consent.

Synovial cells were isolated from diced tissue by digestion in 0.2mg ml^-1 type I collagenase in DMEM/F12 +5% foetal calf serum (FCS). Following digestion, cells were isolated then suspended in the synovial fluid to help lubricate the joint. During osteoarthritis, along with a change in cellular architecture of the synovium, there is a decrease in the UDPGD activity of the synovial fibroblasts leading to a subsequent decrease in HA synthesis (5). This adds to the loss of joint mobility and knee pain associated with osteoarthritis.

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Results: First, results from strained, static control and flow control cells were analysed using a one-way ANOVA and Scheffe post hoc test. This showed there was no difference in hyaluronan concentrations between each of the individual strain plates, no difference between each of the static controls and no difference between the flow control plates. Comparisons of static control cells and flow control cells showed no significant differences in their media hyaluronan concentrations.

From the several cell lines subjected to the 3 different strains it can be seen that the three strains tested it was the lowest strain of 4000µε that gave the greatest significant increase between strained and static control cells. The highest strain (10000µε) produced a significant decrease in hyaluronan media concentration at 24 hours.

Selected cell lines were then followed over a time course of 24 hours. The HA media from static cells could be seen to increase with time. However when cells were subjected to the 0.4% strain significantly higher hyaluronan media concentrations could be seen. For the 0.4% strain, this increase in HA media levels were significantly different between strained and static cells at each of the time points. All data were analysed using a one-way ANOVA followed by Tukey post hoc test.

Discussion: These results demonstrate that although the synovial cells have been cultured from the synovium of osteoarthritic patients which show reduced levels of hyaluronan synthesis they are able to alter their hyaluronan synthesis when subjected to mechanical stimuli. The upregulation of HA levels was seen predominately in the cells subjected to the lowest strain while a decrease in HA levels was seen at a higher strain. This result suggests that the loss of mobility in osteoarthritic joints could be a contributory factor in the decrease of synovial fluid hyaluronan yet the synovial cells from OA synovium can be seen to increase hyaluronan synthesis on the reintroduction of mechanical stimuli. The determination of an appropriate strain and frequency required to restore hyaluronan levels to those of the normal synovial joint will be important in generating exercise based therapies for osteoarthritis.


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