Hyaluronan (HA) is widely used in the treatment of osteoarthritis (OA) while its mechanisms of action is poorly understood. Since chondrocyte apoptosis seems involved in the pathogenesis of OA we investigated the in vitro effect of a 500-730 kd fraction of therapeutic hyaluronan (HA) on anti-Fas induced apoptosis of chondrocytes from OA patients and its mechanism of action analyzing the role of the two HA receptors, CD44 and CD54 (ICAM-1).

Methods: Chondrocytes isolated from human OA knee were cultured and the effect of HA was evaluated both on spontaneous and anti-Fas induced apoptosis. Apoptosis was analyzed by JAM test (for quantitative analysis of fragmented DNA), cell death detection immunohasay (for quantitative analysis of oligonucleosome), TUNEL assay and electron microscopy. Blocking experiments with anti-CD44 and anti-CD54 alone or in combination were performed to investigate the HA action mechanism.

Results: Both quantitative tests demonstrated that anti-Fas significantly induced apoptosis of isolated OA chondrocytes. HA at 1000 mg/ml significantly reduced anti-Fas induced apoptosis of chondrocytes, but did not affect spontaneous chondrocyte apoptosis. These data were also confirmed by TUNEL staining and by electron microscopy. Anti-apoptotic effects of HA on anti-FAS induced chondrocyte apoptosis were significantly decreased by both anti-CD44 (67 ± 14% of inhibition) and CD54 (39 ± 30% of inhibition). The mixture of the two antibodies had an additive effect, since the rate of inhibition increased to 87 ± 13%.

Conclusions: The anti-apoptotic effect of HA mediated by its specific receptors can account for its therapeutic action in OA.