

P023 A novel role for COX-2 regulating HA synthesis and binding in developing joints

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Cells in mechanically challenging developing joint environments elaborate hyaluronan (HA)-rich matrices. We have shown that constitutive ERK activation promotes HA synthesis/binding in articular surface (AS) cells; such constitutive ERK activation is typically restricted to joint pathology. Herein, we examine the hypothesis that COX-2 (inducible cyclo-oxygenase), another factor expressed pathologically, also regulates local HA turnover and also contributes to normal joint development.

Immunocytochemistry disclosed strong COX-2 expression at developing articular surfaces, which co-distributed with phospho-ERK. To address whether PGE₂ (COX-2 product) modifies AS cell behaviour, we examined HA release/retention *in vitro* and found that PGE₂ significantly increased medium HA accumulation and cell HA-retention. Cell: matrix area ratios, a measure of pericellular matrix elaboration, were markedly enhanced by PGE₂ but reduced by NS-398 (COX-2 inhibitor). Using FITC-HA as a probe, we found that PGE₂ increased total HA-binding sites and promoted full occupancy. This suggests close association between COX-2 and ERK in control of AS cell behaviour. Furthermore, stable transfection to promote constitutive ERK activation in human chondrocytes produced increases in COX-2 expression. Our findings suggest a role for constitutive expression of COX-2 and PGE₂ in regulating HA synthesis/binding at the developing joint and lead us to speculate that COX-2 mediates the mechano-dependent process of normal joint development.