studies such as these may suggest different therapeutic targets for treatment of later-stage OA.

236

AML1 IS HIGHLY EXPRESSED IN HUMAN OSTEOARTHRITIC CARTILAGE AND RESPONDS TO MECHANICAL LOADING

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Purpose: AML1 is known to be essential for the normal development of hematopoietic stem cells. Pathologically, AML1 is one of the most frequent targets of chromosome translocations associated with leukemia. Although its role in chondroprogenitor cells was established early on, few papers have since emerged more clearly defining its role in articular cartilage and more importantly, osteoarthritis (OA). In this study, we have undertaken to examine the functional expression patterns of AML1 in normal vs. OA articular cartilage and its role in cartilage mechanotransduction, a feature shared by other genes involved in cartilage homeostasis and OA.

Methods: Medial vs. lateral human OA cartilage samples were analyzed and compared through immunoblot analysis for the relative expression levels of AML1 on a knee-by-knee basis. Bovine articular cartilage discs were harvested from the knees of newborn male calves and compressed ex vivo in compression chambers, to test whether AML1 is a mechanically-regulated gene. Samples were then subjected to AML1 immunoblot analysis. Normal knee articular cartilage from animal sources (bovine and mouse) as well as human knee OA samples (comparing medial vs. lateral distal femoral compartments) were analyzed IHC localization of AML1.

Results: Fig. 1 shows a significant increase in AML1 protein in the medial compartment of human OA varus knees. Similar results were obtained in n=4 human OA knees. These initial results suggested that AML1 is a potentially mechanically regulable gene product. Therefore, we tested the responsiveness of AML1 expression under increasing strains in bovine articular cartilage (Fig. 2). Results indicated that AML1 is extremely sensitive to load, demonstrating a 5-fold increase in AML1 protein expression at 25 and 50% strain values. IHC data (Fig. 3) showed that in normal bovine and mouse cartilage, the highest expression of AML1 is localized in the most superficial zone of articular cartilage. It is interesting to note that it is the superficial zone which experiences the highest degree of tissue strain under mechanical load. Human lateral (varus) OA cartilage showed patchy expression of AML1, but was limited to the superficial zone. Medial OA cartilage showed that AML1 expression was limited to osteoarthritic ‘clones’ or aggregates of chondrocytes in areas immediately adjacent to focal areas of superficial fibrillation.

Conclusions: Here we show that AML1 protein is normally expressed in a narrow margin of cells at the weight-bearing surfaces of articular cartilage in both human and animal samples. Recent studies have shown that stem cell markers (CD155+/CD166+), indicative of the presence of mesenchymal progenitor cells, also co-exist in the same narrow zone. Given these findings and AML1’s known role in cell proliferation, it is interesting to speculate that AML1 may be marking a progenitor cell population localized in surfaces of articular cartilage. In osteoarthritic tissue, AML1 is overexpressed, particularly in the ‘non-spared’ compartments of malaligned knees. Within this compartmentally-restricted expression pattern another sub-pattern of enhanced expression in chondrocyte clones is seen which could be interpreted as an indication that AML1 plays a role in phenotypic plasticity of chondrocytes in sub-populations of cells in both normal articular and osteoarthritic cartilage.

237

POSITIVE REGULATION OF HUMAN OSTEOARTHRITIC CHONDROCYTES UPON ACTIVATION OF THE EphB4 RECEPTOR BY ITS SPECIFIC LIGAND EPHRIN B2

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Purpose: Osteoarthritis (OA) is characterized by cartilage degradation resulting from an increase in catabolic factors and decreased anabolic properties. It has recently been demonstrated that ephrin B2 and its specific receptor EphB4 are involved in the control of bone homeostasis. Our group further revealed that this ephrin system inhibits the pro-resorptive activity of human OA chondrocyte subchondral bone.

To our knowledge, there has been no study on the implication of ephrins in OA cartilage tissue. Thus, we investigated the possible...