

APOPTOSIS IN OSTEOARTHROSIC HUMAN CARTILAGE: POTENCIAL INVOLVEMENT IN MATRIX DEGRADATION. Magdalena Miranda-Sánchez*, Juan B. Kouri**. * Biologist, Assistant, **DSc. Professor and Chairman of the Department of Experimental Pathology; *,**CINVESTAV-IPN, Mexico City . E-mail: bkouri@mail.cinvestav.mx

Summary:

Cell death and matrix degradation are directly responsible for cartilage breakdown, a major cause of osteoarthritic (OA) joint dysfunction. We investigated whether apoptotic cell death in human OA chondrocytes could be involved in matrix degradation. Methods. Knee samples from twelve OA patients, and six fresh cadavers were studied. Chondrocytes were assessed from cartilages damaged regions where proteoglycans (PG) depletion was detected using safranin O staining. In these regions chondrocytes frequently were clustered. Cells were analyzed to find out the prevailing morphology associated with MMP-3 (proteoglycanase involved in matrix degradation) synthesis and *in situ*, cell death detection (TUNEL). Colocalizations of live-dead/MMP-3 and MMP-3/TUNEL procedures were assessed. For immunofluorescence technique, confocal microscope CAS/MRC program, and semi-quantitative analysis were used for statistical assessments.

Results: Upper chondrocytes located in proteoglycan (PG)-depleted OA cartilage regions, displayed a statistical significant increase of MMP-3 immunolabeling (mean = 3.864 ± 0.3980) compared to normal (mean = 0.472 ± 0.2406). Live dead/MMP-3 displayed a similar labeling pattern as MMP-3/TUNEL, which showed pattern of fully labeled (living cells), faintly and scarce labeling (dying chondrocytes) and absent labeling within dead chondrocytes.

Our findings indicated that alive chondrocytes were associated with MMP-3 synthesis, which diminished in dying cells and were absent in dead chondrocytes. These results suggested that apoptosis in OA chondrocytes might be the final stage of the life span of a cell involve in the degradation its own tissue.

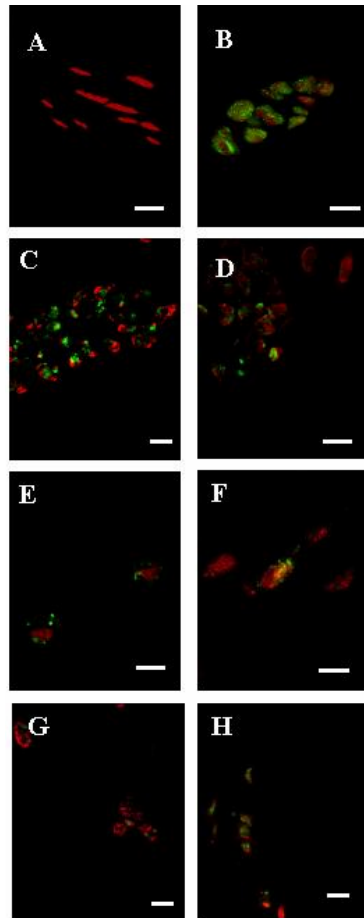


Fig. 1 A-B Detection of MMP-3. Immunolabeling patterns from normal cartilage (A) and OA clustered chondrocytes (B) . Nuclei were stained in red with propidium iodide

C-D: Colocalization of TUNEL-FITC MMP-3(nuclei)/ TRITC (cytoplasm) labelings from clustered OA chondrocytes.

E-F: MP-3 -FITC cytoplasm labeling from non-clustered OA chondrocytes, nuclei were stained in red with propidium iodide.

G-H: TUNEL labeling from non clustered OA chondrocytes.

Bars = 25 μ m