

A NEW ROLE FOR CHONDROCYTES AS NON-PROFESSIONAL PHAGOCYTES. AN *IN VITRO* STUDY. Elena Cristina González Castillo and Juan B. Kouri. Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional (CINVESTAV-IPN), P. O. Box 14-740, C. P. 07360. Mexico City, Mexico. E-mail: mizu40@yahoo.com

There are several aspects regarding the cell biology of the chondrocytes that remain poorly understood; such is the case of phagocytosis, one of the most important processes in the maintenance of an organism's homeostasis that is carried out by macrophages and sometimes by neighboring cells.

Because the articular cartilage is an avascular and alymphatic tissue, there is no evidence of the presence of macrophages or other inflammatory cells. Therefore, it is believed that the chondrocytes could be implicated in clearing out matrix and cellular remains coming from cell death by necrosis, apoptosis, and/or chondroptosis, which occurs during several processes such as: cartilage development, cartilage turnover, and cartilage degradation. The concept of chondroptosis indicates that cell disintegration depends on phagocytic vacuoles or the elimination of cell remnants to the extracellular space as an alternative mechanism and seems to be the major mechanism of cell death within the cartilage, although classical apoptosis might be present in a limited proportion. Previous reports have observed an osteoarthritic human chondrocyte, within the cartilage, probably engulfing another chondrocyte with apparent apoptotic changes and small particles, as well as an osteoarthritis-induced rat chondrocyte with a vacuole containing part of a collagen fiber. In our *in vitro* results, we observed that chondrocytes phagocytosed latex particles as evaluated by confocal microscopy and flow cytometry (data not show). In addition, we observed that chondrocytes phagocytosed articular cartilage detritus and necrotic and apoptotic VP-16 induced-chondrocytes, as observed by bright field microscopy ((Fig. 1)) and transmission electron microscopy (Fig. 2). This data make us speculate that, within this pathological scenario, where a remarkable degradation of the extracellular matrix takes place chondrocytes could be rendered as sort of "free floating," which would facilitate the cell movement necessary for phagocytosis by neighbor chondrocytes.

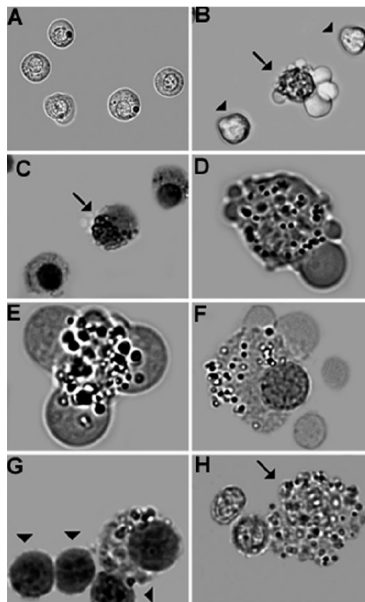


Fig. 1. Phase contrast. Control: **A**: Typical morphology of a normal chondrocytes. **B**: Two normal chondrocytes (arrowheads) and another one displaying spontaneous blebbing (arrow). **C**: Dead chondrocyte (arrow) with small spontaneous blebbing. X40. Chondrocytes treated with VP-16, 1mM: **D**, **E**: Chondrocyte blebbing. **F**: Cell fragmentation. **G**: Naked nuclei are observed (arrowheads). **H**: Edematous infiltration in a necrotic chondrocyte (arrow). X63.

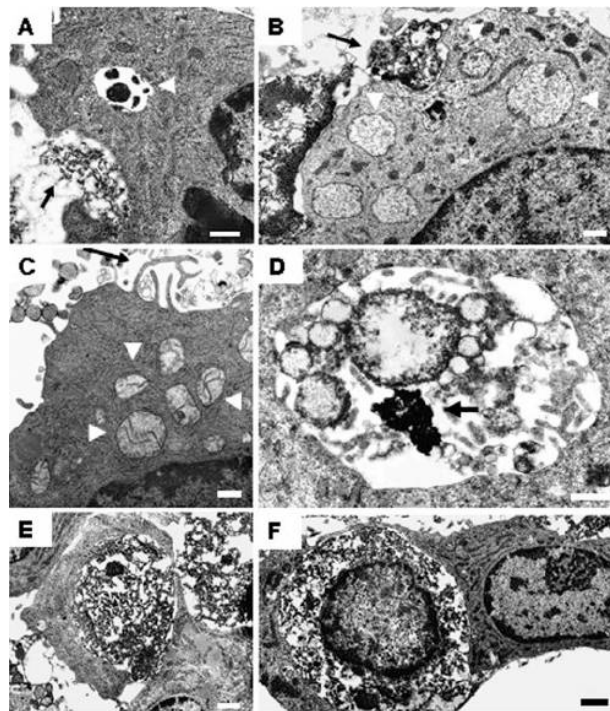


Fig. 2. Electron microscopy. **A**: Chondrocyte engulfing cellular detritus by plasma membrane invagination (arrow); phagocytic vacuoles within apoptotic remains were observed (arrowhead). **B**: Chondrocyte engulfing cells detritus by the invagination of the plasma membrane. **C**: Phagocytosis of cell detritus by the emission of filopodia; edematized mitochondria were observed (arrowheads). **D**: A phagosome with apoptotic remains and a chromatin fragment (arrow) within a phagocytic vacuole. **E**, **F**: Phagocytosis of cell detritus and a whole necrotic chondrocyte. Scale bars = 500 nm (A–D) and 1 μ m (E, F).