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# The Biology of Articular Cartilage: An Overview?

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Articular cartilage is the tissue that allows for a smooth gliding of articulating surfaces of a joint in order to withstand high loads during a lifetime. The structural integrity of the articular cartilage is essential to perform physical activity throughout life. Due to its structural and functional complexity, articular cartilage is extremely difficult to reproduce in the laboratory, and models for experimental testing are generally gained from clinical or animal samples.

Hyaline articular cartilage is formed by the chondrocytes (~5% of the cartilage wet weight and <10% of the cartilage tissue volume) surrounded by an intricate network of extracellular matrix (ECM). The cartilage matrix is rich in proteoglycans (~10%) (mostly aggrecan, but also decorin, biglycan, and fibromodulin) and collagen fibrils (~15%) (Mostly type-II collagen, but also type-IX, -XI, -VI, and -XIV collagens) and a number of additional molecules for stabilization (link protein, cartilage oligomeric matrix protein - COMP, fibronectin, tenascin) [1-3]. Interestingly, some differences in ECM components have been reported between joints like knee and ankle [4]. The molecules that interact with the receptors at the surface of the chondrocytes form the pericellular matrix. Further from the cells but in close distance lies the territorial matrix while at largest distance is the interterritorial matrix [5]. Normal hyaline articular cartilage contains about 70-80% water mainly bound to proteoglycans, but a proportion of which can move freely for joint lubrication and for nutrition of the chondrocytes. Remarkably, adult hyaline articular cartilage is a vascular and a neural tissue that does not possess a lymphatic drainage [6]. The chondrocytes thus derive oxygen and nutrition from the synovial fluid by diffusion. The cartilage (~2-5 mm thick) (Figure 1) is structurally divided in three zones, each with a unique cell morphology and type-II collagen fibers that depend on the expression of specific molecules (parathyroid hormone-related protein - PTHrP, Indian hedgehog - Ihh, Runx2) [7]. The superficial/tangential zone (~10-20%) contains flattened chondrocytes (at the highest density and expressing lubricin essential for lubrication) and fibers parallel to the surface. The intermediate/transitional zone (~40-60%) is formed of round-shaped cells and oblique, less organized fibers. The deep/basal zone (~30%) (Including the calcified zone) also contains round-shaped cells (at the lowest density) and fibers, both in vertical columns perpendicular to the surface. Remarkably, the chondrocytes exist at low oxygen tension, especially those in the deep/basal zone, but are capable of adaption in APRT by up regulating the hypoxia-inducible factor-1α (HIF-1α) that regulates cartilage-specific genes (SOX9, vascular endothelial growth factor - VEGF).

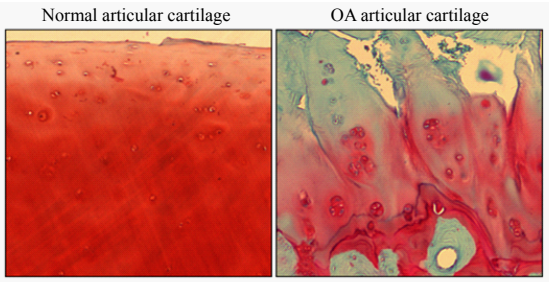


**Figure 1:** Histological sections of normal ans osteoarthritic (OA) cartilage stained with safranin O/fast green to detect matrix proteoglycans. Chondrocytes are also depicted.

In normal adult cartilage, the chondrocytes do not show proliferative activity and the network of type-II collagen fibers is extremely stable, with a half-life of several years, and also the turnover of aggrecan is not excessive (months to years) [3], making cartilage a very consistent tissue. Nevertheless, the adult chondrocytes are capable of adjusting the metabolic (structural and functional) cartilage homeostasis by regulating the balance of ECM components (synthesis *versus* degradation) depending on the (complex) presence and influence of various factors including the composition of the matrix itself, mechanical loads, local hormones, growth factors (transforming growth factor beta - TGF-β, insulin-like growth factor I - IGF-I, the bone morphogenetic proteins 2 and 7 - BMP-2, -7), and cytokines (interleukin 1 - IL-1, tumor necrosis factor alpha - TNF-α), disease (osteoarthritis) (Figure 1) or injury, and aging [3,5,7-16]. The chondrocytes respond for instance to mechanical forces by interactions between their cell surface integrins and the components of the matrix or to local factors (hormones, growth factors, cytokines) by interactions with specific cell surface receptors. As a consequence, these cells can either secrete matrix molecules or the enzymes that degrade them (matrix metalloproteinase's - MMPs, aggrecanases) by undergoing phenotypic changes [3,7,17,18]. Increased chondrocyte proliferation activity is also often observed in altered physiological conditions [3], but cell death by apoptosis has also been reported when the cartilage undergoes pathological processes like in the case of osteoarthritis [3,19,20]. The molecular mechanisms of cartilage remodeling are under active investigation but still only partly understood, showing the need for continuous research to improve our understanding of these processes in this highly specialized tissue.

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