Basic Science of Articular Cartilage

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KEYWORDS

• Articular cartilage • Chondrocytes • ECM • Chondrogenesis • Cartilage injuries

KEY POINTS

- Articular cartilage has highly organized structure composed of 4 zones. The chondrocyte phenotype, cell shape, and the extracellular matrix (ECM) structure vary among the 4 zones.
- The biomechanical behavior of articular cartilage is viewed as a biphasic medium.
- Chondrocytes are responsible for maintenance of cartilage homeostasis through ECM production.
- The cytokine–matrix metalloproteinase relationship seems to contribute to the intrinsic process of cartilage degeneration.
- Several strategies have been studied to identify the optimal method to maintain the chondrocyte differentiation status and to prevent mesenchymal stem cell hypertrophy and maintain their ECM environment.

BASIC MACROSCOPIC AND MICROSCOPIC STRUCTURE OF HYALINE CARTILAGE

The hyaline cartilage is the most abundant type of cartilage in the body. It is responsible for the bone formation in the embryo (endochondral ossification) and in adults, it can be found in costal cartilages, respiratory system (trachea), and covering the bone articular surface (articular cartilage). A gross inspection of healthy articular cartilage from the joints of a young adult mammal shows the surface to be smooth, shiny, and dense white (**Fig. 1**A). The color of immature articular cartilage is somewhat bluish, and in aged animals, the cartilage becomes yellowish. Articular cartilage has a highly organized structure composed of 4 zones: the superficial (tangential) zone, middle (transitional) zone, deep (radial) zone, and calcified zone (see **Fig. 1**B). The chondrocyte phenotype, cell shape, and the extracellular matrix (ECM) structure

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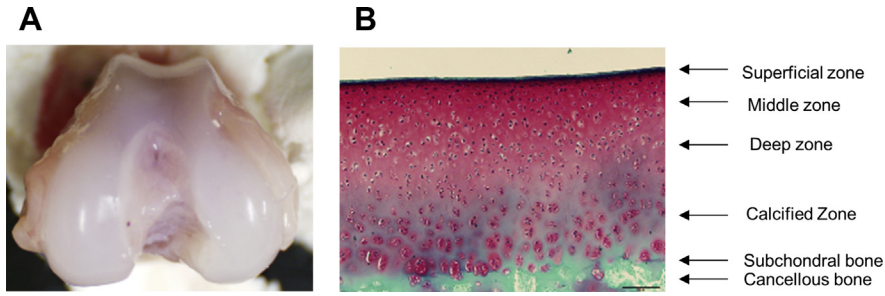

Fig. 1. Normal cartilage of the distal femur in a young adult pig. (*A*) Gross specimen. The surface of the cartilage is dense white, glistening, and smooth. (*B*) Histology stained with safranin-O (original magnification, ×40). Matrix and chondrocytes are well organized in each zone. The superficial zone has no safranin-O staining. In the middle zone, where safranin-O staining appears, the cells are rounded or ovoid and seem to have random distribution; in contrast, in the deep zone, the cells are arranged in short columns.

vary among the different zones.[1,2] The dominant load carrying structural components of the ECM are collagen (75% of the dry weight) and proteoglycan (20%–30% of the dry weight), the concentrations of which vary with depth from the articular surface.[3,4] Collagen content is highest in the superficial zone, decreasing by 20% in the middle and deep zones. Proteoglycan content is lowest at the superficial zone, increasing by as much as 50% into the middle and deep zones.[3,4]

The superficial zone typically stains for fast green only, and does not for safranin-O. Note the lamina splendens, a layer of fine collagen fibers at the very surface of this zone (**Fig. 2**A), in which the cells are elongated and tangentially arranged (**Fig. 2**B). In the middle zone, where safranin-O staining first appears, the cells are rounded or ovoid and seem to have a random distribution, whereas in the deep zone the cells are arranged in short columns[5] (**Fig. 2**C).

The tidemark is a thin basophilic line that usually can be seen in a slide stained with hematoxylin and eosin, represents the boundary between the mineralized and unmineralized regions, and separates the deep zone from the calcified zone.

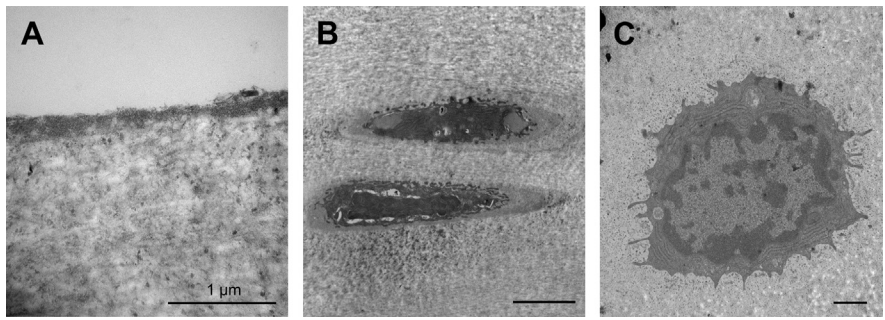

Fig. 2. Transmission electron microscopy images of the distal femur in a normal rat. (*A*) Lamina splendens, the fine fibers and filaments in the surface of articular cartilage. (*B*) Elongated cells in the superficial zone. (*C*) A round cell in the deep zone. (*Reprinted from* Nakagawa Y, Muneta T, Otabe K, et al. Cartilage derived from bone marrow mesenchymal stem cells expresses lubricin in vitro and in vivo. PLoS One 2016;11(2):e0148777; with permission.)