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Short Commentary Open Access

New Perspectives in Cartilage Medicine: Latest Biology Insights can re-direct Future Cartilage Medical Strategies?

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Commentary

Adult cartilage, a connective tissue with origin in mesenchymal cells, exists in all the entire articular surface of bones. Composed by a small number of a unique cellular type – chondrocytes – this tissue appears to be of high simplicity. This apparent simplicity masks a convoluted balance between anabolic and catabolic processes which are needed to maintain metabolically active the tissue and its extracellular matrix (ECM).

The first observation reported in literature goes back to the eighteen century, when the structure of articular cartilage and its diseases were published by Proceedings of the Royal Society [1]. Since then and until recently, it was mainstream to consider that this unvascularized, aneural, and alymphatic tissue presented a poor reparative potential due to the lack of stem/progenitor cells within its ECM and the nonexistence of a vasculature which, should supply circulating stem cells to the site of damage [2].

Chondrocytes are the only responsible cells for the growth and maintenance of the extensive ECM composed primarily by water, aggrecans and collagen type II. Full embedded in single lacunae, articular chondrocytes do not have the capacity to migrate to the lesion site, proliferate and start a repair process, which results in a very low inherent capacity of self-regeneration of this adult tissue [3]. To overcome chondrocytes intrinsic properties in the attempt to repair articular cartilage, Peterson et al. [4] proposed, in 1984, the first cell based therapy in cartilage orthopedic field. Such modus operandi was developed to overcome the limitations of the already existing approaches in the early 90's. Brittgerg et al. published the initial results regarding the follow up after 39 months of 23 patients in 1994 [5].

Since then the notion of cartilage engineering by using stem cells, biomaterials and combination of these has evolved [6-8].

The paradigm shift came with the seminal research performed by the group of Archer. The fundamental observation of the presence of chondrogenic progenitor cells (CPCs) within the superficial articular cartilage layer was by many considered the Willy Wonka ticket to win the battle of cartilage repair strategies [9]. Relaying on this approach, cartilage could be repaired from the roof (superficial layer) and no longer only from the foundations (bone/cartilage calcified layer). With a deeper characterization of chondrocytes the first therapeutic approach based on the presence of a resident stem cell population within articular cartilage was documented for cell-based cartilage therapy [10]. Following this original work, other researchers have very recently shown and confirmed, using different markers methodologies, the presence of CPCs on articular cartilage, i.e. the use of human platelet lysate (PL) as a serum substitute increases the percentage of CPCs cells over 2D expansion with high expression of CD133 [11]. Contrary to resident human articular chondrocytes CPCs keep their chondrogenic memoir, even with high proliferative capacity, demonstrated by the appetence to form cartilage in vivo by the use of a nude mice model [11].

More recent, the identification of CPCs derived from adult human chondrocytes was highlighted by dynamic variations in expression of the mature chondrocyte marker, such as collagen type II and mesenchymal stromal cell (MSC) marker, CD146 [12]. Researchers have accessed cellular stemness grade and differentiation status by novel physical and biochemical cues during 2D cell culture. In the reported study, CPCs showed similar phenotype as bone marrow mesenchymal stromal cells but with a greater chondrogenic potential. More important, the same study provided evidences that CPCs were able to repair large knee cartilage defects in 15 patients, which undoubtedly make a successful translation between bench cartilage biology and cartilage medicine [12].

All together, this more recent work on CPCs increases our understanding of cartilage biology and allow us to develop more of chondrocyte-medical based therapies for near future clinical applications.

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