

Cartilage Healing and Joint Injectables

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It has been understood that that polypeptide growth factors are of key importance in articular cartilage homeostasis and repair. It has been shown that the growth factors responsible for regulating cartilage are themselves regulated by growth factors. When insulin-like growth factor I (IGF-I), fibroblast growth factor-2 (FGF-2), and/or transforming growth factor- β 1 (TGF- β 1) were delivered to adult bovine articular chondrocytes in culture, these growth factors differentially regulated their own growth as well as the differentiation of each other. Of major importance was that these interactions ranged from inhibitory to synergistic indicating that joint and cartilage repair is a delicate balance that needs to be respected. “These studies suggest that interactions among IGF-I, FGF-2, and TGF- β 1 substantially modulate their regulatory functions.” [1]

Joint chondrocytes take a big burden in our life, but unfortunately have a poor repair capacity. Once the articular cartilage substance is lost, the damage is often permanent, and as the biomechanical forces are now ‘off’, creating progressive degeneration. Orthopedic medicine has been researching ways to solve this problem for years. Currently injecting into the joint some type of ‘healing’ substance such as platelet rich plasma (PRP), stem cells or hyaluronic acid is the standard of care with hopes that lubrication or these individual cells will stimulate repair. Recently focus has turned to exosomes derived from human mesenchymal stem cells. Liu et al., discovered the contents of the exosomes and that the healing molecule was *exosomal KLF3-AS1*. [2] The theory was that healing was promoted via chondrocyte migration and proliferation stimulated by this exosomal product.

Cartilage growth in the joint, however, is more complicated than just stimulation by a single factor. The pericellular matrix (PCM), a narrow tissue region surrounding chondrocytes in articular cartilage, together with the enclosed cell(s) is of key importance in biological and biomechanical functions. [3] This matrix is kept viable and healing with polypeptides, proteoglycans and the growth factors described above. In normal aging, the size and number of proteoglycans and chondroitin sulphate content decreased, as well as the production and quality of healthy polypeptides. [4,5]

Plasma from young donors, young Fresh Frozen Plasma (yFFP®), contains all the healing peptides (human peptide GHK (glycyl-l-histidyl-l-lysine), cells, exosomes and balance of growth factors necessary to stimulate chondrocytes and repair joints. [6,7] “The decreased level of IGF-1 may play a critical role for maintaining the balance between catabolic and anabolic processes in cartilage metabolism during the development of osteoarthritis.” [8] It is not driving a force of independent factors, but the balance of the optimal young factors that minimize inflammation and rejuvenate the traumatized tissue.

[1] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2652312>

[2] <https://portlandpress.com/biochemj/article-abstract/475/22/3629/49824/Exosomal-KLF3-AS1-from-hMSCs-promoted-cartilage?redirectedFrom=fulltext>

- [3] <https://pubmed.ncbi.nlm.nih.gov/16831947>
- [4] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1184203>
- [5] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6925077>
- [6] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6073405>
- [7]. <https://www.upmc.com/media/news/120621-ambrosio-evs-muscle>
- [8] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6100760>
- [9] The effect of aging on the bone healing properties of blood plasma:
<https://pubmed.ncbi.nlm.nih.gov/34049703/>

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