Young Plasma Exosomes

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Osteoarthritis and degenerative joint diseases affect millions of people worldwide. [1] Chronic pain in these cases seriously reduces the quality of life of patients. Additionally, the socioeconomic burden of these patients is considerable. Present management is currently divided into 3 categories: nonpharmacological, pharmacological, and surgical interventions. [2] Pharmacological treatments are focused on pain control until surgical treatment must be employed for severely impaired patients with serious functional disability. Rebuilding and reversal of disease with PRP has very limited success, showing no real statistically significant improvement as reviewed in a JAMA published review study. [3] Recent work has focused on extracellular vesicles or exosomes as the new optimal healing answer. [4]

A recent 2021 review of exosomes was published:

"Exosomes are cell-secreted nanoparticles (generally with a size of 30–150 nm) bearing numerous biological molecules including nucleic acids, proteins and lipids, which are thought to play important roles in intercellular communication. As carriers, exosomes hold promise as advanced platforms for targeted drug/gene delivery, owing to their unique properties, such as innate stability, low immunogenicity and excellent tissue/cell penetration capacity. However, their practical applications can be limited due to insufficient targeting ability or low efficacy in some cases." [5]

Exosomes are carrier nanoparticles acting as intracellular messengers. [6] Once thought of as cellular waste disposal mechanisms, they now have been discovered to also be a tissue signaling molecule. This property has made them extremely important in the joint healing space as they seem to have immunomodulatory effects. [7] Exosomes contain lipids proteins and nucleic acids. The mRNA when released to the target tissue appears to have an effect upregulating gene expression. This genetic material in the exosomes is endowed with a type of regulatory capacity on the genomes of the target cells. Mesenchymal stem cell exosomes appear to suppress proinflammatory mediators and increase anti-inflammatory factors. [8] However, the upregulation of the receiving tissue, in this case the aging and damaged joint cartilage, needs to employ its own growth factors and other budling blocks to optimize repair. The stimulus of the exosome cannot do much if the tissue itself has lost its vital components to regrow.

Loeser et al wrote in Nature Reviews:

"Age-related factors that contribute to osteoarthritis development

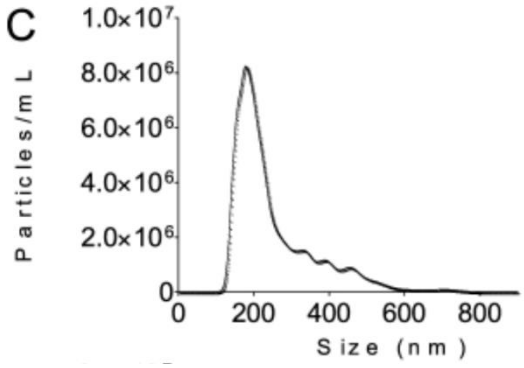
- Reduced muscle mass and increased fat mass alter joint loading and are associated with an increase in adipokine and cytokine production, resulting in low-grade systemic inflammation.
- Changes in the extracellular matrix, including accumulation of advanced glycation end-products, reduced aggrecan size, reduced hydration, and increased collagen cleavage alter the mechanical properties of cartilage and make it more susceptible to degeneration.

- Extracellular matrix disruption and reduced cell density in the meniscus and ligaments promote degeneration and can potentially alter joint mechanics.
- Impairment in the function of subchondral bone due to reduced numbers of osteocytes and altered mineral composition.
- Mitochondrial dysfunction, oxidative stress and reduced autophagy in chondrocytes alters their function, promoting catabolic processes and cell death over anabolic processes." [9]

Young fresh frozen plasma contains all the desired exosomes along with the other factors needed for the tissue to heal.

Producing a large enough amount of exosomes to be used to ensure therapeutic results in patients is very difficult. The literature describes that there is "…difficulty in producing the vesicles not only in a large quantity, but also in high purity and consistent quality. The large scale production for clinical studies and commercialization can become expensive. The typical yield of an exosome isolation can be less than 1 µg of exosomal protein from 1 ml of culture medium, whereas the therapeutic dose of exosomes is usually in the range of 10–100 µg of protein in mouse model. In humans, the effective dose could be an order of magnitude or more to compensate for the rapid clearance of exosomes from the body. [10]

Cosenza et al. studied the effects of exosomes in their paper, Mesenchymal stem cells derived exosomes and microparticles protect cartilage and bone from degradation in osteoarthritis. [11] They found protection from joint damage in mice using the exosome volume as shown below.



Young plasma contains 37 billion exosomes in a 20 ml unit and 370 billion in a 200 ml unit. These exosomes in young plasma are not only in higher volume, but they have not been damaged by any processing. Along with the superior exosome volume, young plasma:

- young plasma "trims down the pro-oxidant markers as well as improves the antioxidant markers". [12]

- responses to young or aged blood in heterochronic parabiosis. Adipose mesenchymal stromal cells, hematopoietic stem cells, hepatocytes, and endothelial cells from multiple tissues appear especially responsive. On the pathway level, young blood invokes novel gene sets in addition to reversing established ageing patterns, with the global rescue of genes encoding electron transport

chain subunits, pinpointing a prominent role of mitochondrial function in parabiosis-mediated rejuvenation. Intriguingly, we observed an almost universal loss of gene expression with age that is largely mimicked by parabiosis: aged blood reduces global gene expression, and young blood restores it. [13]

Rejuvenating factors affecting all tissues are apparent in the literature. [14] Combining these factors with a high volume of exosomes is an extremely promising, easy and affordable modality to treat all conditions of joint degeneration or damage.

[1] https://www.sciencedirect.com/science/article/pii/S0140673618322256

[2] https://www.oarsijournal.com/article/S1063-4584(20)30007-8/fulltext

[3] https://jamanetwork.com/journals/jama/article-abstract/2786501

[4] https://www.karger.com/Article/FullText/491469

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8531489/

[6] https://www.nature.com/articles/nri855

[7] https://doi.org/10.1016/j.lfs.2019.116861

[8] https://stemcellres.biomedcentral.com/articles/10.1186/s13287-019-1445-0

[9] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4938009/

[10] https://www.frontiersin.org/articles/10.3389/fphar.2019.01368/full

[11] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5701135/

[12] https://www.liebertpub.com/doi/10.1089/rej.2020.2354

[13] https://www.nature.com/articles/s41586-022-04461-2

[14] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7746393

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