

Regenerative Medicine: Attacking Osteoarthritis from Within

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Being the most common joint disease worldwide, Osteoarthritis (OA) affects the knee more than any other joint. Recent studies have noted the global prevalence of knee OA in individuals aged 15 and over with the prevalence and incidence increasing with age. The ratios of prevalence and incidence are higher in females than males [1]. OA is a disease of the whole joint that targets the cartilage, the synovial membrane, the subchondral bone, muscles, ligaments, and the menisci. Over time there is a loss of the ability to tolerate compressive loading due to the wearing of the cartilage, thinning of the synovial fluid, hypertrophy of adjacent bone, and thickening of the joint capsule. This leads finally to biomechanical joint failure [2].

OA is a progressively degrading condition over a lifetime that requires long-term treatment. As a result of this, a person's tolerance becomes a crucial consideration with regards to the treatment options. Treatments focus on pain relief, along with improvement of joint function. So, the goal of treatments is to help to slow down the costly loss of function. Initial and conservative recommendations include weight loss, physical and or occupational therapy, exercise, patient education, simple analgesics, and non-steroidal anti-inflammatory drugs (NSAIDs) [3,4]. Most recently, a new form of treatment for OA has been emerging: Regenerative Medicine.

Regenerative Medicine consists of many substances that restore tissue integrity and at the same time, reducing inflammation. The focus will be on hyaluronic acid (HA), adipose-derived stem cells (ASCs), platelet rich plasma (PRP) and extracellular vesicles (EVs) with a brief description of the physiological reactions that can lead to healing of the tissues affected by OA. These substances are introduced via intra-articular injection (IA), thus healing in paracrine manner.

As a glycosaminoglycan with viscoelastic properties, hyaluronic acid (HA) is the primary component of synovial fluid. During slow joint movements, the synovial fluid provides lubrication and during rapid joint movements it reduces compressive loading forces. Additionally, HA is a primary ingredient of the cartilage's extracellular matrix, creating elasticity and decreasing shear and compression forces [7]. The hyaluronan level in the synovial fluid of an osteoarthritic joint is lower than that of a healthy joint. As a result, there is a loss of shock absorption and lubricating abilities. Thus, the cartilage's superficial layer deteriorates [5,6]. Restoring the integrity of synovial fluid is the rationale for viscosupplementation with HA [6,7].

Adipose-derived stem cells (ASCs) can be readily harvested from the subcutaneous region of the abdomen. A stem cell has the capacity to renew and differentiate into various cells needed in the affected region. As a therapeutic intervention for OA, ASCs are injected into an affected joint or tissue, releasing multiple substances that stimulate recovery. The ASCs stimulate the recruitment of local stem cells to the affected area, promoting their differentiation into the needed cells. The experimental evidence from *in vitro* and *in vivo* studies demonstrates the high level of specificity of ASCs from adipose tissue harvested from humans. These include the adipocyte, chondrocyte, hematopoietic supporting, neuronal-like, osteoblast and skeletal myocyte pathways [8].

Platelet-rich plasma (PRP) is plasma with a higher than average platelet concentration in peripheral blood [9]. There are more than 800 proteins and molecules, some of which are cytokines, growth factors (GFs) and numerous soluble proteins [10]. In addition to their

role in coagulation and hemostasis, they also trigger an immune response, angiogenesis and tissue regeneration, among other healing processes [11-13].

Extracellular vesicles (EVs) are among several classes of vesicles, such as exosomes [14]. These vesicles contents are internalized by other cells as a form of intercellular communication, making these vesicles potential therapeutic agents or delivery vehicles of therapeutic agents [15]. The intercellular communication is through protein-protein interactions and the exchange of proteins and genetic materials including tissue repair [14].

The reality of remarkable healing for OA ravaged joints is found in these substances. In addition to healing intra-articular tissues, associated soft tissues, such as extra-articular ligaments, tendons, bursae, skeletal muscle, and retinacula, have exhibited dramatic healing. This author has witnessed firsthand this dramatic healing of damaged joints and the surrounding soft tissues with the accompanying return of normal biomechanical functioning of the targeted joints and tissues.

Future research in Regenerative Medicine will reveal even more remarkable uses of these and other substances. In time, other body structures will experience the noteworthy healing that is seen with OA today.

Note: The author is part of a multidisciplinary Regenerative Medicine practice.

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