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Revolutionizing Orthopaedics: Exploring the Therapeutic Potential of Stem Cells

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The development of stem cells holds the key to a revolutionary era in medicine, unlocking multisystem processes that will help restore normal function in the human body. Stem cells are undifferentiated cells that have the capability to give rise to cells of the same type, and from which new cells can arise through the process of differentiation. Several sources of stem cells can be broadly categorized into three main types: embryonic stem cells (ESC), adult stem cells, and induced pluripotent stem cells (iPSCs).[1]

ESCs, also known as pluripotent stem cells, are self-renewing cells derived from the embryo and give rise to all different cell types during development. Adult (or somatic) stem cells are multipotent cells found in various tissues of the body and generate specific cell types within the respective tissue. Unlike ESCs, adult stem cells have less proliferative potential and are often limited to a specific cell line. Examples include hematopoietic stem cells in bone marrow and neural stem cells in the brain.[2] In recent years, scientists have been able to genetically re-engineer adult stem cells to display the pluripotent characteristics of embryonic stem cells. These are known as induced pluripotent stem cells.

Ongoing clinical trials are exploring stem cell usage for conditions such as coronary artery disease, pulmonary emphysema, and infertility. In orthopedics, stem cell therapy is being investigated for osteoarthritis, as well as bone, tendon, and cartilage repair.

Mesenchymal stem cells, a type of adult stem cell derived from the mesoderm, hold particular interest in orthopedics. They can differentiate into bone, ligament, tendon, and cartilage cells while promoting essential growth factors such as bone morphogenic proteins (BMP), TGF-Beta, and VEGF.[3] These profound effects can serve as targets for treatments in conditions such as osteoarthritis and tendonitis.

Osteoarthritis (OA) affects over 32.5 million adults in the US. 73% of people living with OA are older than 55, and 94.5% experience severity levels (moderate or severe) that could benefit from rehabilitation. In a study performed by Zhou et al., surgically induced OA in rat knees was shown to be alleviated by adipose-derived mesenchymal stem cells. Results indicated that adult mesenchymal stem cells (ADMSCs) alleviated cartilage deterioration and OA, as evidenced by histological analysis. When injected, these stem cells upregulated transcription factors col-2 and sox-9, important regulators in collagen and protein production, while causing proinflammatory cytokines such as IL-6 and TNF-α to decrease. Harmful markers that lead to tissue destruction, such as matrix metalloproteinase 13 (MMP-13), were also shown to be downregulated.[4] In a similar study conducted by Saulnier et al., MMP gene expression was found to be downregulated following intra-articular stem cell injection.[5] By increasing the amount of collagen and protein through these transcription factors, and by reducing the factors that lead to their destruction, stem cells were found to alleviate OA.

Current clinical trials show promise toward the potential use of stem cell injections for OA and in many other orthopaedic diagnoses. Though limited, clinical studies are showing the benefits of stem cell therapies such as injectable MSC therapy for OA. Dr. Al-Najar et al. performed a study using intra-articular marrow-derived MSCs in 13 patients with end-stage OA (bone-on-bone contact with no cartilage protecting the knees in the joint). The results showed that Knee Injury and Osteoarthritis Outcome Score (KOOS) significantly improved, as well as cartilage thickness measurements using T2-weighted MRIs.[6] In a prospective, randomized, open-label study conducted by Garay-Mendoza et al., patients in the treatment group showed significant improvement in pain, stiffness, and physical function at both one and six months. The treatment group received G-colony stimulating factor (G-CSF) for bone marrow stimulation, followed by bone marrow aspiration for a single intra-articular injection, and the control group received oral acetaminophen alone.[7] This study was one of the first to show the potential of G-CSF as a stimulant for MSC harvest.

Lateral epicondylitis, also referred to as "tennis elbow", is a condition characterized by pain and inflammation on the outer part of the elbow near the forearm extensors origin. Tennis elbow can develop in any patient who repeatedly uses their forearm muscles and tendons through gripping, in addition to repetitive arm movements. As the condition progresses, lateral epicondylitis can lead to weakened grip strength, decreased range of motion (ROM), and increased pain, all of which can hinder a patient's ability to perform daily tasks. In a prospective study performed by Dr. Ajit Singh et al., a cohort of 30 patients with untreated tennis elbow were injected with bone marrow aspirate containing plasma with growth factor and MSCs. Patient-rated Tennis Elbow Evaluation (PRTEE) surveys were recorded at

baseline, 2, 6, and 12 weeks, measuring three dimensions: pain, function in the affected arm, and usual activities (lower score correlates with less pain and greater ability to perform tasks). The results showed that at 2, 6, and 12 weeks, the PRTEE score significantly decreased from 72.8 ± 6.97 at baseline to 14.86 ± 3.48 at 12 weeks.[8]

Amongst the promising developments of MSC therapy, it is important to note studies that have reported adverse events. Peeters et al. reported in a cohort of 844 patients treated with MSC therapy, one patient developed a pulmonary embolism and another became infected following bone marrow aspiration.[9] Systemic reviews, such as one completed by Pas et al. found that there were no serious adverse events associated with MSC injections; however, some minor adverse events were found including swelling in the treated area.[10] Though still underway, clinical trials and current medical applications have shown stem cells are safe to use by trained providers.

Ethical issues regarding the source of cells, cloning, commercialization, and the need for regulatory oversight present major obstacles to application in everyday practice. Adult MCS pose less ethical concerns than embryonic stem cells which are highly controversial due to the destruction of embryos during extraction. Rapid advancements in gene editing technologies raise ethical questions about the potential misuse or unintended consequences of altering genetic information within adult stem cells. Balancing these ethical considerations with scientific progress is crucial for responsible stem cell research in the future.

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