

OSTEOARTHRITIS & STEM CELLS: FACT SHEET

INTRODUCTION

Osteoarthritis (OA) is a common, chronic, and incurable degenerative disorder of the joints. The main presenting symptoms are pain, swelling, and stiffness. Disability, difficulty with activities of daily living and self-care, and chronic pain arise as the disease progresses. Early arthritic changes in bone, cartilage, synovium, and other joint tissues typically do not produce consistent symptoms. Thus, patients often do not realize they have OA until symptoms worsen and the disease is widespread, irreversible, and more prominent on x-rays. While cartilage damage and loss are important components to OA development and explain the loss of joint space on x-rays, all joint tissues are affected. Various factors, such as genetics and weight gain, increase OA risk, but the specific mechanisms to OA in individual patients remain unknown, which substantially limits treatment options. Consequently, patients experiencing significant pain and limitations in work, self-care, or even walking may consider biologic and cell-based therapies as alternatives to traditional care, such as anti-inflammatory medications, corticosteroid injection (which can have significant side effects), weight loss, bracing, activity modification, or in severe cases, total knee replacement.

RATIONALE FOR USING CELL-BASED THERAPIES FOR OA

Frequently cited goals of cell therapies for OA include pain relief, anti-inflammatory effects, and regeneration of joint tissues. The role of cell therapy in joint tissue regeneration and repair has primarily been explored in the treatment of small, focal, or “pothole”-like defects in the joint surface cartilage, rather than the more generalized cartilage loss and joint damage seen in OA^{1,2}. This is an important distinction.

With a few notable exceptions, currently available cell therapies for knee OA have not been shown to regenerate joint tissues in widespread arthritis. Targeting joint inflammation and regulating the inflammatory and degradative processes from altered gene expression and metabolism of joint tissue cells may be appropriate therapeutic strategies. Mesenchymal stromal cells (MSC) are defined by the International Society for Cell Therapy (ISCT) as culture-expanded cell populations that are plastic-adherent, express certain cell markers but not others, and are able to differentiate into bone, cartilage, and fat forming cells³. Numerous laboratory studies have shown that cells meeting this definition of MSCs can be derived from the heterogeneous connective tissue progenitors present in native tissues such as bone marrow, fat, and synovium. These culture-expanded populations have been reported to have immunomodulatory and anti-inflammatory properties and can stimulate other cells to improve repair processes⁴. Despite these preclinical successes, human trials have not yet demonstrated definitive clinical efficacy of these cell therapy-based treatments.

In an effort to develop cell therapies via simpler approaches without laboratory expansion of MSCs, direct injections of mixed, uncultured, and uncharacterized cells from patient’s blood, fat, or bone marrow have been utilized clinically and in most cases are marketed incorrectly as “stem cell” or “MSC” therapies. The clinical use of these poorly understood injections to treat OA ranges widely among practitioners, from highly trained orthopedic and sports medicine providers to those without proper qualifications. The biological properties and therapeutic potential of both culture expanded MSCs and uncultured directly injected cells remain controversial and in need of substantial additional scientific inquiry⁵.

CLINICAL STATUS OF CELL-BASED THERAPIES AND CLINICAL TRIALS FOR OA

Unproven cell-based therapies to treat OA are used worldwide despite limited evidence from high-quality studies. In the United States, current experimental cell therapies for OA primarily involve cells obtained from autologous, minimally manipulated tissues, such as concentrated bone marrow aspirate (BMAC) and micro-fragmented adipose tissue (MFAT). When administered by appropriately trained clinicians, these treatments appear largely safe. Studies have demonstrated pain relief with cell therapies for knee OA, but more rigorous randomized trials have mostly revealed similar pain relief compared to standard care of treatments, and none have shown significant cartilage regeneration indicative of an arthritis cure.

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ADDITIONAL RESOURCES

About Stem Cells

<https://aboutstemcells.org>

American College of Rheumatology

<https://rheumatology.org/patients/osteoarthritis>

Arthritis Foundation

<https://www.arthritis.org/diseases/osteoarthritis>

Mayo Clinic

<https://www.mayoclinic.org/diseases-conditions/osteoarthritis/symptoms-causes/syc-20351925>

Gupta PK, et al. Efficacy and safety of adult human bone marrow-derived, cultured, pooled, allogeneic mesenchymal stromal cells (Stempeucel®): preclinical and clinical trial in osteoarthritis of the knee joint. Arthritis Res Ther. 2016 Dec 20;18(1):301. doi: 10.1186/s13075-016-1195-7. PMID: 27993154; PMCID: PMC5168586.

Pers YM, et al. Adipose Mesenchymal Stromal Cell-Based Therapy for Severe Osteoarthritis of the Knee: A Phase I Dose-Escalation Trial. Stem Cells Transl Med. 2016 Jul;5(7):847-56. doi: 10.5966/sctm.2015-0245. Epub 2016 May 23. PMID: 27217345; PMCID: PMC4922848.

Shapiro SA, et al. A Prospective, Single-Blind, Placebo-Controlled Trial of Bone Marrow Aspirate Concentrate for Knee Osteoarthritis. Am J Sports Med. 2017 Jan;45(1):82-90. doi: 10.1177/0363546516662455. Epub 2016 Sep 30. PMID: 27566242.

The most recent systematic review of a concentrated bone marrow cell therapy injection for knee OA analyzed eight randomized controlled trials involving 937 patients. The review found improvements in pain and function but did not outperform other standard of care pain relieving injections⁶. Mautner et al performed a large multi-center randomized controlled trial comparing cell therapies derived from autologous bone marrow, fat, or allogeneic human umbilical cord tissue-derived MSCs, and conventional corticosteroid injections. All of these procedures were able to relieve patient's pain at one-year follow up, but none of the cell-based procedures outperformed a corticosteroid injection⁷. Overall, further development of cell therapy products and high-quality clinical studies for efficacy are required before these treatments can be recommended for treatment for knee OA.

Finally, it should be noted that many orthopedic and sports medicine practitioners frequently utilize a biologic product called platelet-rich plasma (PRP)⁸. PRP, made from a patient's own blood, is a cocktail of growth factors released during platelet activation and has been shown in over 40 randomized trials to improve pain and function in patients with knee OA⁹. Although biologically derived, PRP is generally not considered a cell therapy, but several studies have shown it achieves outcomes comparable to some cell-based therapies. PRP is now commonly used in routine practice but often mistaken or falsely promoted as a stem cell therapy.

CENTERS WORKING ON THE CLINICAL APPLICATION OF STEM CELLS FOR OA

- [Cedars Sinai](#)
- [Cleveland Clinic](#)
- [Emory University](#)
- [Hospital for Special Surgery \(HSS\)](#)
- [Mayo Clinic](#)
- [University of Colorado](#)

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