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AN MCI WHITE PAPER

The Role of Dezawa MuseCells® in Orthopedics and Longevity

A Comprehensive Review

Why an endogenous, non-tumorigenic pluripotent stem cell may be uniquely suited to musculoskeletal repair — and to extending healthy lifespan.

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Introduction

Multilineage-differentiating stress-enduring Dezawa MuseCells® are endogenous pluripotent stem cells first identified in mesenchymal tissues such as bone marrow, skin fibroblasts, and adipose tissue (Kuroda et al., 2010). These cells possess the capacity to differentiate into cells from all three germ layers, express pluripotency markers such as Oct3/4, Nanog, and Sox2, and crucially, are non-tumorigenic and immunologically tolerant. This positions them as an attractive option for regenerative medicine.

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An aging population and the case for regeneration

As the global population continues to age, the burden of musculoskeletal disorders such as osteoarthritis, osteoporosis, and degenerative disc disease is projected to rise substantially. Traditional orthopedic interventions, including joint replacement and bone grafting, provide mechanical solutions, but do not address the underlying biological decline. This has fueled interest in regenerative medicine approaches, with stem cell-based therapies offering a promising frontier.

Uniquely suited for orthopedic applications

Dezawa MuseCells® are uniquely suited for orthopedic applications because of their dual ability to integrate into injured tissue and modulate the local immune and inflammatory milieu. Unlike conventional MSCs, Dezawa MuseCells® do not require genetic reprogramming to exhibit pluripotency, and they display superior survival in oxidative environments, making them an ideal candidate for repair of aged or chronically inflamed tissue. Their non-tumorigenic nature further positions them as a safer alternative to induced pluripotent or embryonic stem cells in clinical applications.

Stress endurance, homing, and immune privilege

Dezawa MuseCells® show stress-endurance, which allows them to survive under harsh conditions including serum deprivation, hypoxia, and low attachment (Kuroda et al., 2013). They are a subset of mesenchymal stem cells (MSCs) and can be isolated by fluorescence-activated cell sorting for the SSEA-3 marker. A hallmark of Dezawa MuseCells® is their ability to home to damaged tissue via the S1P-S1PR2 axis, a mechanism elucidated by Yamada et al. (2018), which enhances their regenerative targeting ability. These cells migrate efficiently to sites of inflammation and injury without the need for external chemotactic agents, making them highly practical for systemic delivery. In contrast to induced pluripotent stem cells, Dezawa MuseCells® do not form teratomas in vivo, thus eliminating a significant risk associated with pluripotent cell therapies. They also express low levels of HLA-DR, which contributes to their immune privilege and allows for allogeneic transplantation without the need for immunosuppressive therapy.

“In contrast to induced pluripotent stem cells, Dezawa MuseCells® do not form teratomas in vivo, thus eliminating a

significant risk associated with pluripotent cell therapies."

Differentiation and tissue regeneration

Dezawa MuseCells® have demonstrated the potential to differentiate into osteocytes, chondrocytes, and myocytes in preclinical models. In the musculoskeletal system, their paracrine effects and ability to contribute to structural tissue regeneration are notable. While direct studies in osteoarthritis remain limited, their lineage potential suggests promising applications in cartilage and bone regeneration. Furthermore, Dezawa MuseCells® contribute to neovascularization in ischemic limbs and injured tissues, aiding in the repair of both hard and soft tissues. Their non-tumorigenic nature makes them suitable for orthopedic applications, especially in long-term joint preservation.

In spinal cord injury models, Dezawa MuseCells® have been shown to differentiate into neuron-like cells, integrate into host tissue, and improve functional outcomes. Their homing capability and regenerative effects also suggest a role in tendon and ligament repair, where poor vascularity typically limits healing capacity.

Longevity and anti-senescent mechanisms

The potential for Dezawa MuseCells® to contribute to longevity lies not only in their regenerative capacity, but also in their anti-senescent mechanisms. Chronic inflammation and loss of cellular homeostasis are key drivers of aging in joint tissues, contributing to cartilage degradation and impaired bone remodeling. Dezawa MuseCells® can help mitigate these effects through secretion of trophic factors, reduction of oxidative stress, and promotion of local angiogenesis. In experimental aging models, Dezawa MuseCells® transplantation has been associated with improved histological markers of tissue health and functional performance. These findings suggest Dezawa MuseCells® may not only repair tissue damage but also help maintain tissue integrity over time, thereby delaying the onset of degenerative diseases and extending healthy lifespan. Recent research by Wakao et al. (2022) highlighted the unique capacity of Dezawa MuseCells® to phagocytose apoptotic fragments, which enhances their differentiation potential and rejuvenated effects—key processes relevant to healthy aging. This mechanism suggests an innate ability of Dezawa MuseCells® to recycle cellular waste into regenerative capacity.

> *"These findings suggest Dezawa MuseCells® may not only repair tissue damage but also help maintain tissue integrity over time, thereby delaying the onset of degenerative diseases and extending healthy lifespan."*

Clinical translation and future directions

Dezawa MuseCells® have been applied in early-phase clinical trials for stroke, acute myocardial infarction, spinal cord injury, and neonatal hypoxic-ischemic encephalopathy. Their intravenous administration without immunosuppression and lack of tumorigenicity are critical advantages. In orthopedic surgery, one of the most compelling uses for Dezawa MuseCells® is in the treatment of large bone defects, cartilage restoration and nonunion fractures, conditions where standard methods often fall short. Their ability to integrate into host tissue without provoking immune rejection could support allogeneic cell banking for off-the-shelf use.

Furthermore, Dezawa MuseCells® can be paired with advanced biomaterials or 3D bioprinting platforms to create complex tissue constructs. When seeded into bioresorbable scaffolds, Dezawa MuseCells® may support osteochondral regeneration in joint defects. Dezawa MuseCells®, along with their exosomes, have been shown to have positive results in treating the spine via intra-discal, intra-articular (into facet joints), or epidural injections. Clinical translation will require standardization of isolation methods, quality control metrics, and long-term outcome studies. Collaboration between cell biologists, surgeons, physicians and regulatory bodies will be essential to navigate the ethical and logistical challenges associated with next-generation regenerative therapies.

References

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DISCLOSURE & ATTRIBUTION

This review synthesizes peer-reviewed research on multilineage-differentiating stress-enduring cell biology and is provided for informational and educational purposes only; it is not medical advice, nor a statement of the regulatory status of any product. Cited studies refer to the broader scientific literature on this cell type. The biological characteristics described reflect authentic Dezawa MuseCells® as developed and characterized under the licensed intellectual property and methodologies of MuseCell Innovations®; only cells originating from MCI's manufacturing ecosystem and distributed through MCI-designated, licensed partners carry the profile described here.

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