MUSECELL® INNOVATIONS

REGENERATING LIFE AT ITS SOURCE

AN MCI SCIENTIFIC BRIEF

Pluripotent Without the Pain: How Dezawa MuseCells® Dodge Tumor Formation

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Overview

Umbilical cord-derived Dezawa MuseCells® (Multilineage differentiating Stress Enduring) are unusual stem cells that combine broad differentiation capacity without tendency to form tumors. They are identified as SSEA-3–positive cells within the mesenchymal stromal compartment and can self-renew from single cells and generate derivatives of all three germ layers. Unlike embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), however, they do not form teratomas when transplanted under conditions where classic pluripotent cells typically do. In other words, Dezawa MuseCells® retain pluripotent-like function, but their biology is organized to keep growth tightly controlled.

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How can UC Dezawa MuseCells® be pluripotent-like yet non-tumorigenic?

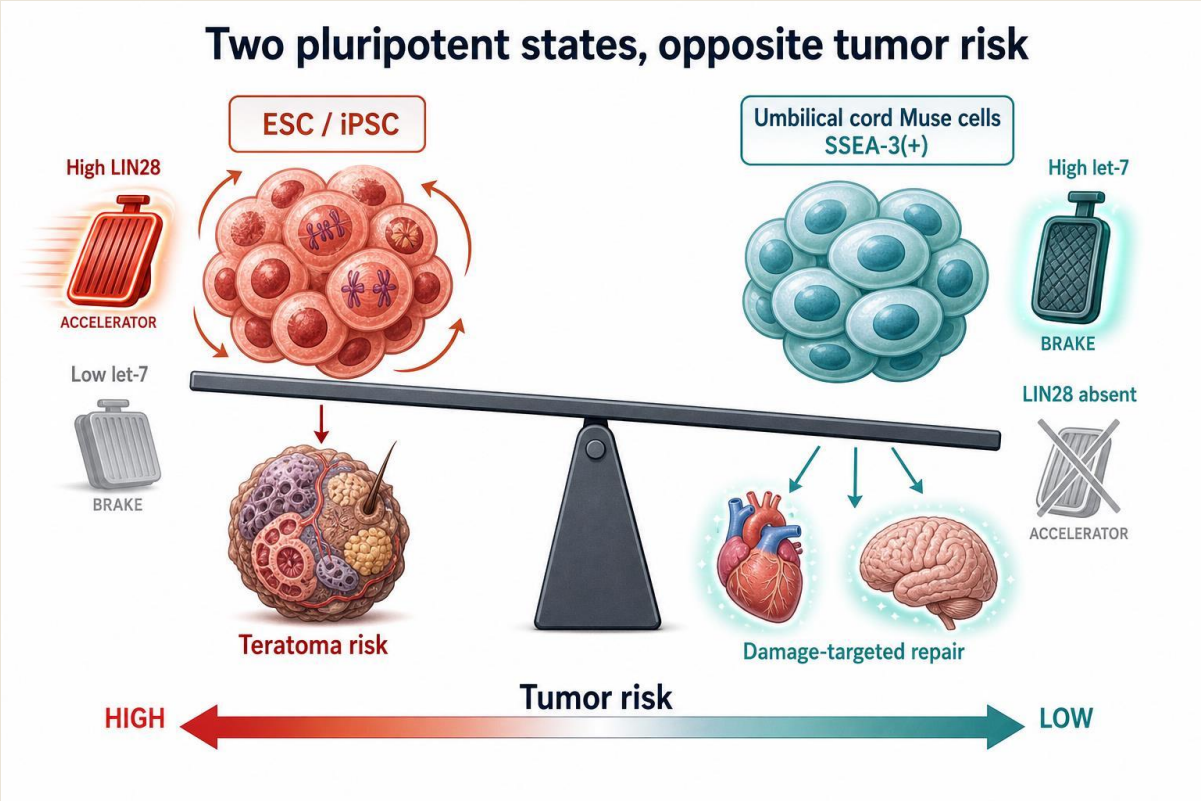

Figure 1. Two pluripotent states, opposite tumor risk — the LIN28-driven "accelerator" of ESC/iPSCs versus the let-7-dominant "brake" of umbilical cord Dezawa MuseCells® (SSEA-3+), and their opposing positions on the tumor-risk axis.

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An endogenous, repair-oriented nature

A first reason for this is their endogenous, repair-oriented nature. Dezawa MuseCells® are not created by forced genetic reprogramming; they arise naturally within tissues such as bone marrow, adipose tissue, amnion, and umbilical cord. Because they develop in a normal tissue environment rather than in an artificial reprogramming process, they avoid much of the genomic and epigenetic instability that can accompany iPSC generation and long-term ESC culture. Functionally, they behave as stress-responsive repair units: they are relatively quiescent at baseline, become activated by tissue injury, home to damaged sites, and differentiate into organ-appropriate cell types. Their proliferation is closely tied to the presence of damage signals and declines as the tissue recovers, rather than continuing indefinitely.

A low proliferative drive

A second key feature is their low proliferative drive. Classic ESCs and iPSCs exhibit high telomerase activity, rapid cell-cycle progression, and symmetric divisions that support large-scale expansion. This is useful for generating large numbers of cells in vitro, but it also means that any cells that remain undifferentiated after transplantation can easily fuel teratoma formation. Dezawa MuseCells®, in contrast, show low telomerase activity and slower proliferation, even though they retain the ability to self-renew and to differentiate broadly. They divide more like somatic stem cells than like embryonic stem cells. This “low-gear” growth pattern makes them far less likely to generate the uncontrolled, space-occupying masses characteristic of teratomas.

> *“They divide more like somatic stem cells than like embryonic stem cells. This ‘low-gear’ growth pattern makes them far less likely to generate the uncontrolled, space-occupying masses characteristic of teratomas.”*

Intact DNA-damage checkpoints and p53 surveillance

Third, Dezawa MuseCells® appear to preserve robust DNA damage checkpoints and p53-dependent genome surveillance. In healthy cells, these systems act as quality-control mechanisms: they pause the cell cycle when DNA is damaged, allow repair, and trigger apoptosis if the damage is too severe. In many cancers and in some pluripotent stem cell lines, these safeguards are attenuated, allowing cells to continue dividing despite accumulating mutations. Dezawa MuseCells®, by contrast, respond to genomic stress by arresting, repairing, or undergoing programmed cell death instead of pushing through the cell cycle with damaged DNA. This is especially important because cells used for regenerative therapy will often encounter hypoxia, inflammation, and oxidative stress in injured tissues. A population that preserves these checkpoints is less likely to progress toward malignant transformation under such conditions.

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The let-7 / LIN28 axis: a two-part growth-control module

The most informative mechanistic insight comes from the let-7/LIN28 axis, which can be thought of as a two-part growth-control module. Let-7 is a family of microRNAs that acts as a tumor-suppressive brake by downregulating genes that promote proliferation, survival, and stem-like behavior. LIN28 is an RNA-binding protein that functions like a growth gas pedal: it blocks the maturation of let-7, thereby lifting that brake and allowing pro-growth, pro-stemness genes to remain highly active. ESCs, iPSCs, and many cancers operate in a “LIN28-high / let-7-low” state, which favors rapid self-renewal, high metabolic drive, and a greater risk of oncogenic behavior.

Dezawa MuseCells® occupy the opposite configuration. They do not express LIN28 detectably, but they do express several let-7 family members at relatively high levels. In Dezawa MuseCells®, let-7 directly dampens the PI3K–AKT pathway, a central driver of proliferation, survival, and glycolytic metabolism in many stem and cancer cells. When PI3K–AKT signaling is restrained, cells divide more slowly and are less likely to

enter a cancer-like, highly glycolytic growth mode. At the same time, the pluripotency regulator KLF4 and its downstream targets (including OCT4, SOX2, and NANOG) remain expressed. This means Dezawa MuseCells® keep key pluripotency genes switched on, but within a molecular context that strongly limits growth. They achieve pluripotency-like gene expression without activating the full embryonic stem cell growth program.

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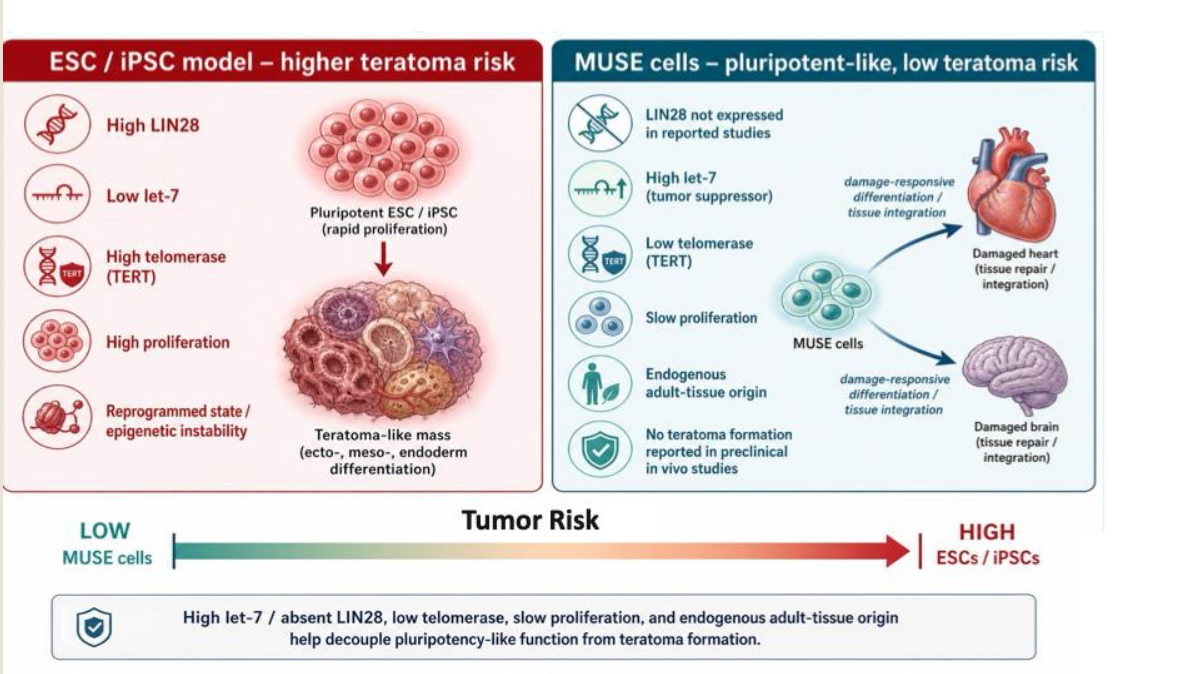

Figure 2. Mechanistic contrast between the ESC/iPSC model (higher teratoma risk) and Dezawa MuseCells® (pluripotent-like, low teratoma risk). High let-7, absent LIN28, low telomerase, slow proliferation, and endogenous adult-tissue origin together decouple pluripotency-like function from teratoma formation.

An additional nuance is that in Dezawa MuseCells®, the MEK/ERK pathway helps support self-renewal and limit senescence but is not under let-7 control. This division of labor, PI3K–AKT constrained by let-7, MEK/ERK available to maintain a modest self-renewal capacity, allows Dezawa MuseCells® to remain functionally plastic without becoming aggressively proliferative. In simple terms, let-7 keeps the growth engine idling at low levels, while other pathways maintain sufficient activity to preserve a stable, reparative stem cell state.

Umbilical cord Dezawa MuseCells® within the framework

Umbilical-cord-derived Dezawa MuseCells® fit squarely within this framework. In umbilical cord tissue, they are isolated as the SSEA-3-positive subset of mesenchymal stromal cells and show the same core features: stress endurance, single-cell triploblastic differentiation, low telomerase activity, slow proliferation, and absence of teratoma formation in relevant in vivo models. The perinatal origin adds practical advantages, young tissue with relatively few accumulated mutations and an ethically straightforward source but does not fundamentally change the mechanistic explanation for their safety. The non-tumorigenic profile is tied to Dezawa MuseCells® identity itself: endogenous origin, preserved checkpoints, low proliferative drive, and a LIN28-negative/let-7-dominant molecular state.

Viewed together, these elements provide a coherent explanation for why Dezawa MuseCells® do not exhibit tumorigenic tendencies despite their pluripotent-like capacity. They are pluripotent-like cells in which every major layer of growth control remains intact: endogenous tissue origin rather than artificial reprogramming, low telomerase activity and slow proliferation, intact DNA-damage and p53 responses, damage-linked activation rather than autonomous expansion, and a let-7-driven microRNA environment that restrains key growth pathways in the absence of LIN28. This architecture allows Dezawa MuseCells® to participate in tissue repair across multiple organs while markedly reducing the risk of teratoma formation and malignant transformation compared with conventional pluripotent stem-cell therapies.

DISCLOSURE & ATTRIBUTION

This scientific brief discusses the biology of umbilical cord-derived Dezawa MuseCells® produced and characterized in line with the licensed intellectual property and methodologies of MuseCell Innovations®. The safety and mechanistic characteristics described reflect authentic Dezawa MuseCells® biology; only cells originating from MCI's manufacturing ecosystem and distributed through MCI-designated, licensed partners carry the profile described here.

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