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Case Report

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Multi-System Biological Age Reversal Following MUSE Stem Cell Therapy: Case Reports

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ABSTRACT

Background: Biological aging can be quantified using DNA methylation "epigenetic clocks," which estimate an individual's biological age based on methylation patterns. These clocks correlate strongly with chronological age and health risks, with Horvath's seminal multi-tissue clock achieving a median error of ~3.6 years. However, traditional clocks may have limited resolution in individuals and do not pinpoint which organ systems are driving aging. Recent advances focus on biological noise – stochastic epigenetic dysregulation that increases with aging – and organ-specific epigenetic biomarkers to more precisely track aging and rejuvenation. Meanwhile, novel regenerative therapies such as multilineage differentiating stress- enduring (MUSE) stem cells have emerged. MUSE cells are endogenous non-tumorigenic pluripotent-like stem cells discovered in 2010 by Professor Mari Dezawa, capable of homing to damaged sites and orchestrating repair via differentiation and immunomodulation.

Keywords: MUSE Cells, Epigenetic Aging, DNA Methylation Clocks, Biological Age Reversal, Stem Cell Therapy, Regenerative Medicine.

CASE PRESENTATION

We present two anonymized cases of middle-aged adults who underwent intravenous MUSE cell therapy and demonstrated marked biological age reversal, as assessed by the SystemAge epigenetic analysis platform. The first case involved a 45-year-old individual who received two intravenous infusions consisting of approximately 1.0×10^{8} allogeneic MUSE cells, 1.0×10^{13} MUSE-derived exosomes, and umbilical cord plasma per infusion [1,2]. The second case, a 60-year- old individual, also received one infusion of the same formulation. DNA methylation-based biological age testing (SystemAge, Generation Lab) was performed for both patients: once before treatment and again at follow-up (3 months post-therapy for Case 1 and approximately 6.5 months post-therapy for Case 2) [3,4]. System Age is a next-generation epigenetic clock that quantifies aging across 19 organ systems by measuring molecular biological noise (epigenetic variability) in blood DNA [5].

CASE 1 PRESENTATION

A 45-year-old individual received two intravenous infusions of MUSE cells, exosomes, and umbilical cord plasma. Before therapy, the patient's

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overall SystemAge was 53.0 years (significantly older than chronological age), with particularly accelerated ages in the brain and immune systems. Following MUSE therapy, the SystemAge analysis demonstrated a profound decrease in biological ages across multiple organs, as shown in Figure 1. Notably, the patient's brain epigenetic age was reduced by 13.6 years (from mid-50s to ~40), approaching parity with chronological age (Figure 2). The immune system age decreased by 6.1 years, and other systems showed substantial rejuvenation. Key organ-specific age changes included:

- Brain system: 13.6-year decrease in biological age
- Immune system: 6.1-year decrease
- Reproductive system: 4.9-year decrease
- Urinary system: 7.5-year decrease

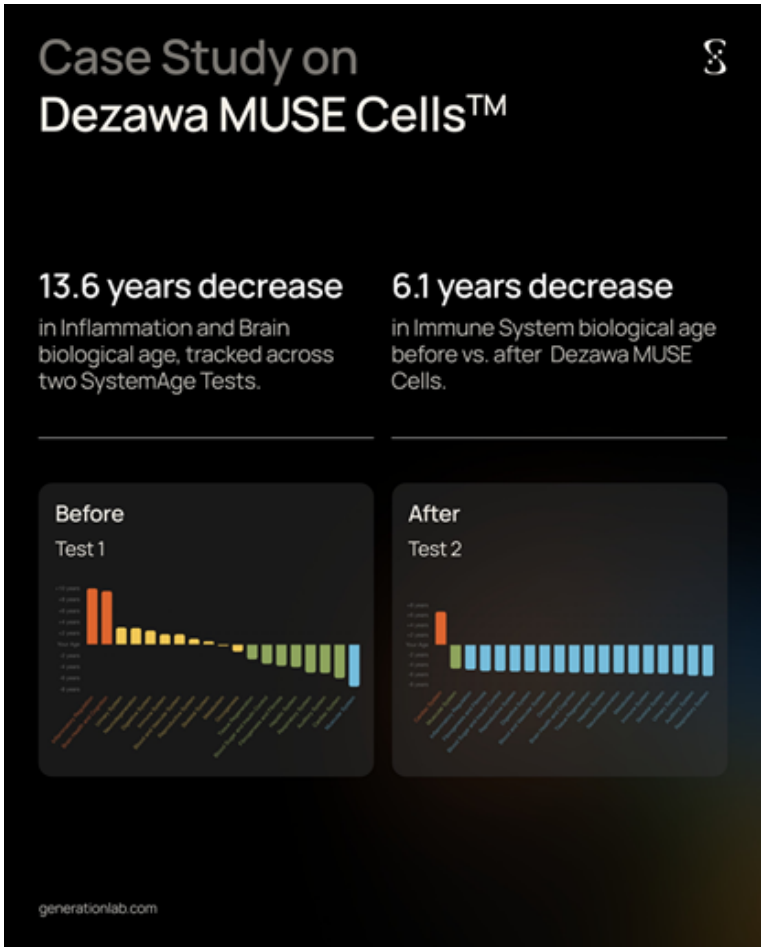

Figure 1. SystemAge biological age changes before (Test 1) and after (Test 2) MUSE therapy, showing significant reductions in inflammation, brain, and immune system biological ages.

Figure 2. Visual summary of biological age reductions following MUSE therapy in the brain (−13.6 years), reproductive system (−4.9 years), and urinary system (−7.5 years).

Additionally, the patient's "inflammation aging index" – an epigenetic indicator of inflammatory/ immune aging – dropped from +13.84% above expected to –4.67%, indicating a shift from pro- aging to rejuvenation in inflammatory status. No adverse events were observed during or after the MUSE cell infusion, and the patient reported subjective improvements in vigor.

CASE 2 PRESENTATION

The second patient was a 60-year-old individual who underwent a single intravenous infusion of approximately 1.0×10^{8} allogeneic multilineage-differentiating stress-enduring (MUSE) stem cells, 1.0×10^{13} MUSE-derived exosomes, and umbilical cord plasma. SystemAge analysis was conducted prior to therapy and again approximately six and a half months post-infusion. This testing evaluates organ-specific biological aging using epigenetic signatures, quantifying the divergence from chronological age.

At baseline, the patient's SystemAge was 63.7 years, surpassing their chronological age of 60.0 years (Figure 3). Multiple organ systems were showing signs of accelerated biological aging, including the reproductive system (69.0), blood and vascular system (68.0), cardiac system (65.5), inflammatory regulation (63.7), and respiratory system (63.2.) The inflammatory regulation profile indicated an accelerated aging status and a heightened risk for chronic immune dysfunction (Figure 4).

Following treatment, SystemAge testing performed six and a half months later revealed substantial biological rejuvenation. The patient's SystemAge decreased to 52.8 years, now significantly younger than their chronological age of 60.9 years (Figure 5). Organ-level analysis demonstrated improvements across several systems, with the most notable

decreases seen in:

- **Reproductive system:** from 69.0 to 59.3
- **Blood and vascular system:** from 68.0 to 57.9
- **Cardiac system:** from 65.5 to 56.8
- **Neurodegeneration (nerve cells):** from 63.7 to 56.3
- **Auditory system:** from 61.5 to 55.5

The inflammatory system also improved significantly, with SystemAge decreasing from 63.7 to 52.8, indicating a transition from an accelerated to a more regulated immune profile (Figure 6). A side-by-side comparison of system-level biological age deviations before and after treatment is illustrated in Figure 7, highlighting the broad multi-system improvements following MUSE cell therapy.

The patient experienced no adverse effects and remained medication-free during the follow-up period. No other therapeutic interventions were introduced between the two tests, suggesting that MUSE therapy was the primary contributing factor to the biological age reversal observed.

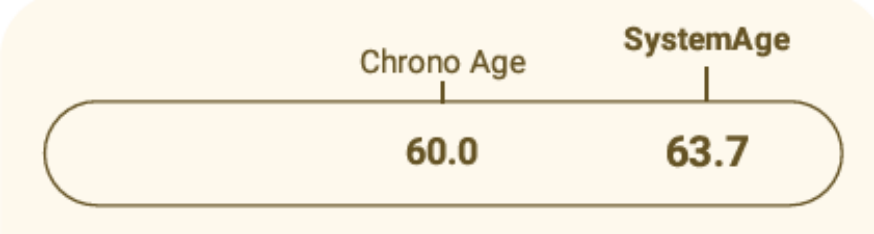

Figure 3. Pre-treatment inflammatory regulation system showing accelerated biological aging prior to MUSE cell therapy.

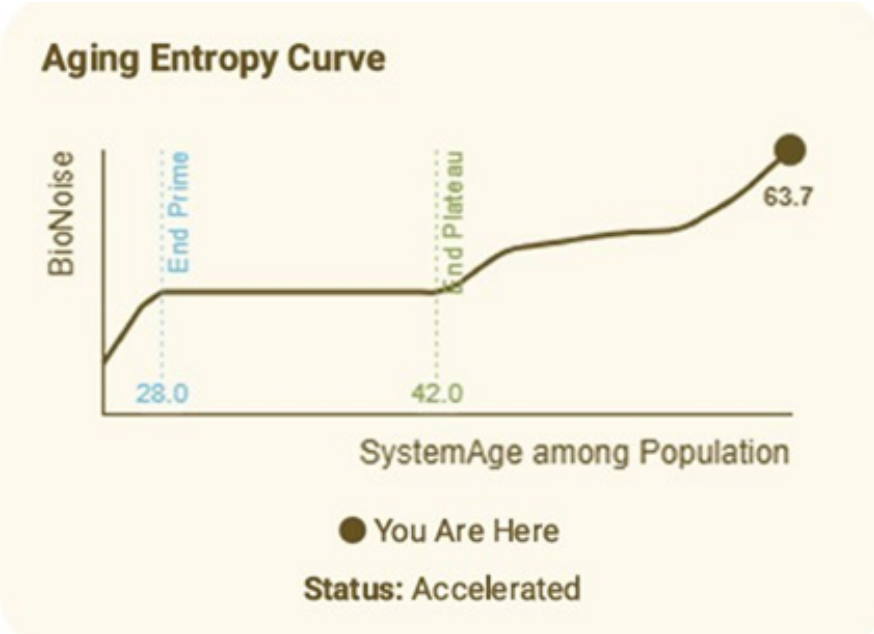

Figure 4. Entropy distribution before treatment demonstrating a rightward shift, consistent with accelerated inflammatory aging.

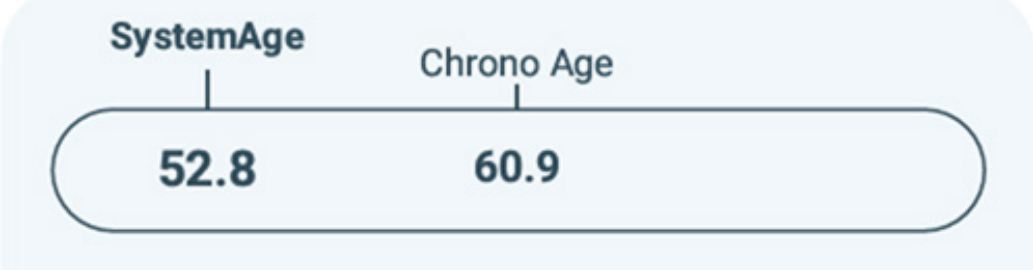

Figure 5. Post-treatment inflammatory regulation profile showing reversal of biological age below the patient's chronological age.

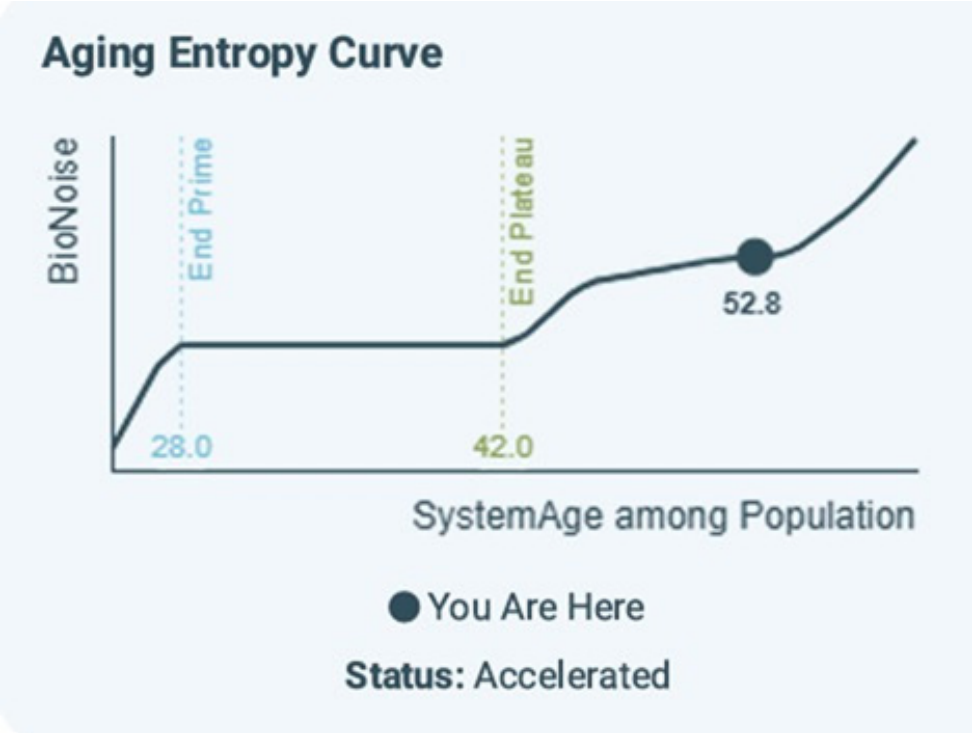

Figure 6. Reduced inflammatory entropy post treatment.

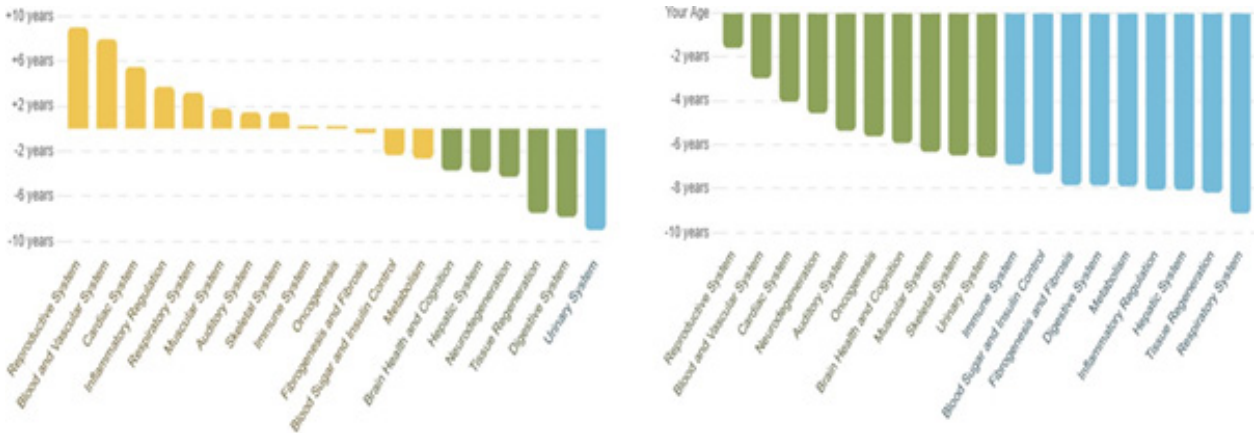

Figure 7. Side-by-side comparison of organ-specific biological age deviations before (left) and after (right) MUSE therapy for Case 2.

DISCUSSION

This case series provides preliminary evidence that MUSE stem cell therapy may be associated with multi-system epigenetic age reversal. The post-treatment epigenetic clock readings suggest that both patients experienced biological age reductions across multiple organ systems, with Case 1 showing notable decreases in brain, immune, reproductive, and urinary system ages. Case 2 similarly demonstrated substantial reductions in biological age across the reproductive, cardiovascular, immune, and auditory systems following a single infusion. These findings align with emerging literature that interventions can produce measurable rejuvenation in epigenetic aging biomarkers [6]. One possible explanation is the high regenerative and anti-inflammatory potential of MUSE cells: MUSE cells can migrate to sites of tissue injury or dysfunction (including possibly microvascular or neuroinflammatory lesions in the brain) and differentiate into functional cells to replace damaged cells [4]. In the brain, even subtle age-related micro- damage or inflammation may trigger homing of MUSE cells, which then contribute to repair and reduced biological age signals [4]. In Case 1, The concurrent 6.1-year reduction in immune age and the pronounced drop in the inflammatory age index support the hypothesis that MUSE therapy ameliorated

"inflammaging," the chronic low-grade inflammation that drives aging and age-related pathology (Figure 8). MUSE cells have documented immunosuppressive and immunotolerant properties, enabling allogeneic transplantation without immunotherapy [7]. By secreting anti-inflammatory factors and possibly phagocytosing senescent or apoptotic immune cells, MUSE cells could reset the immune system towards a more youthful state [7]. In Case 2, this pattern of immune modulation was also evident. The patient's immune system SystemAge decreased from 60.3 years to 53.9 years, despite a chronological age increase from 60.0 to 60.9 years, suggesting a rejuvenated immune profile and reduced inflammatory burden. This parallels the changes observed in Case 1 and reinforces the role of immune restoration as a core mechanism of action. This immunomodulation may have systemic effects, as the immune system heavily influences aging in other organs through inflammatory cytokines [4]. The improvements observed in the reproductive and urinary system biological ages in case 1 may likewise stem from systemic reductions in inflammation and direct tissue repair by MUSE cells in those organ systems (e.g. MUSE cells potentially engrafting in the kidneys or gonads to rejuvenate tissue function). Mechanistically, MUSE cells combine advantages of mesenchymal stem cells (paracrine repair, anti-inflammatory effects) with true pluripotent regenerative capacity [4,7].

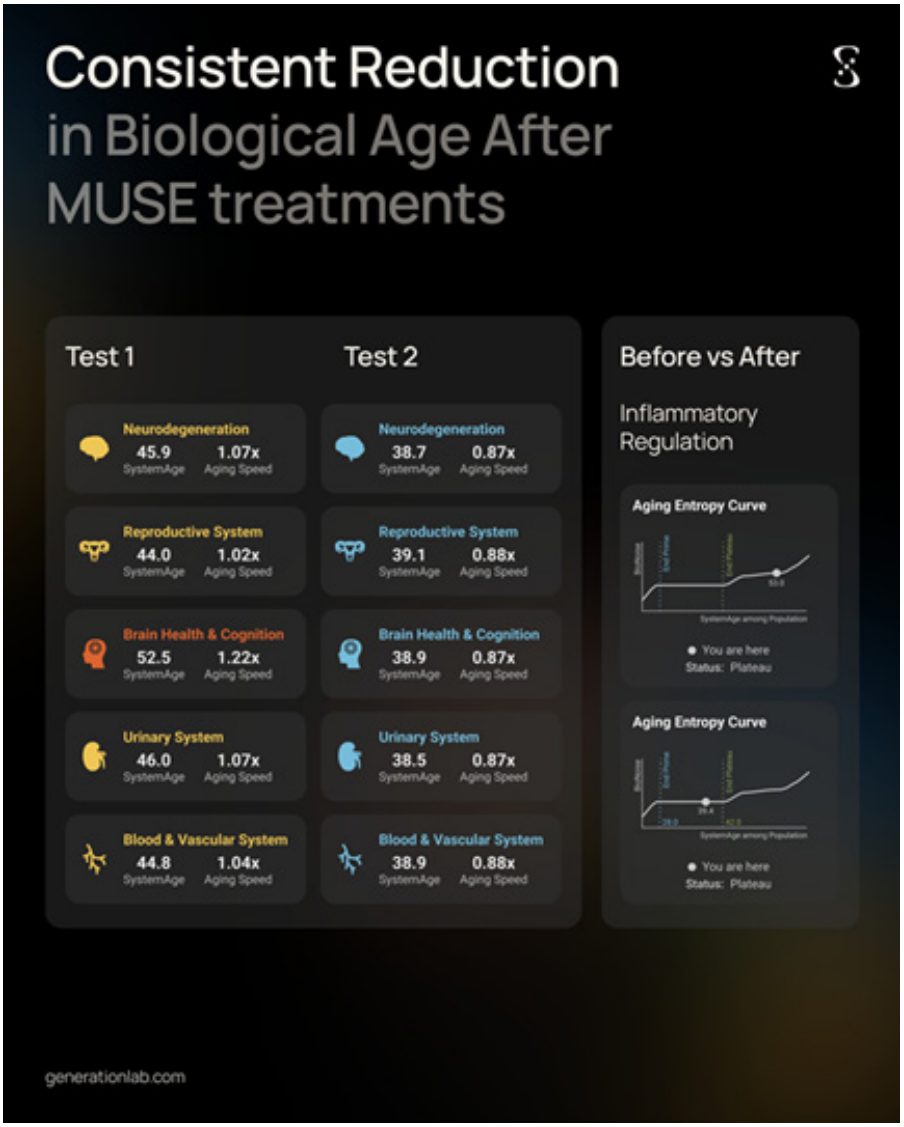

Figure 8. Comparison of SystemAge scores and aging speeds before and after MUSE therapy across five organ systems. Also shown are improvements in the Aging Entropy Curve, indicating a reduction in biological noise and epigenetic variability.

They can sense sphingosine-1-phosphate released by damaged cells and actively home to injured tissues [4]. Once at a target site, MUSE cells exhibit a unique macrophage-like function: they phagocytose debris and dying cells and then replace them by differentiating into the same cell type needed for that tissue [4]. This direct replacement of damaged cells with healthy ones could restore tissue integrity and genomic stability, thereby reducing the epigenetic "noise" that accumulates with age. In both patients, such processes may have occurred broadly, given that multiple organ biological ages regressed toward a younger baseline. The concept of measuring biological noise rather than just age-related methylation changes is critical here: by targeting fundamental dysregulation, MUSE therapy may have globally reduced the variability in methylation at age-stable sites, as per the noise barometer model [2]. A reduction in epigenetic noise reflects a return toward homeostasis and cellular network coherence, which is consistent with the observed multi-organ age "reset." Our findings are in concordance with the idea that aging is a multi-system, asynchronous process: different organs can age at different rates and contribute variably to overall aging. In Case 1, the immune system and brain were biologically older than the patient's chronological age at baseline and showed strong rejuvenation after therapy; similarly, in Case 2, the immune system exhibited marked age acceleration pre- treatment and demonstrated significant improvement following the infusion, suggesting these systems were principal drivers of the patient's biological aging. This supports the emerging paradigm of "ageotypes," where individuals have particular organ systems that drive their aging process (Figure 9) [3]. Identifying and targeting such ageotypes with interventions like MUSE cells could yield personalized geroprotection. Notably, MUSE cells have already shown therapeutic benefits in clinical trials for age-related conditions (e.g. cardiac ischemia, stroke, frailty-related skin ulcers) without significant side effects [4,7]. These trials reported improved tissue function (e.g. better cardiac ejection fraction in myocardial infarction) and functional recovery in stroke, lending credence that MUSE-induced regeneration can translate to tangible health benefits in humans. Our case extends this by linking MUSE therapy to objective epigenetic rejuvenation metrics [5,6].

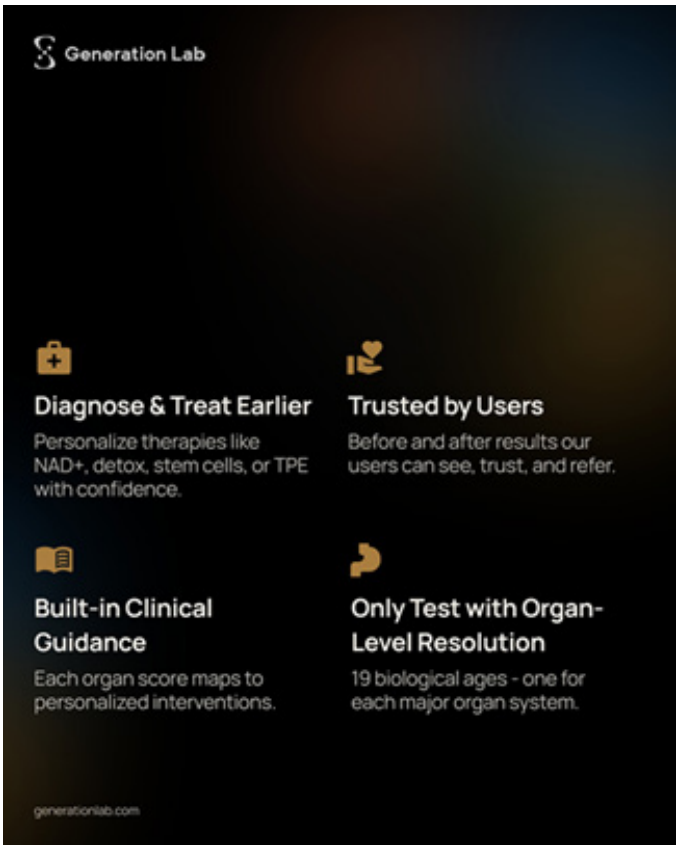

Figure 9. Overview of Generation Lab's SystemAge platform, highlighting its clinical utility for personalized anti-aging interventions and its unique organ-level resolution across 19 biological systems.

LIMITATIONS

As a case series involving two patients, these results must be interpreted with caution. Epigenetic clock analyses, while reproducible, can have technical and biological variability. The large magnitude of age reduction observed here (e.g. >13 years in brain age) in Case 1 and the >10- year systemic improvement in Case 2- exceeds typical test-retest variation reported for most DNA methylation clocks, suggesting a true biological effect; however, placebo effects or lifestyle changes cannot be fully excluded. Both patients were concurrently advised on general health optimization (diet, exercise, etc.) as part of longevity care, which could synergize with MUSE cell effects. We did not have a control clock (e.g. Horvath or GrimAge) run in parallel; using multiple epigenetic aging measures in future cases or trials would strengthen the evidence for true age reversal. Nonetheless, SystemAge's multi-organ readouts provided granular insight that a single composite epigenetic age might miss – For example, a conventional blood-based methylation age could have masked system-specific changes—such as the dramatic brain age reversal in Case 1 or the broad multi-system rejuvenation in Case 2. Another limitation is the relatively short follow-up. It is unknown if these rejuvenation effects are lasting or transient. Longitudinal tracking will be important to see if biological ages remain low or if additional MUSE doses are needed to maintain the gain.

CONCLUSION

This report illustrates the potential of MUSE stem cell therapy to reverse aspects of biological aging, as measured by cutting-edge epigenetic clocks. Both patients experienced notable de- aging of multiple organ systems, particularly the brain and immune system, alongside a reduction in inflammatory epigenetic markers. These findings support the concept that aging may be modifiable and even reversible in specific biological domains. MUSE cells' unique dual role – regenerative and immunomodulatory – may simultaneously address degenerative changes and chronic inflammation, two key hallmarks of aging. While acknowledging this is a limited two- case observation, it provides a compelling rationale for further research: formal clinical trials with larger cohorts and control groups should investigate MUSE cell therapy as a potential geriatric intervention. Such studies should incorporate comprehensive epigenetic clock panels and functional health outcomes to validate if MUSE-induced epigenetic rejuvenation correlates with clinical rejuvenation. In summary, this report adds to growing evidence that biological age is not immutable and raises the exciting possibility that cellular therapies can induce meaningful age reversal, opening new avenues in regenerative medicine and longevity science.

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