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CASE REPORT

Multi-Differentiating Stress-Enduring (MUSE) Cell and Exosome Therapy in Inflammatory Disease: A Two-Patient Case Series with Epigenetic Biomarker Assessment

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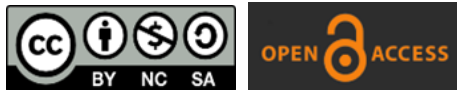

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Abstract

Background: DNA methylation–based epigenetic clocks are increasingly used to estimate biological age and to track aging-related physiology in both chronic disease management and longevity-focused care. These assessment tools are heterogeneous: some models prioritize chronological-age prediction, whereas others emphasize morbidity/mortality risk, methylation variability ("biological noise"), organ-system aging patterns, or pace-of-aging metrics. In rheumatoid arthritis (RA), inflammation has been associated with epigenetic age acceleration, including findings reported using second-generation clocks such as GrimAge and GrimAge2. Multilineage-differentiating stress-enduring (MUSE) cells are endogenous, non-tumorigenic reparative stem cells with reported damage-site homing and immunomodulatory effects; contemporary reviews and clinical-trial experience describe intravenous administration of donor MUSE cells without human leukocyte antigen (HLA) matching or immunosuppression in select indications.

Objective: To describe the clinical outcomes and epigenetic aging findings observed following MUSE cell and exosome therapy in two patients undergoing regenerative and longevity-focused treatment.

Case presentation: We present two patients who underwent MUSE cell and exosome therapy. The first patient was a 45-year-old male with rheumatoid arthritis and chronic multisite inflammatory musculoskeletal pain. The second patient was a 52-year-old female pursuing longevity-focused care after demonstrating elevated biological age estimates and unfavorable pace-of-aging metrics.

Conclusion: In this two-patient case series, following MUSE cell and exosome therapy, favorable patient-reported and epigenetic aging outcomes were reported. These outcomes included improved mobility, reduced inflammatory symptoms, decreased analgesic use, and improvements in biological aging metrics such as OrganSystemAge, OmniAge, and pace-of-aging outputs. These findings support further investigation into the relationship between regenerative therapies and biological aging metrics.

Keywords: MUSE cells; Exosomes; Rheumatoid arthritis; Immune system aging; Epigenetic aging; DNA methylation biomarkers; SystemAge; TruDiagnostic; Glucocorticoids; Metabolic dysfunction; Regenerative medicine.

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1. Introduction

DNA methylation–based epigenetic clocks have garnered attention in both chronic disease research and longevity-focused medicine as tools for estimating biological age and aging-related physiologic decline [1], [2]. In contrast to chronological age, biological age is intended to reflect the cumulative effects of inflammation, cellular stress, and systemic dysfunction on tissues and organ systems over time [2], [3]. A growing number of epigenetic clock platforms have been developed, each with differing methodologies and clinical applications. While some models are designed primarily to predict chronological age, others assess factors such as morbidity and mortality risk, methylation variability ("biological noise"), organ-system aging patterns, and pace-of-aging metrics such as SystemsAge [1], [4]. One example is SystemsAge, which utilizes a single blood methylation test to characterize physiological aging across multiple body systems [5]. As a result, epigenetic age testing is being utilized as a marker of aging and to investigate its potential in monitoring disease burden and responses to therapeutic interventions.

Rheumatoid arthritis (RA) is a complex inflammatory autoimmune disease associated with chronic joint inflammation and systemic inflammatory burden [6]. In addition to its musculoskeletal manifestations, chronic inflammation in RA has also been linked to accelerated biological aging [6]. Studies using second-generation epigenetic clocks, including GrimAge and GrimAge2, have demonstrated evidence of epigenetic age acceleration in inflammatory disease states, suggesting that persistent inflammation may contribute to physiologic decline and increased morbidity risk [6]. These findings have generated growing interest in therapies aimed at both reducing inflammation and promoting tissue repair. One emerging approach involves multilineage-differentiating stress-enduring (MUSE) cells, a unique endogenous subset of mesenchymal stem cells with pluripotent-like differentiation potential, non-tumorigenicity, and selective homing to sites of tissue injury [7]. Similar to prior mesenchymal stem cell–based therapies investigated in rheumatoid arthritis, MUSE cells also demonstrate immunomodulatory and reparative properties that may support systemic recovery and reduction of inflammatory burden [8]. Early clinical experience has further described the intravenous administration of donor-derived MUSE cells without the need for HLA matching or immunosuppression in select conditions, highlighting their potential therapeutic versatility and safety profile [9].

In this case series, we present two patients undergoing MUSE cell–based regenerative therapy for rheumatoid arthritis and longevity-focused care, who have shown reductions in serial DNA

methylation–based epigenetic aging assessments. This paper presents a case series exploring the potential impact of MUSE cell and exosome therapy on RA and longevity-focused care, utilizing DNA methylation-based measures of biological age.

2. Case Presentations

We report two patients who received MUSE cell and exosome therapy: an individual with rheumatoid arthritis and chronic inflammatory musculoskeletal pain (Case 1) and an individual seeking longevity-focused care with serial epigenetic aging assessments (Case 2). Epigenetic aging assessments were obtained using commercially available DNA methylation-based platforms, which estimate biological age using blood-derived methylation signatures. Reported outputs included OrganSystemAge estimates, composite biologic age metrics (TruDiagnostic, OmniAge/System Age), and pace of aging measures.

3. Case 1 Presentation

A 45-year-old male presented for evaluation of chronic inflammatory and autoimmune-related musculoskeletal pain involving the shoulders and knees, with associated plantar fasciitis and heel spur symptoms. The patient had a diagnosis consistent with rheumatoid arthritis and was treated with tocilizumab in combination with chronic systemic corticosteroids [10]. The shared therapeutic goal was to pursue regenerative interventions while reducing long-term steroid dependence. The patient subsequently underwent regenerative therapy incorporating MUSE cells and exosomes. He first received an intravenous infusion containing 80 million MUSE cells and exosomes. On the following day, he underwent fat grafting to the knee and shoulder with targeted local administration of approximately 40 million MUSE cells and 200 billion exosomes to the treated regions.

The dosing and route of administration were selected based on available preclinical studies and early-phase clinical trials of Muse cell–based therapies, which have reported intravenous dosing within the range of approximately 1.5×10^6 to 1.5×10^7 cells per administration and support the use of systemic delivery approaches [12]. Muse cells are also known to preferentially home to sites of tissue injury following intravenous administration, providing a mechanistic rationale for this route [12].

Given the evolving nature of regenerative therapies, the specific dosing and combination of systemic and local administration used in this case were guided by clinical judgment and institutional experience, as standardized protocols for higher dosing strategies, local delivery, and exosome administration have not yet been established.

To characterize systemic biologic response, epigenetic aging was assessed using the SystemAge platform, which derives organ-system–specific biological aging signatures from blood-based epigenetic markers. At baseline, the patient demonstrated accelerated immune system biological aging relative to chronological age (Fig. 1), consistent with an immune-system aging profile elevated relative to chronological age. Following regenerative therapy, repeat testing demonstrated a shift in immune aging metrics toward a comparatively younger pattern: the immune system profile showed a lower estimated immune system biological age relative to baseline (Fig. 2), and the post-treatment immune summary visualization was also consistent with improvement, reflecting an immune aging signature that moved toward (and below) chronological age expectations (Fig. 3). In addition, analysis of epigenetic variability demonstrated stabilization of the aging entropy curve following treatment (Fig. 4), which may reflect changes in methylation variability and reduced "biological noise" within aging-related dynamics.

System-level deviations between estimated biological age and chronological age were also evaluated. On the post-treatment multi-system deviation plot, the immune system demonstrated a marked negative deviation (Fig. 5), indicating that immune system biological age was estimated to be several years younger than the patient's chronological age at the time of testing (45.7 years). Importantly, this immune system deviation ranked among the more pronounced "younger-than-chronological" systems within the profile, suggesting a comparatively younger immune-system aging profile relative to chronological age following treatment (Fig. 5). At the overall level, the patient's post-treatment SystemAge was 38.9 years compared with a chronological age of 45.7 years, indicating an overall biological age estimate approximately 6.8 years younger than chronological age at the time of measurement (Fig. 6). No adverse events were reported during or after infusion and procedural interventions, and the patient described subjective improvement in vitality.

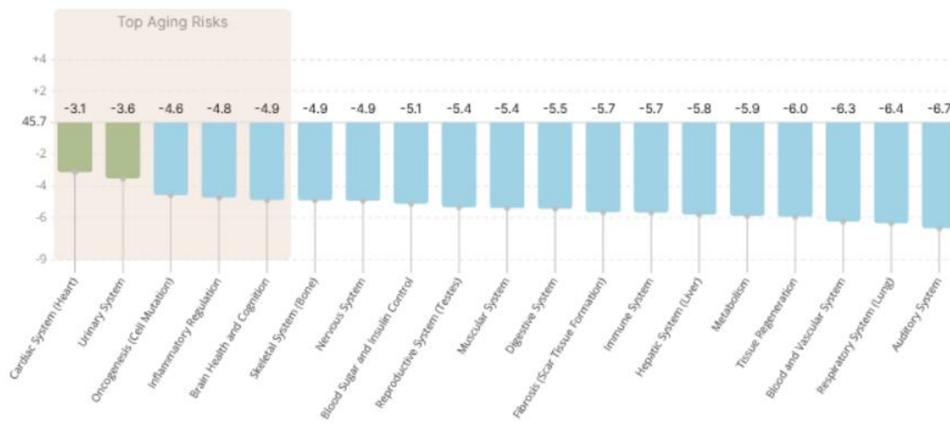

Fig. 1. SystemAge profile prior to MUSE cell and exosome therapy, demonstrating accelerated biological aging relative to chronological age.

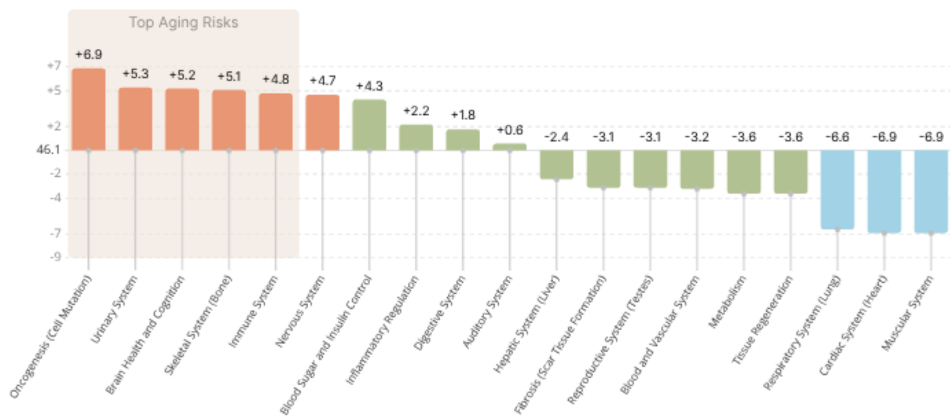

Fig. 2. SystemAge profile following MUSE cell and exosome therapy, demonstrating reduction in biological age compared with baseline.

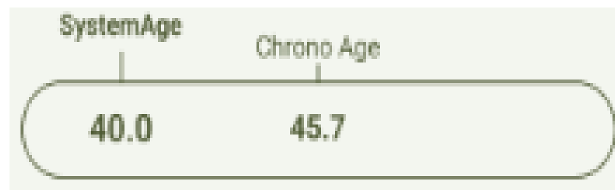

Fig. 3. Post-treatment immune age summary illustrating improvement in immune system biological aging following regenerative therapy.

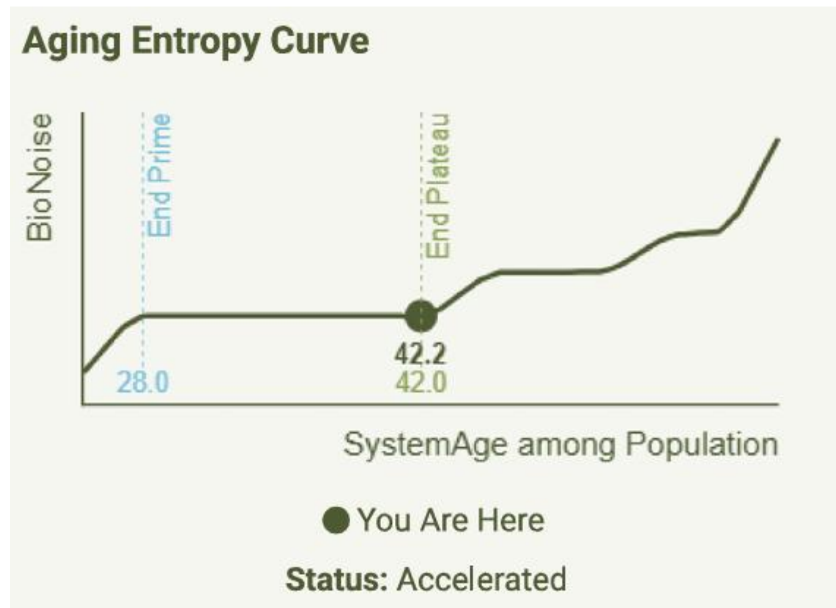

Fig. 4. Post-treatment aging entropy curve demonstrating stabilization of biological noise and improved epigenetic aging dynamics following MUSE cell and exosome therapy.

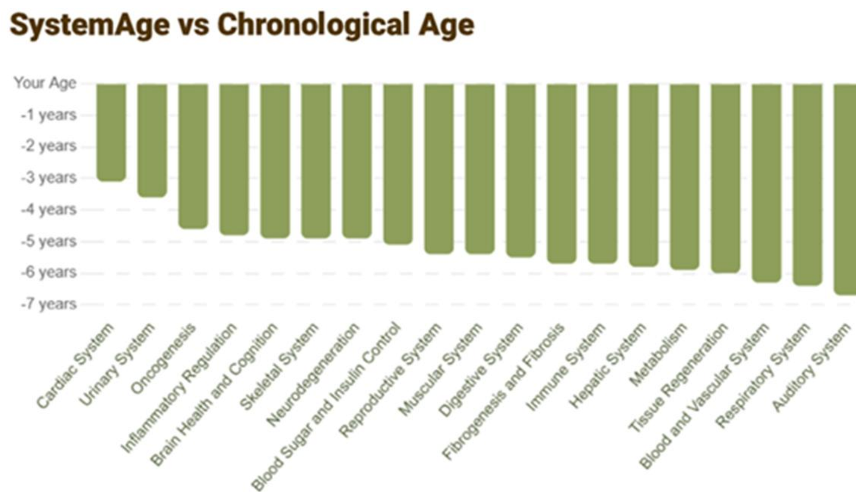

Fig. 5. The bar graph shows system-level differences (years) between estimated biological age and chronological age at the time of testing, where negative values denote biological age younger than chronological age. The immune system exhibits a marked negative deviation, indicating a biologically younger immune aging profile relative to chronological age.

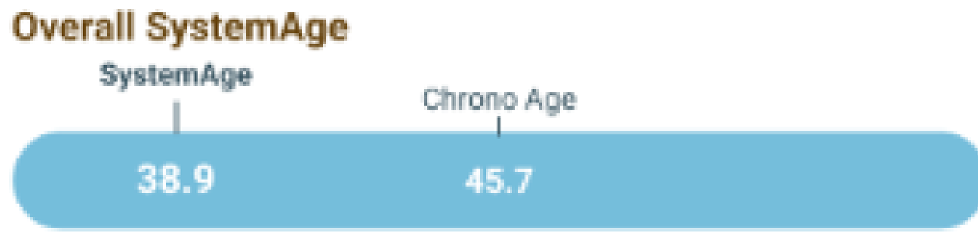

Fig. 6. Overall SystemAge following MUSE cell and exosome therapy. The summary visualization depicts the patient's estimated post-treatment SystemAge (38.9 years) compared with chronological age at the time of testing (45.7 years), demonstrating an overall biological age that is approximately 6.8 years younger than chronological age and consistent with a global shift toward a more favorable biological aging profile following regenerative therapy.

4. Case 2 Presentation

A 52-year-old female presented seeking longevity-focused regenerative treatment and biologic age optimization. Relevant medical history and concomitant medications were not available in the provided record. The patient underwent intravenous regenerative therapy consisting of 20 million MUSE cells followed by administration of 200 billion MUSE-derived exosomes. The dosing and route of administration were selected based on emerging evidence from preclinical studies and early-phase clinical trials demonstrating the safety and therapeutic potential of intravenously delivered Muse cells. Prior studies have reported intravenous dosing in the range of approximately 1.5×10^6 to 1.5×10^7 cells per administration, supporting the use of similar dosing strategies in clinical contexts [12]. Muse cells have also been shown to preferentially home to sites of tissue injury following systemic administration, providing further rationale for the intravenous route [12]. At present, standardized dosing guidelines for Muse-derived exosomes remain limited; therefore, the exosome dose was determined based on available translational literature and institutional clinical practice. Current literature on Muse-derived exosomes highlights their emerging role as a cell-free therapeutic platform but does not establish definitive dosing parameters.

To characterize systemic biologic response, longitudinal aging-biomarker testing was obtained using commercial epigenetic aging reports supplied by the patient via TruDiagnostic (TruDiagnostic.com), including OrganSystemAge outputs, ChronoAge versus OmniAge comparison, and pace-of-aging

metrics. Baseline and most recent follow-up results are summarized in Figs 7–9. On OrganSystemAge profiling, the patient demonstrated improvement across reported organ-system age estimates; for example, estimated liver biological age decreased from 46.2 years at baseline to 38.5 years at follow-up (Fig. 7). Additional OrganSystemAge domain values also shifted toward younger biological-age estimates on follow-up (Fig. 7). On the composite epigenetic age output, OmniAge decreased on serial testing relative to baseline (Fig. 8). Pace-of-aging outputs also improved on follow-up testing, consistent with a shift toward a slower estimated aging rate relative to age-matched norms (Fig. 9) [11].

Fig. 7 provides a baseline-versus-follow-up OrganSystemAge comparison from TruDiagnostic. In addition to the improvement in liver age (46.2 years at baseline to 38.5 years at follow-up), all other displayed organ-system age estimates in the provided report shifted toward younger biological-age values at the most recent follow-up (Fig. 7). Fig. 8 compares chronological age with the OmniAge estimate on serial testing and demonstrates a downward shift in OmniAge from baseline to the most recent measurement (Fig. 8). Fig. 9 summarizes the pace-of-aging output, which also improved on follow-up, supporting a more favorable estimated aging-rate trajectory compared with the baseline report (Fig. 9). These results are descriptive and hypothesis-generating and do not establish causality.

ORGAN SYSTEM	Apr 09, 2026	Feb 18, 2026	Dec 29, 2025	Aug 02, 2025
Blood	39.6	39.3	40.9	42.2
Brain	38.3	44.3	42.4	43.7
Inflammation	41.2	46.9	42.5	46.5
Heart	43.8	46.7	43.4	43.9
Hormone	44.8	46.7	48.4	47.9
Immune	42.2	47.3	43.9	44.9
Kidney	40.9	45	43.9	44.7
Liver	38.5	46.9	43.3	46.2
Metabolic	38.7	45.2	43	43.4
Lung	42	47.4	50.2	47.1
Musculoskeletal	40.1	43.8	45.9	44.7

Note: *Original data were supplied by the authors as a figure and reformatted by the editorial office into a table for improved readability.*

Fig. 7. Case 2 OrganSystemAge report (TruDiagnostic): baseline versus most recent follow-up organ-system aging profile comparison. Reported domain estimates shifted toward younger biological-age values on follow-up; for example, liver biological age decreased from 46.2 years at baseline to 38.5 years at follow-up.

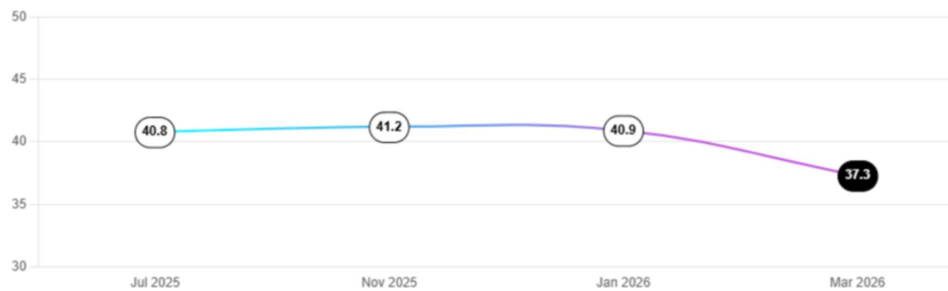

Fig. 8. Case 2 chronological age versus OmniAge (TruDiagnostic) on serial testing. OmniAge decreased from baseline to the most recent follow-up measurement.

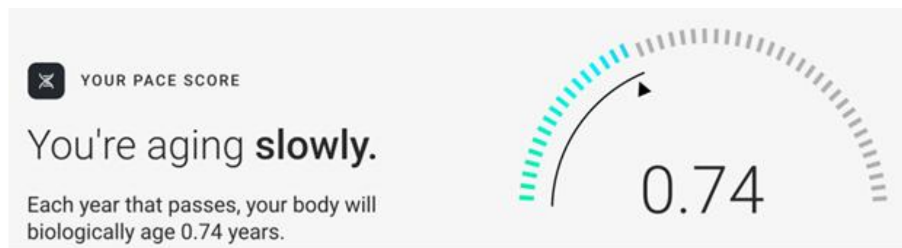

Fig. 9. Case 2 pace-of-aging output (TruDiagnostic). The follow-up output showed improvement versus baseline, consistent with a slower estimated aging rate relative to age-matched norms.

5. Discussion

This two-patient case series describes the clinical experiences and outcomes of: (1) a middle-aged male with rheumatoid arthritis (RA) and chronic inflammatory multisite musculoskeletal pain who underwent combined intravenous and local regenerative biologic therapy using MUSE cells and exosomes**,** followed by a structured recovery program and later major metabolic intervention (gastric bypass); and (2) a 52-year-old female who pursued longevity-focused regenerative treatment using intravenous MUSE cells and exosomes with serial epigenetic age reporting over time. MUSE cells are characterized in contemporary reviews as endogenous reparative stem cells with pluripotent-like and macrophage-like functions, including damage-site homing through sphingosine-1-phosphate signaling and tissue repair via phagocytosis-coupled differentiation and immunomodulatory effects [12], [13]. These proposed reparative and immunomodulatory properties provide a potential explanation for the evaluation of clinical changes observed following treatment in this series. For example, in Case 1, the

clinical course documented progressive functional improvement (shoulder mobility), pain resolution (knee), and improvement in inflammatory hand symptoms, alongside the ability to taper corticosteroids and analgesics.

A key contextual factor in improving Case 1's status is the patient's baseline exposure to chronic systemic glucocorticoids and the resulting metabolic consequences. Long-term glucocorticoid therapy is strongly linked to adverse metabolic outcomes, including insulin resistance, diabetes, and weight gain [14], [15]. The patient's later course included bariatric surgery with substantial weight loss and a reduced inflammatory burden; systematic review evidence suggests that bariatric/metabolic surgery may be associated with improved RA disease activity and inflammatory markers in obese cohorts, although the evidence remains limited and heterogeneous [16]. RA itself is associated with increased cardiometabolic risk and systemic inflammation that can influence multiple organ systems, supporting a rationale for multidomain outcome tracking [17]. Therefore, a potential biological explanation is that both bariatric surgery and reduced steroid exposure with weight loss contributed to improvements in systemic inflammation and symptom burden, independent of regenerative interventions.

In terms of the epigenetic aging measurements, the current findings should be considered hypothesis-generating given the limited direct evidence linking regenerative biologic therapies to changes in epigenetic age. DNA methylation–based clocks estimate biological age and correlate with health risks, with Horvath's multi-tissue work serving as a foundational demonstration of strong chronological-age correlation [18]. More recent studies emphasize that clock predictions may have limitations in individual-level resolution and suggest that alternative approaches focusing on methylation variability ("biological noise") may better reflect dysregulation associated with aging and disease states [19]. Commercial platforms increasingly provide multi-output reports (e.g., organ-system aging, composite biological age, and pace-of-aging); however, interpretation frameworks vary and are not yet standardized across clinical settings [12], [20]. In rheumatoid arthritis, second-generation clocks (e.g., PhenoAge/GrimAge and related accelerations) have shown associations with disease status and adverse outcomes, supporting the biological plausibility of inflammation-linked age acceleration signals [6], [21]. Within this case series, improved immune system aging signals were observed in the context of MUSE cell/exosome treatment alongside concurrent steroid reduction and weight loss in Case 1, while Case 2 involved longitudinal monitoring through serial commercial epigenetic aging assessments after MUSE cell/exosome treatment in a longevity-focused patient.

Mechanistically, an immunomodulatory and reparative pathway is biologically plausible for both MUSE cells and exosomes. Contemporary reviews describe MUSE cells as possessing reported immune-tolerant behavior, proposed damage-site homing, and anti-inflammatory paracrine effects, while early clinical-trial programs have reported intravenous administration of donor-derived MUSE cells without the need for HLA matching or immunosuppressive therapy in select indications [9], [13], [14]. Exosomes, a subtype of extracellular vesicles, act as carriers of proteins, RNAs, and other bioactive cargo that have been implicated in the modulation of immune responses, cellular signaling, and tissue repair processes [22], [23]. Together, these findings provide a biologically plausible rationale for continued investigation of MUSE cell and exosome-based therapies, though causal clinical effects cannot be established from the present case series.

6. Limitations

This report is limited by its uncontrolled, two-patient case-series design and reliance on clinical documentation rather than standardized prospective outcome measures. Independent validation across diverse clinical cohorts remains limited [12], [19].

Major confounders include medication changes (corticosteroid taper), intensive adjunctive rehabilitation modalities, and subsequent bariatric surgery and weight loss, which has published associations with improved RA outcomes and inflammatory markers [14]. Additionally, chronic systemic glucocorticoids can worsen metabolic status and inflammation-linked risk profiles, so discontinuation itself may have improved both clinical symptoms and system-level aging signals [14], [15]. Future work would be strengthened by standardized RA disease activity scoring, validated functional outcomes, serial inflammatory biomarkers, and parallel epigenetic clocks (e.g., multi-clock panels) to contextualize measurement variability [18], [19].

Since direct evidence linking MUSE/MSC therapy to improvements in proprietary organ-system methylation clocks such as SystemAge or OmniAge remains limited, observed changes in organ-system epigenetic age should be interpreted as exploratory and hypothesis-generating rather than causal.

7. Conclusion

In this two-patient case series, combined MUSE cell and exosome therapy was associated with improvement in patient-reported symptoms in a patient with rheumatoid arthritis and chronic

inflammatory musculoskeletal pain (Case 1), including improved mobility, reduced pain, and decreased corticosteroid and analgesic use. In a second patient pursuing longevity-focused treatment (Case 2), serial epigenetic aging reports were available for longitudinal assessment (OrganSystemAge profiles, ChronoAge vs OmniAge, and pace-of-aging outputs). Although limited by the case-series design and concurrent interventions, these findings support further controlled investigation of regenerative therapies and epigenetic aging outcomes in inflammatory disease.

8. Patient Consent

Written informed consent was obtained from the patients for publication of this case report and accompanying images.

9. Conflicts of Interest

The authors declare no conflicts of interest.

10. References

1. Chen BH, Marioni RE, Colicino E, et al. DNA methylation-based measures of biological age: meta-analysis predicting time to death. Aging (Albany NY). 2016;8(9):1844-1865. PubMed | CrossRef
2. Jylhävä J, Pedersen NL, Hägg S. Biological age predictors. EBioMedicine. 2017;21:29-36. PubMed | CrossRef
3. Yamada H. Epigenetic clocks, resilience, and multi-omics ageing: A review and the EpiAge-R conceptual framework. Int J Mol Sci. 2026;27(4):1908. PubMed | CrossRef
4. Oblak L, van der Zaag J, Higgins-Chen AT, et al. A systematic review of biological, social and environmental factors associated with epigenetic clock acceleration. Ageing Res Rev. 2021;69:101348. PubMed | CrossRef
5. Sehgal R, Markov Y, Qin C, et al. Systems Age: a single blood methylation test to quantify aging heterogeneity across 11 physiological systems. Nat Aging. 2025;5(9):1880-1896. PubMed | CrossRef
6. Ou Y, Wang Z, Yuan Y, et al. Epigenetic age acceleration and rheumatoid arthritis: An NHANES-based analysis and survival prediction models. Clin Epigenetics. 2025;17(1):111. PubMed | CrossRef
7. Alanazi RF, Alhwity BS, Almahlawi RM, et al. Multilineage differentiating stress enduring (Muse) cells: A new era of stem cell-based therapy. Cells. 2023;12(13):1676. PubMed | CrossRef
8. Sarsenova M, Issabekova A, Abisheva S, et al. Mesenchymal stem cell-based therapy for rheumatoid arthritis. Int J Mol Sci. 2021;22(21):11592. PubMed | CrossRef

9. Minatoguchi S, Fujita Y, Niizuma K, et al. Donor Muse cell treatment without HLA-matching tests and immunosuppressant treatment. Stem Cells Transl Med. 2024;13(6):532–545. PubMed | CrossRef
10. American College of Rheumatology. Tocilizumab (Actemra): Patient information; 2025.
11. TruDiagnostic. TruDiagnostic epigenetic testing and biological age analysis platform [Internet]. [cited 2026 Apr]. Available from: https://www.trudiagnostic.com/
12. Dezawa M. Macrophage- and pluripotent-like reparative Muse cells are unique endogenous stem cells distinct from other somatic stem cells. Front Bioeng Biotechnol. 2025;13:1553382. PubMed | CrossRef
13. Kuroda Y, Oguma Y, Hall K, et al. Endogenous reparative pluripotent Muse cells with a unique immune privilege system: Hint at a new strategy for controlling acute and chronic inflammation. Front Pharmacol. 2022;13:1027961. PubMed | CrossRef
14. Pofi R, Caratti G, Ray DW, et al. Treating the side effects of exogenous glucocorticoids; can we separate the good from the bad? Endocr Rev. 2023;44(6):975-1011. PubMed | CrossRef
15. Li J-X, Cummins CL. Fresh insights into glucocorticoid-induced diabetes mellitus and new therapeutic directions. Nat Rev Endocrinol. 2022;18:540–557. PubMed | CrossRef
16. Miladi S, Makhlouf Y, Boussaa H, et al. Effect of bariatric and metabolic surgery on rheumatoid arthritis outcomes: A systematic review. PLOS One. 2023;18(11):e0294277. PubMed | CrossRef
17. Corrao S, Calvo LL, Giardina A, et al. Rheumatoid arthritis, cardiometabolic comorbidities, and related conditions: need to take action. Front Med. 2024;11:1421328. PubMed | CrossRef
18. Horvath S. DNA methylation age of human tissues and cell types. Genome Biol. 2013;14(10):R115. PubMed | CrossRef
19. Mei X, Blanchard J, Luellen C, Conboy MJ, Conboy IM. Fail-tests of DNA methylation clocks, and development of a noise barometer for measuring epigenetic pressure of aging and disease. Aging (Albany NY). 2023;15(17):8552–8575. PubMed | CrossRef
20. Generation Lab. Generation Lab introduces SystemAge platform measuring aging speed and "biological noise" across 19 organ systems [Internet]. GlobeNewswire. 2024 May 31 [cited 2026 Apr]. Available from: https://www.globenewswire.com/
21. Mukherjee N, Harrison TC. Epigenetic aging and rheumatoid arthritis. J Gerontol A Biol Sci Med Sci. 2024;79(1):glad213. PubMed | CrossRef
22. Kalluri R. The biology and function of extracellular vesicles in immune response and immunity. Immunity. 2024;57(8):1752–1768. PubMed | CrossRef
23. Kumar MA, Baba SK, Sadida HQ, et al. Extracellular vesicles as tools and targets in therapy for diseases. Signal Transduct Target Ther. 2024;9(1):27. PubMed | CrossRef