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Systemic aging delay and anti-aging therapy using allogeneic stem cells

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ABSTRACT

Allogeneic stem cells derived from umbilical cord tissue, placenta, and umbilical cord blood have shown potential in treating delayed systemic aging and aging-related diseases. Aging induces cellular senescence, oxidative stress, chronic inflammation, and stem cell depletion, all of which contribute to tissue damage and functional decline. Recent advances in regenerative medicine suggest that allogeneic stem cells can mitigate these aging processes through immunomodulation and tissue regeneration. In particular, umbilical cord-derived mesenchymal stem cells have gained attention for clinical applications owing to their strong immunomodulatory properties and low immunogenicity. These cells can repair damaged tissues and enhance metabolic and cognitive function by secreting various cytokines, growth factors, and exosomes, offering potential treatment for aging-related conditions such as osteoporosis and neurodegenerative disorders. Both clinical and preclinical studies indicate that allogeneic stem cells play a critical role in alleviating these diseases, including osteoporosis, osteoarthritis, cardiovascular diseases, and neurodegenerative disorders. Despite their therapeutic potential, challenges remain, such as immune compatibility, long-term safety, and the lack of standardized protocols for large-scale production. This review outlines the biological mechanisms by which allogeneic stem cells contribute to delayed aging, summarizes current clinical research, and explores future prospects. Allogeneic stem cells may offer novel strategies for delaying aging and extending lifespan.

Keywords: Allogeneic Transplantation; Anti-aging; Stem Cells; Mesenchymal Stem Cells; Umbilical Cord

Introduction

Aging is a complex biological process characterized by the gradual decline of organ and tissue function, along with an increased risk of disease [1]. As global life expectancy continues to rise, the need for effective strategies to delay aging and extend healthspan has become increasingly imperative. Allogeneic stem cells, obtained from donor sources, have garnered attention given their applicability in regenerative medicine for delaying aging and treating age-related disorders [2]. Systemic aging involves complex biological mechanisms, including cellular senescence, oxidative stress, inflammation, telomere shortening, and impaired stem cell function. Together, these factors disrupt tissue homeostasis and organ function [3]. Understanding the molecular and cellular mechanisms underlying aging is essential for both understanding the aging process and developing therapeutic approaches to counteract it. Recent studies have demonstrated the rejuvenating potential of various allogeneic stem cell sources—such as the umbilical cord, placenta, and adipose tissue—in aging tissues [4]. Advances in stem cell biology and regenerative medicine continue

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to harness the therapeutic potential of these cells to mitigate the signs of aging and restore the function of multiple organ systems [5].

Characteristics and Classification of Allogeneic Stem Cells

Definition and benefits of allogeneic stem cells

Allogeneic stem cells are derived from a donor who is genetically distinct from the recipient. Unlike autologous stem cells, which are sourced from the patient's body, allogeneic stem cells from sources such as umbilical cord blood, placental tissue, bone marrow, and adipose tissue are obtained from healthy donors. These cells possess the remarkable ability to differentiate into multiple lineages, such as osteogenic, chondrogenic, adipogenic, and neurogenic, enabling their use in tissue repair and regeneration [6].

Among the many advantages of allogeneic stem cells, immediate availability is a key benefit. Without the need for patient-specific harvesting and processing, they can be prepared, stored, and readily deployed for clinical use. This feature is particularly valuable in medical settings, where timely intervention is critical. Moreover, stem cells derived from umbilical cord or placental sources are considered immunologically immature, thereby reducing the risk of immune rejection compared to other cell types [7]. In the context of anti-aging therapy, allogeneic stem cells help replenish damaged or senescent cells, thereby supporting tissue homeostasis and preserving organ function [8]. Furthermore, these cells secrete a diverse array of bioactive molecules—anti-inflammatory cytokines, growth factors, and extracellular vesicles—that modulate inflammation, reduce oxidative stress, and improve the cellular microenvironment [9]. Additionally, allogeneic stem cells contribute to the regeneration of aged tissues and organs by enhancing angiogenesis, improving mitochondrial function, and stimulating endogenous stem cells [10]. These combined effects support improvements in skin elasticity, cognitive function, and overall physiological resilience against age-related decline. Recent advances in cell processing technologies, including gene editing and immune modulation strategies, have further increased the safety and efficacy of allogeneic stem cell therapies in anti-aging applications. As a result, these therapies are being more actively explored for clinical use to extend healthspan and improve quality of life in aging populations.

Umbilical cord-derived MSCs or Wharton's jelly-derived MSCs

Umbilical cord-derived mesenchymal stem cells (UC-MSCs), particularly those isolated from Wharton's jelly—a gelatinous connective tissue within the umbilical cord—are a valuable noninvasive source of stem cells for regenerative therapies. Characterized by a high proliferation rate, UC-MSCs enable the production of large quantities of cells, which is essential for therapeutic applications [11]. These cells have demonstrated significant immunomodulatory effects, capable of influencing both innate and adaptive immune responses. This is especially important for reducing inflammation and preventing immune-mediated tissue damage [11]. One major advantage of UC-MSCs is their low immunogenicity, allowing their use in allogeneic transplantation with minimal risk of rejection. Additionally, as the umbilical cord is a postnatal structure, UC-MSCs are not associated with ethical concerns surrounding embryonic stem cells [11]. In the context of the anti-aging therapy, UC-MSCs show considerable potential owing to their ability to differentiate into various lineages, including osteoblasts, chondrocytes, adipocytes, and neurons [12]. This multipotency supports the regeneration of damaged tissues across multiple organ systems. In addition, UC-MSCs secrete a wide range of paracrine factors—such as growth factors, cytokines, and extracellular vesicles—that contribute to tissue repair, increased angiogenesis, and oxidative stress modulation [13]. These secretions play a pivotal role in rejuvenating aged tissues by enhancing skin elasticity, improving cardiovascular function, and ameliorating neurodegenerative changes associated with aging [13].

Placenta-derived MSCs

Placenta-derived mesenchymal stem cells (P-MSCs) represent a promising and emerging source of stem cells for both regenerative and anti-aging therapies [14]. These cells originate from the placenta—an organ typically discarded after birth—and thus provide an abundant and ethically noncontroversial source of MSCs. P-MSCs can be readily isolated from various placental tissues, including the amniotic membrane, chorionic villi, and decidua, making their procurement relatively simple and scalable [14]. P-MSCs hold significant potential in mitigating systemic aging processes characterized by chronic low-grade inflammation and acute immune dysfunction, owing to their potent immunomodulatory and anti-inflammatory properties [15]. Through the secretion of anti-inflammatory cytokines and the modulation of immune cell activity, P-MSCs help reduce systemic inflammation, thereby decreasing age-related tissue damage and promoting healthspan extension. These cells exhibit considerable proliferative capacity and the ability to differentiate into multiple lineages, including adipogenic, osteogenic, and neurogenic cells [14]. These features enable P-MSCs to repair and regenerate aged tissues and organs, potentially leading to improvements in cognitive function, bone density, and metabolic health in older individuals. Furthermore, the bioactive factors secreted by P-MSCs can augment mitochondrial function, improve vascular integrity, and promote endogenous repair mechanisms, further reinforcing their role in anti-aging interventions [16].

Umbilical cord blood-derived MSCs

Umbilical cord blood-derived mesenchymal stem cells (UCB-MSCs) represent another promising source of allogeneic stem cells with significant potential for anti-aging applications. Collected non-invasively from umbilical cord blood at the time of delivery, UCB-MSCs are readily accessible and can be cryopreserved for future therapeutic use [17]. These cells are known for their high plasticity, enabling differentiation into various cell types, including hematopoietic, neural, and mesenchymal lineages [17]. One of the most notable characteristics of UCB-MSCs is their remarkable immunosuppressive capacity, which allows them to modulate immune responses, thereby reducing the risk of graft-versus-host disease (GVHD) in allogeneic transplantation settings [18]. This immunomodulatory property is particularly relevant for treating age-related immune dysfunction and chronic inflammation. In addition, UCB-MSCs have demonstrated strong neuroprotective effects [19], making them valuable candidates for treating neurodegenerative diseases such as Alzheimer's and Parkinson's, which are commonly associated with aging. Through the paracrine secretion of neurotrophic factors, UCB-MSCs support neuronal survival, synaptic plasticity, and cognitive function. Beyond their neurological applications, UCB-MSCs contribute to systemic rejuvenation by enhancing vascular regeneration, improving metabolic function, and promoting tissue repair across multiple organ systems [20]. Additionally, their ability to improve mitochondrial efficiency and reduce oxidative stress represents another important mechanism for delaying aging-related physiological decline.

Immunological characteristics and safety of umbilical cord-derived MSCs

UC-MSCs possess highly favorable characteristics for allogeneic transplantation and regenerative therapies [21]. One of their most notable features is low immunogenicity. This is primarily due to their low expression of major histocompatibility complex (MHC) class II antigens and co-stimulatory molecules such as CD40, CD80, and CD86, which are responsible for the activation of T lymphocytes [22]. As a result, the likelihood of eliciting an immune response against the graft is significantly reduced, enabling broader clinical application of UC-MSCs without the need for intensive immunosuppression. Taken together, these attributes allow UC-MSCs to attenuate harmful immune responses while preserving crucial host defense mechanisms. These unique immunological properties make UC-MSCs particularly valuable for minimizing the risk of GVHD, a major complication following allogeneic stem cell transplantation [22].

Regarding safety, UC-MSCs have been rigorously evaluated in both preclinical models and clinical trials, consistently demonstrating a favorable safety profile [23]. Studies report minimal adverse effects following intravenous or local administration. Potential concerns, such as ectopic tissue formation or tumorigenicity, have been thoroughly investigated, with current evidence indicating a low risk when the cells are properly processed and administered. Furthermore, their noninvasive derivation from postnatal tissues such as the umbilical cord significantly lowers the risk of donor-site morbidity and addresses many of the ethical concerns associated with other stem cell sources [24]. The combination of low immunogenicity and a well-established safety record strongly supports the future clinical use of UC-MSCs in anti-aging therapy, immune-mediated conditions, and tissue regeneration [25]. Ongoing research and the development of standardized clinical protocols may further enhance the efficacy and safety of UC-MSC-based treatments.

Mechanisms of Systemic Aging Delay by Allogeneic Stem Cells

Anti-inflammatory and immunomodulatory effects

Aging is closely associated with chronic low-grade inflammation, a phenomenon known as "inflammaging," which contributes to various age-related pathologies such as cardiovascular diseases, neurodegenerative disorders, and metabolic syndrome. Allogeneic stem cells—particularly UC-MSCs, P-MSCs, and UCB-MSCs—exhibit potent anti-inflammatory and immunomodulatory effects that are critical in delaying systemic aging [26,27]. These effects are primarily mediated through the secretion of a diverse array of bioactive molecules, including anti-inflammatory cytokines such as interleukin-10 (IL-10), transforming growth factor-beta, growth factors, and immunoregulatory factors [28]. By modulating the activity of immune cells—including T cells, B cells, natural killer cells, and macrophages—these stem cells suppress the production of pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), thereby fostering an anti-inflammatory milieu. Additionally, these cells promote the expansion of regulatory T cells (Tregs) and inhibit the maturation of dendritic cells, which prevents excessive immune activation [29]. Such mechanisms are essential for mitigating chronic inflammation, a major driver of tissue degeneration and organ function dysfunction. Multiple clinical studies have demonstrated that systemic administration of allogeneic stem cells can reduce inflammatory markers and restore immune homeostasis, ultimately leading to improved physical function and an extended healthspan [30].

Aging has been associated with pervasive but relatively subtle inflammation—an idea often referred to as "inflammaging." This degenerative phase of normal development contributes to the onset of cardiovascular diseases, neurodegenerative disorders, and metabolic syndrome. In particular, allogeneic stem cells—particularly those from UC-MSCs, P-MSCs, and UCB-MSCs—exhibit potent anti-inflammatory and immunomodulatory properties. These effects further support the immune suppression afforded

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by enhanced Treg activity and concurrent inhibition of dendritic cell maturation, which together help suppress excessive immune activation [26]. In the context of aging, these mechanisms are instrumental in counteracting the harmful effects of chronic inflammation, which would otherwise accelerate tissue degeneration and impair organ function. Several clinical studies have reported that systemic administration of allogeneic stem cells reduces inflammatory markers and promotes immune homeostasis, resulting in improved physical function and an extended healthspan [27].

Reduction of oxidative stress and antioxidant mechanisms

Oxidative stress—arising from an imbalance between the production of reduction of oxidative stress (ROS) and the body's antioxidant defenses—plays a central role in aging. Elevated levels of ROS damage cellular components, including DNA, proteins, and lipids, ultimately leading to cellular dysfunction and tissue degeneration [28]. Allogeneic stem cells help mitigate oxidative stress through both direct and indirect mechanisms. They upregulate the expression of endogenous antioxidant enzymes, such as superoxide dismutase, catalase, and glutathione peroxidase, which are particularly vital under conditions of oxidative challenge [29]. Allogeneic stem cells also secrete antioxidant peptides and factors that enhance the resilience of surrounding tissues to oxidative stress [29]. Furthermore, these cells improve mitochondrial function, thereby reducing mitochondrial-derived ROS production [30]. By preserving mitochondrial integrity and bioenergetic efficiency, these cells maintain cellular homeostasis and delay the onset of age-related functional decline [31].

Regulation of cellular senescence and apoptotic pathways

Cellular senescence—the irreversible cessation of cell division—and apoptosis (programmed cell death) are key features of aging and are implicated in tissue dysfunction and age-related diseases [1]. The accumulation of senescent cells within tissues leads to the release of pro-inflammatory factors known as senescence-associated secretory phenotype (SASP), which amplify inflammation and contribute to tissue degradation [32]. Allogeneic stem cells have been shown to modulate these processes through the secretion of factors that promote cell survival, enhance DNA repair mechanisms, and suppress SASP expression [33]. UC-MSCs, specifically, have demonstrated expression of telomerase reverse transcriptase [34], which helps maintain telomere length, thereby delaying replicative senescence. By protecting telomere integrity, these stem cells limit the buildup of dysfunctional cells in aging tissues. In addition, allogeneic stem cells can inhibit pro-apoptotic pathways while activating anti-apoptotic signaling, promoting the survival of cells in aging tissues. These effects are mediated through paracrine signaling that regulates key apoptotic proteins such as Bcl-2 and Bax [35,36]. By reducing cellular senescence and apoptosis, such stem cells may help preserve tissue integrity and maintain functional capacity over time.

Promotion of tissue regeneration and repair

Allogeneic stem cells possess distinctive anti-aging mechanisms, particularly through tissue regeneration and repair. These cells exhibit multipotent lineage differentiation and can replenish damaged or lost cells in various tissues such as the skin, bone, muscle, and the cardiovascular system [37]. Beyond direct differentiation, allogeneic stem cells exert powerful paracrine effects by secreting growth factors (e.g., vascular endothelial growth factor, hepatocyte growth factor, insulin-like growth factor 1) that enhance the recruitment of endogenous progenitor cells, stimulate angiogenesis, and improve extracellular matrix remodeling. Such paracrine signals are vital for accelerating wound healing, restoring normal tissue architecture, and reversing age-related degenerative changes [38]. Collectively, through improving physical performance, reducing frailty, and enhancing the quality of life, these regenerative effects significantly contribute to the well-being of aging populations [39].

Effects on aging-related genes and signaling pathways

Aging is regulated by several key molecular pathways and genes that regulate cellular longevity, metabolism, and stress responses. Allogeneic stem cells can modulate these aging-related pathways, thereby contributing to systemic aging delay. One of the primary pathways affected by stem cells is the mechanistic target of rapamycin (mTOR), which plays a central role in regulating cell growth, metabolism, and autophagy. Autophagy-stimulating factors secreted by stem cells inhibit mTOR signaling, which promotes autophagy, enhances mitochondrial function, and improves metabolic efficiency, all of which are associated with increased longevity and delayed aging [40]. Furthermore, allogeneic stem cells are known to enhance the expression of sirtuins, which are NAD^+-dependent deacetylases that regulate gene expression, DNA repair, and metabolic homeostasis. Increased sirtuin activity, particularly that of SIRT1 and SIRT3, has been linked to improved mitochondrial function, enhanced stress resistance, and prolonged cellular lifespan [41]. Stem cells also influence the p53 pathway, a major regulator of cell cycle arrest, apoptosis, and genomic stability. Modulating p53 activity by allogeneic stem cells promotes wound repair while preventing cellular, thereby maintaining tissue homeostasis throughout aging [42]. Collectively, their effects contribute to cellular resilience of cells, improved metabolic function, and delayed onset of age-related diseases, positioning allogeneic stem cells as highly promising agents for systemic anti-aging interventions.

Clinical Studies and Application Cases of UC-MSCs

Reduction of systemic inflammation

Clinical trials involving UC-MSCs have demonstrated significant reductions in systemic inflammation, a key marker of aging. Additionally, transplantation of UC-MSCs has been associated with decreased levels of pro-inflammatory cytokines such as IL-6, TNF-α, and C-reactive protein, while levels of anti-inflammatory cytokines such as IL-10 have increased (Table 1) [23,42-51]. These immunomodulatory effects help balance the immune system, enhancing both innate and adaptive immune responses. Clinical evidence also suggests improvements in T-cell proliferation, restoration of Tregs, and increased natural killer cell activity following UC-MSC therapy. Collectively, these changes contribute to better immune surveillance and reduced susceptibility to infections, supporting the reduction of chronic inflammation and delaying the onset of age-related diseases [38].

Metabolic health and physical fitness improvement

Clinical studies indicate that UC-MSC therapy significantly improves metabolic health and physical performance in patients. UC-MSC transplantation has been shown to enhance insulin sensitivity and improve glucose regulation by lowering fasting blood glucose levels [44]. Patients treated with UC-MSCs also exhibited improved lipid profiles, with reductions in total cholesterol, low-density lipoprotein, and triglycerides, whereas their high-density lipoprotein levels were increased [42]. These metabolic benefits help mitigate the risk of type 2 diabetes and cardiovascular disease. In addition, treated individuals showed improvements in muscle mass, hand grip strength, and endurance capacity, as evaluated through physical performance tests such as the 6-minute walk test and handgrip strength assessments [48]. These findings suggest that UC-MSC therapy may counteract age-related sarcopenia and other metabolic declines (Table 1) [50].

Treatment of other conditions

UC-MSC therapy is increasingly being explored for a range of other medical conditions. In randomized clinical trials (RCTs), UC-MSCs have demonstrated both efficacy and safety in treating cesarean section scars, with positive outcomes in scar appearance and skin quality (Table 1) [51]. Additionally, UC-MSC treatment has been expanded to address both symptoms and underlying inflammation of rheumatoid arthritis [38]. UC-MSC therapy has demonstrated significant and safe improvements in disease outcomes for conditions such as Crohn's disease [42].

Potential in preventing and treating geriatric diseases

There is growing evidence supporting the potential of UC-MSCs in the treatment and prevention of various geriatric conditions, including osteoporosis, osteoarthritis, and cognitive decline. Encouraging early results have been reported in clinical practice regarding the use of UC-MSCs to improve bone mineral density, regulate calcium metabolism, and enhance osteoblast activity in patients with osteoporosis, ultimately leading to stronger bone formation and a reduced risk of fractures [46]. In osteoarthritis, intra-articular injections of UC-MSCs have shown significant effects in alleviating joint pain, improving joint function, and promoting cartilage regeneration, as confirmed by MRI and arthroscopic evaluations (Table 1) [45]. In cases of cognitive decline—particularly in the early stages of Alzheimer's disease—UC-MSC treatment has shown potential in preserving cognitive function by reducing amyloid-beta deposition and modulating neuroinflammatory markers [49]. Other clinical reports on patients treated with UC-MSCs indicate general improvements in the quality of life and functional capacity affected by age-associated conditions [46].

Safety and Adverse Effects Reports

Although UC-MSCs have demonstrated significant promise in both preclinical and clinical trials, safety remains an important consideration. Most clinical studies report only minimal adverse effects, typically limited to transient fever, localized swelling at the injection site, and mild fatigue [47]. Immunogenic reactions are rare, largely due to the immunomodulatory properties of UC-MSCs and their low expression of MHC class II molecules [46]. Despite these reassuring findings, long-term safety data are still required to rule out potential risks, such as tumorigenicity, ectopic tissue formation, or organ dysfunction.

Comparison of Current Anti-Aging Therapies and Allogeneic Stem Cell Treatments

Current anti-aging interventions encompass a wide range of drugs, hormones, lifestyle changes, and aesthetic procedures targeting different aspects of the aging process [52]. Pharmacological agents such as retinoids and senolytic compounds aim to protect cells from damage and eliminate senescent cells. Metabolic modulators such as metformin and rapamycin have also been investigated for their potential anti-aging effects [53]. Hormonal therapies—including growth hormone and hormone replacement therapy—seek to counteract age-related hormonal decline; however, they carry potential risks such as metabolic dysregulation

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Table 1. Clinical studies on UC-MSC therapy

Disease category	Study name	Disease/condition	Study type	Injection route	Key findings	Reference
Autoimmune and inflammatory diseases	UC-MSC & Crohn's disease study	Crohn's disease	RCT	Intravenous	Reduced inflammation & symptom improvement	Zhang et al. [42] (2018)
Cardiovascular diseases	RIMECARD trial	Heart failure	Phase 1/2 RCT	Intravenous	Improved cardiac function	Bartolucci et al. [23] (2017)
	UC-MSC & severe systolic heart failure study	Severe systolic heart failure	Clinical study (RCT)	Intracoronary	Improved cardiac function, reduced NT-proBNP levels, & lower mortality rate	Zhao et al. [43] (2015)
Metabolic and liver diseases	UC-MSC & NAFLD/ diabetes study	Type 2 diabetes + NAFLD	Retrospective analysis	Intravenous	Improved liver function & metabolic markers	Zhao et al. [44] (2024)
Musculoskeletal and regenerative medicine	UC-MSC & knee osteoarthritis study	Osteoarthritis	Phase 1/2 RCT	Intraarticular	Improved joint function & pain relief	Matas et al. [45] (2019)
	UC-MSC & bone regeneration study	Osteoporotic bone defects	Experimental treatment	Local injection	Promoted bone regeneration	Hendrijantini et al. [46] (2018)
	UC-MSC & teriparatide study	Osteoporotic vertebral fractures	Phase 1/2a study	Intravenous + subcutaneous	Increased bone density & functional recovery	Shim et al. [47] (2021)
Neurological diseases	UC-MSC & cerebral palsy study	Cerebral palsy	RCT	Intrathecal	Enhanced motor function	Gu et al. [48] (2020)
	UC-MSC & multiple sclerosis study	Multiple sclerosis	Phase 1/2 dose exploration study	Intravenous	Neuroprotective & immunomodulatory effects	Jamali et al. [49] (2024)
Pulmonary diseases	UC-MSC & idiopathic pulmonary fibrosis study	Idiopathic pulmonary fibrosis	Case report	Intravenous	Symptom relief & improved quality of life	Zhang et al. [50] (2017)
Skin and wound healing	UC-MSC & cesarean section scar study	Skin regeneration	RCT	Local injection	Reduced scar formation	Fan et al. [51] (2020)

UC-MSC, umbilical cord-derived mesenchymal stem cell; RCT, randomized controlled trial; NT-proBNP, N-terminal pro B-type natriuretic peptide; NAFLD, non-alcoholic fatty liver disease.

and malignancy [54]. Lifestyle modifications, including caloric restriction and fasting, along with nutraceuticals such as NAD^+ precursors and resveratrol, have been associated with enhanced repair mechanisms and longevity pathways [55]. Aesthetic treatments, such as platelet-rich plasma injections, botulinum toxin injections, and laser procedures, primarily offer superficial improvements without addressing the underlying biological aging process [56]. In contrast, allogeneic stem cell therapies, particularly those using UC-MSCs, adopt a regenerative approach aimed at reducing inflammation, promoting tissue repair, and ultimately reversing certain aspects of age-related degeneration [57]. While these therapies may be viewed as superior due to their distinct mechanisms compared to conventional anti-aging interventions, they remain largely experimental, as robust and sustained clinical evidence is still lacking.

Reality and Limitations of UC-MSC Therapy

Clinical challenges in UC-MSC therapy

Although UC-MSCs are generally considered to have lower immunogenicity than other allogeneic stem cells, concerns regarding immunological rejection remain. The long-term safety of UC-MSC therapy is still unclear, as only a limited number of high-quality RCTs have evaluated post-transplantation complications [58]. Some RCTs have shown promising therapeutic effects; however, these studies were limited by small sample sizes, short follow-up periods, and heterogenous study designs [59]. To better understand complications such as GVHD and tumorigenicity, more extensive, controlled, and long-term safety studies are necessary [59]. The lack of standardization in the isolation, expansion, and characterization of UC-MSCs further complicates the reproducibility and scalability of their clinical application [60]. Variations in donor gestational age, culturing conditions, and cell passage number affect both the quality and potency of UC-MSCs, necessitating robust quality control (QC) measures and standardized protocols [61]. Without these, clinical outcomes may continue to vary across studies. Additionally, economic and ethical barriers are expected to hinder the widespread adoption of UC-MSC therapies. The costs associated with large-scale cell culture, processing, and storage are barriers to scalability, especially in resource-constrained settings [62]. Ethical and legal concerns also restrict the availability of regenerative therapies, emphasizing the importance of comprehensive long-term safety data to support informed consent practices [63]. While UC-MSCs are derived from a noncontroversial source—the umbilical cord post-delivery—their commercial use must still be appropriately regulated to prevent exploitation and unethical practices [64].

Clinical reality and public expectations

A critical challenge in the implementation of UC-MSC therapy lies in the gap between public expectations and clinical reality, particularly in the context of anti-aging applications. Stem cell therapies are often portrayed as "revolutionary" solutions that can regenerate tissues, extend lifespan, and rejuvenate the body. However, scientific evidence supporting these claims remains inconclusive. Most clinical studies investigating the anti-aging effects of stem cells have been limited by cohort size and period of observation, making it difficult to draw conclusions regarding long-term efficacy and safety. While preclinical studies suggest that UC-MSCs can facilitate tissue regeneration through paracrine signaling and immunomodulatory mechanisms, it remains uncertain whether these findings can be translated into reliable and effective human therapies. Furthermore, key considerations such as cellular senescence, sustained engraftment, and potential complications, including fibrosis and tumor formation, require more rigorous investigation before UC-MSCs can be adopted in anti-aging clinical settings [65]. In parallel, regulatory frameworks must evolve to support innovation in stem cell therapies while prioritizing patient safety and preventing premature commercialization [65].

The Role of Family Physicians in Advising Patients about Stem Cell Therapy

Given the current level of scientific evidence, stem cell-based anti-aging therapies should not be recommended as part of routine clinical practice. Although stem cell treatments show promise, their effectiveness for anti-aging applications remains unproven, primarily due to the lack of large-scale, long-term studies demonstrating both efficacy and safety. Family physicians play a critical role in guiding patients by offering evidence-based information and helping to manage expectations regarding these treatments. Physicians should be prepared to counsel patients on the experimental nature of stem cell interventions. Most claims related to rejuvenation and extended longevity are not adequately substantiated. Potential risks, such as immune reactions or exploitation of vulnerable patients through unregulated commercial practices, should also be discussed. Furthermore, physicians can assist patients in distinguishing between legitimate, regulated clinical trials and unproven therapies promoted with exaggerated or misleading claims of success [66]. As stem cell research advances, it is essential for family physicians to stay informed and provide balanced, up-to-date guidance. Until more conclusive clinical evidence becomes available, a cautious, patient-centered approach is warranted to ensure informed decision-making and the minimization of harm to patients.

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Future Perspectives and Directions for Improvement

Potential for gene editing and personalized anti-aging therapies

Gene editing technologies—in particular, clustered regularly interspaced short palindromic repeats/Cas9—hold immense potential for enhancing the therapeutic efficacy of MSCs [67]. By precisely editing genes associated with aging or age-related conditions, it may become possible to significantly boost the regenerative capacity of UC-MSCs [68]. Furthermore, gene editing could allow for the correction of individual genetic predisposition to age-related diseases, thereby personalizing UC-MSC therapy.

Stem cell-derived exosome-based strategies

Exosomes derived from UC-MSCs are gaining growing recognition as a viable alternative to live cell transplantation. The exosomes can carry bioactive molecules, such as proteins, lipids, and RNA, which mediate regenerative effects [69]. A key advantage of exosomes is their ability to cross biological barriers more easily than whole cells, enabling more precise targeting of damaged or diseased tissues and enhancing therapeutic delivery [70].

Combination therapy with senolytic drugs

Senolytic drugs are compounds that selectively eliminate senescent cells—cells that have lost their capacity to divide and contribute to tissue aging [53]. These drugs are emerging as promising tools in regenerative medicine and anti-aging treatments. In combination with UC-MSC therapy, these senolytic drugs may enhance treatment outcomes by addressing both cellular and molecular contributors to aging [71].

Integration with personalized medicine

The integration of UC-MSC therapies with personalized medicine represents one of the most promising developments in regenerative medicine [72]. Personalized medicine seeks to tailor treatment strategies based on the individual's genetic makeup, lifestyle, and comorbid conditions. Recent reports suggest that UC-MSCs can be modified according to patient-specific characteristics, thereby enhancing their therapeutic efficacy while minimizing adverse effects. Through precision approaches, UC-MSC therapy has the potential to improve treatment outcomes in age-related and degenerative diseases [73]. Combining targeted regenerative therapies with individualized patient profiles yields more effective and safer interventions that maximize the regenerative benefits of stem cell treatment [74].

Conclusion

Looking ahead, these emerging therapeutic strategies may help resolve challenges such as immune rejection, standardization, scalability, and cost in stem cell-based anti-aging therapy. UC-MSCs stand out among regenerative modalities due to their safety profile, potent regenerative capacity, and immunomodulatory properties. Continued advancements in gene editing, exosome-based therapies, and combination treatments are likely to increase the clinical applicability of UC-MSCs. Ultimately, these personalized and effective anti-aging therapies are expected to be centered around UC-MSCs.

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Author contribution

Conceptualization: SH, SWK. Formal analysis: SH, SWK. Investigation: SH, SWK. Validation: SH, SWK. Writing–original draft: SH, SWK. Writing–review & editing: SH, SWK. Final approval of the manuscript: all authors.

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