AHEAD OF PRINT

Internal peacekeepers and external mediators: A new model of peripheral immune tolerance involving regulatory T cells and mesenchymal stem cells

Phuc Van Pham[A–F]

VNUHCM-US Stem Cell Institute, University of Science, Vietnam National University Ho Chi Minh City, Vietnam

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

Advances in Clinical and Experimental Medicine, ISSN 1899–5276 (print), ISSN 2451–2680 (online) *Adv Clin Exp Med*. 2026

Address for correspondence
Phuc Van Pham
E-mail: phucpham@sci.edu.vn

Funding sources
None declared

Conflict of interest
None declared

Received on November 17, 2025
Reviewed on January 9, 2026
Accepted on January 11, 2026

Published online on January 23, 2026

Abstract

The 2025 Nobel Prize in Physiology or Medicine honored the seminal discovery that regulatory T cells (Tregs) restrain immune responses and prevent autoimmunity through peripheral immune tolerance. However, to obtain a holistic view of peripheral immune tolerance, it is also necessary to consider the role of mesenchymal stem/stromal cells (MSCs) in this process. Therefore, I propose a two-tier model that incorporates both Tregs and MSCs, with Tregs acting within the immune system as an "internal checkpoint" to temper effector cell activity, and tissue-resident MSCs – or "master signaling cells" – serving as an "external checkpoint." Injury- or pathogen-induced inflammation activates MSCs, which in turn secrete a broad repertoire of immunomodulatory molecules, create a local anti-inflammatory milieu, promote tissue repair, and directly dampen excessive immune activity at the site of damage. The concerted actions of Tregs and MSCs are essential for effective peripheral immune tolerance, shielding the host from pathogens and collateral tissue injury. This model helps explain the pathophysiology of autoimmunity and tumor immune evasion, as well as the therapeutic potential of MSC-based interventions.

Key words: inflammation, immune tolerance, autoimmunity, regulatory T cells, mesenchymal stem/stromal cell

Cite as
Pham PV. Internal peacekeepers and external mediators: A new model of peripheral immune tolerance involving regulatory T cells and mesenchymal stem cells [published online as ahead of print on January 23, 2026]. *Adv Clin Exp Med*. 2026. doi:10.17219/acem/216728

DOI
10.17219/acem/216728

Highlights

- This editorial expands on the 2025 Nobel Prize-recognized role of regulatory T cells by introducing mesenchymal stem/stromal cells (MSCs) as critical "external checkpoints" in immune regulation.
- Tissue-resident MSCs respond to inflammation by secreting immunosuppressive mediators, promoting tissue repair, and locally dampening excessive immune responses, complementing Treg-mediated immune control.
- The integrated Treg–MSC tolerance model provides new insights into autoimmune disease mechanisms and tumor immune evasion, and highlights the therapeutic potential of MSC-based immunomodulatory strategies.

Introduction

The 2025 Nobel Prize in Physiology or Medicine was awarded to Mary E. Brunkow, Fred Ramsdell, and Shimon Sakaguchi for their groundbreaking discovery of regulatory T cells (Tregs) and their role in maintaining immune homeostasis through peripheral immune tolerance.[1] Tregs monitor and suppress effector immune cells, preventing excessive immune responses and shielding host tissues from collateral damage.

Recent studies have revealed the widespread presence of another specialized cell population in most organs: mesenchymal stem/stromal cells (MSCs).[2–7] These adult stem cells possess potent immunomodulatory capacities and have been shown to directly curb excessive inflammatory responses within tissue niches.[8–11]

Building on these observations, I have developed a two-tier model of peripheral immune tolerance that integrates both Tregs and MSCs, with Tregs acting within the immune system as an "internal checkpoint" and tissue-resident MSCs serving as an "external checkpoint." I argue that durable peripheral immune tolerance – particularly in the context of pathogen-induced tissue injury – can be achieved only through the combined activities of these complementary regulatory cell types.

Tregs: The peacekeepers of the immune system

A brief overview of the immune system

The immune system functions as a living shield that protects the host from both exogenous pathogens and aberrant endogenous cells. It is composed of highly specialized cellular subsets that together form a multilayered defense mechanism. The first barrier consists of innate effector cells – macrophages, dendritic cells (DCs), and natural killer (NK) cells – that are capable of immediately eliminating exogenous threats.[12,13] Concomitantly, localized inflammation is initiated, facilitating leukocyte recruitment and the containment and destruction of the pathogen. The complement system, which enhances phagocytosis and helps regulate inflammation, is also an integral component of the innate immune response. Pathogens that evade the first line of defense are targeted by the antigen-specific (adaptive) immune response. Although slower to develop than innate immunity, the adaptive response is both potent and exquisitely targeted and confers long-term immunological memory. Two principal types of lymphocytes mediate adaptive immunity: B cells and T cells. B cells are activated by professional antigen-presenting cells (APCs), such as DCs and macrophages. Once activated, B cells secrete large quantities of antibodies that neutralize pathogens and opsonize them for phagocytosis. Some activated B cells differentiate into long-lived memory B cells, which enable more rapid responses upon re-exposure to the same antigen.[12] T cells are also activated by APCs. $CD4^+$ T helper (Th) cells orchestrate the adaptive immune response, whereas $CD8^+$ cytotoxic T lymphocytes (CTLs) directly lyse infected or transformed cells. Memory T cells are generated in parallel, ensuring a rapid response upon re-exposure to the antigen.[12] Collectively, the generation of memory B and T cells enables faster and more robust protection during subsequent encounters with the same pathogen.

Regulatory control of immune activity

The immune system must be tightly regulated to prevent collateral damage to host tissues, particularly in cases of molecular mimicry (i.e., when a pathogen expresses self-like antigens). A key regulatory mechanism that limits such "friendly fire" was elucidated by Brunkow, Ramsdell, and Sakaguchi, who were awarded the 2025 Nobel Prize in Physiology or Medicine for this work. They identified Tregs, a cell population that restrains autoreactive immune effector cells. This discovery helps explain why most individuals do not develop autoimmunity and how neoplastic cells can sometimes exploit immune tolerance.

Sakaguchi first postulated the existence of a suppressive T-cell subset in 1995, challenging the prevailing view that central immune tolerance in the thymus is sufficient.[14,15] In 2001, Brunkow and Ramsdell identified the genetic mutation in a mouse strain prone to fulminant autoimmunity: a loss-of-function mutation in the transcription factor FOXP3, a defect that was also found in humans.[16–18]

Sakaguchi subsequently demonstrated that FOXP3 is the master regulator specifying the lineage he had previously described, now formally termed regulatory T cells (Tregs).[19,20]

Tregs monitor and curb aberrant immune activity through multiple non-redundant mechanisms.[21–23] First, they modulate immune responses via cytokine-mediated suppression. Tregs secrete interleukin (IL)-10, which inhibits Th cells and macrophages; transforming growth factor beta (TGF-β), which limits T- and B-cell proliferation and activation; and IL-35, which restrains effector T (Teff) cells. Second, Tregs suppress immune effector cells through direct cell–cell contact. Tregs express CTLA-4 and thus outcompete Teff cells for binding to APCs by engaging the costimulatory ligands CD80/CD86. They also sequester IL-2 via the high-affinity IL-2 receptor α-chain (CD25), depriving effector cells of essential growth signals. Third, in certain contexts, Tregs can directly eliminate autoreactive T cells or overactivated APCs through granzyme- and perforin-dependent cytolysis. Finally, Tregs can exert suppressive effects through metabolic modulation. The ectonucleotidases CD39 and CD73 expressed on Tregs catalyze the conversion of pro-inflammatory extracellular ATP into immunosuppressive adenosine, which dampens Teff cell activity by binding to adenosine receptors. Through these varied mechanisms, Tregs modulate immune responses to ensure they are potent enough to eradicate pathogens, yet sufficiently restrained to preserve host tissue integrity. Thus, Tregs act as an indispensable "brake" on immune activation.

MSCs: Internal custodians of tissue homeostasis and external mediators of immune activity

Mesenchymal stem cells or master signaling cells?

Mesenchymal stem/stromal cells have long been appreciated for their capacity for self-renewal and multilineage differentiation. However, their more consequential properties may be mediated by their secretome – the rich repertoire of soluble factors and extracellular vesicles they release. Accordingly, it has recently been proposed that MSCs be renamed "master signaling cells".[24]

Colony-forming, plastic-adherent stromal cells were first reported by Friedenstein et al. in the late 1950s and 1960s[3]; however, it was not until 1991 that Caplan isolated such cells from bone marrow and characterized them.[4] Subsequently, MSC-like populations were identified in adipose tissue,[6] umbilical cord blood,[25] Wharton's jelly,[26] the placenta,[27] dental pulp,[28] the dermis,[29] and even hair follicles.[30] To harmonize the nomenclature, the International Society for Cell and Gene Therapy proposed 3 minimal criteria in 2006: 1) plastic adherence and fibroblast-like morphology; 2) expression of CD105, CD73, and CD90, with absence of CD14, CD34, CD45, and HLA-DR; and 3) trilineage differentiation in vitro into osteoblasts, chondrocytes, and adipocytes.[31]

Due to their favorable properties, MSCs are now used clinically across a broad range of applications. For example, off-the-shelf products such as Prochymal, Ryoncil, and Temcell HS are used to treat graft-versus-host disease,[32–34] whereas Cartistem[35] and StemOne[36] are utilized to treat osteoarthritic degeneration. The development of MSC-based therapies has ushered in a new era of regenerative medicine.

Intriguingly, the therapeutic efficacy of MSCs appears to depend less on their stemness (i.e., their capacity to directly replace lost cells) than on their potent secretome-mediated anti-inflammatory and immunomodulatory functions. This realization has prompted a terminological shift from referring to these cells as mesenchymal stem/stromal cells to referring to them as medicinal signaling cells. In a previously published article, this concept was further developed, and the term "master signaling cells" was proposed as a more accurate description of MSCs, given their role as ubiquitous tissue sentinels that orchestrate signaling networks to preserve organismal equilibrium.[24]

The immunomodulatory activity of MSCs

With regard to the anti-inflammatory and immunoregulatory effects of MSCs, they have been shown to promote immune tolerance.[32–36] Accordingly, MSCs functionally parallel Tregs by helping to maintain local immune quiescence.

When exposed to a pro-inflammatory milieu rich in interferon-gamma (IFN-γ), tumor necrosis factor alpha (TNF-α), and IL-1, MSCs become activated and upregulate inhibitory ligands, such as programmed death ligand 1 (PD-L1), Fas ligand (FasL), galectin-1, CD73, and human leukocyte antigen G (HLA-G).[37–39] Concurrently, MSCs secrete a spectrum of soluble mediators, including indoleamine 2,3-dioxygenase, prostaglandin E2, nitric oxide, TGF-β, and hepatocyte growth factor.[39,40] Through these factors, as well as direct cell–cell contact, MSCs suppress pro-inflammatory effector cells (i.e., Teff cells, NK cells, B cells, and DCs) while promoting the expansion of Tregs.[10,41,42] The net result is an anti-inflammatory, tolerogenic microenvironment that promotes tissue repair and minimizes immune-mediated collateral damage.

Discussion

Given that both Tregs and MSCs play vital roles in maintaining immune homeostasis, I propose a two-tier model of peripheral immune tolerance that incorporates these internal and external checkpoints acting sequentially

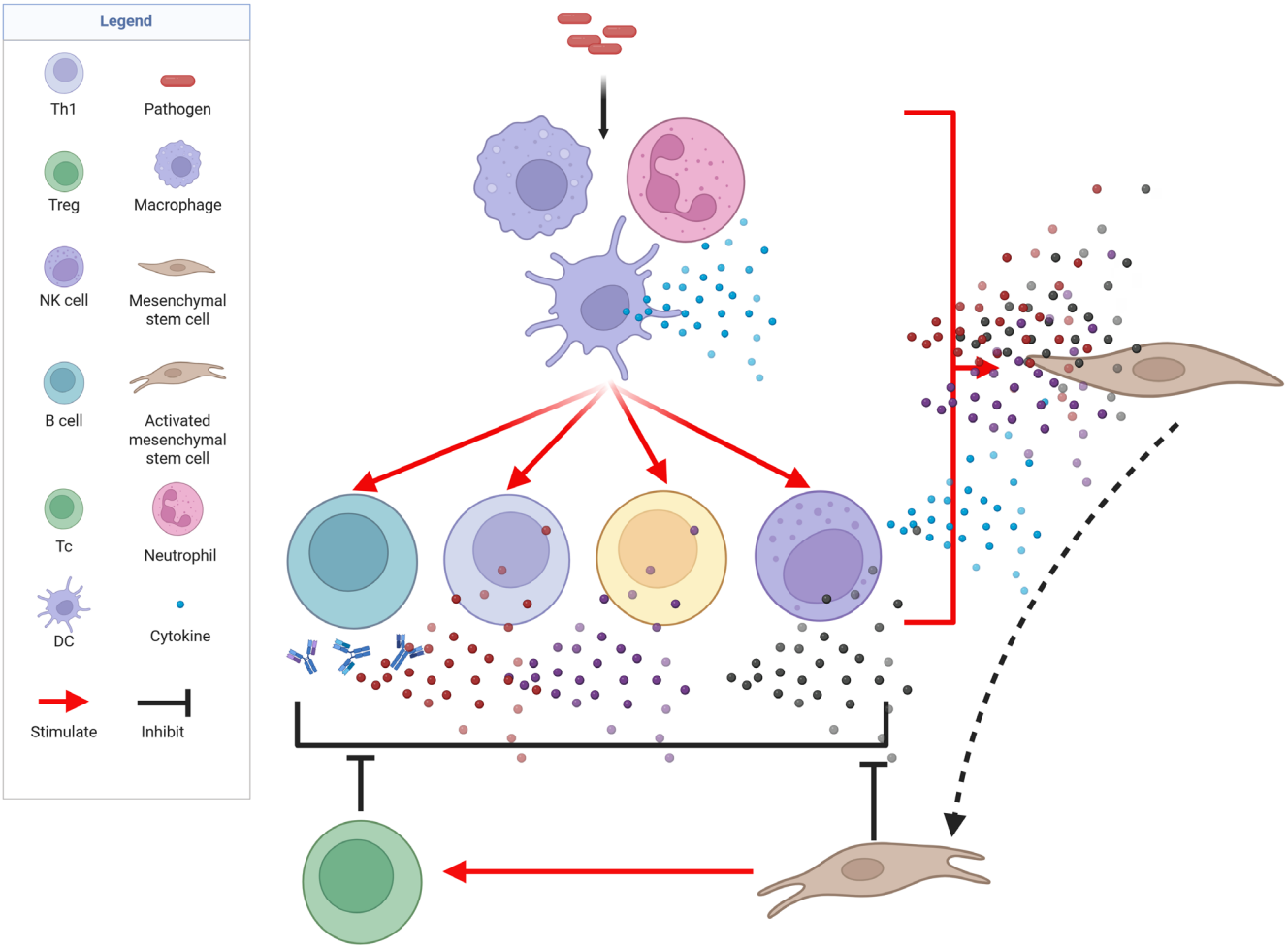

Fig. 1. A two-tier model of peripheral immune tolerance. When a pathogen invades the body, the immune system is activated to eradicate the harmful intruder. Concomitantly, regulatory T cells (Tregs) are induced in lymphoid organs to prevent excessive immune activation and systemic immunopathology. In parallel, inflammatory mediators released by immune cells reach the affected tissue and activate resident mesenchymal stem/stromal cells (MSCs). These MSCs adopt an anti-inflammatory, immunoregulatory phenotype that protects parenchymal cells from immune-mediated collateral damage during pathogen clearance (created with BioRender.com)

(Fig. 1). First, Tregs in secondary lymphoid organs curb the activity of adaptive immune effector cells. Then, once activated immune cells reach the site of infection or inflammation, resident or infiltrating MSCs are stimulated to locally dampen their effector functions.

This model helps explain the encouraging clinical outcomes observed with MSC infusion in several autoimmune settings.[43–47] However, a potential downside of MSC infusion is that the resulting broad immunosuppression may create a favorable environment for malignant cells, shielding them from CTL surveillance. The model also implies that autoimmune pathology may arise when both checkpoints are concurrently compromised.

The ubiquity of MSCs across virtually all organs likely reflects the critical importance of the tissue-level safeguard provided by these cells. Even in organs in which MSCs have not been conclusively identified, it is plausible that cells of analogous ontogeny persist in a dormant state or have differentiated into tissue-adapted subsets. Under homeostatic conditions, MSCs remain quiescent and help maintain local tissue equilibrium. When injury occurs, pro-inflammatory cytokines released by infiltrating immune cells activate MSCs, inducing a potent anti-inflammatory and immunomodulatory phenotype. Thus, MSCs provide a secondary defense mechanism within tissues. In contrast to Tregs, which primarily function to suppress inflammation, MSCs are multifunctional: they simultaneously temper immune activity and orchestrate tissue repair through a repertoire of paracrine and direct cell–cell mechanisms. Therefore, we propose that MSCs be regarded as a specialized, tissue-resident extension of the immune system – a gatekeeper population that shields host tissues from collateral damage inflicted by excessive immune activation.

Conclusions

The 2025 Nobel Prize in Physiology or Medicine was awarded for the identification of Tregs, which play a critical role in peripheral immune tolerance. Mesenchymal

stem cells also make substantial contributions to this process, serving as an external checkpoint in peripheral tissues. Thus, to more accurately describe the mechanisms underlying peripheral immune tolerance, I propose a two-tier model in which Tregs restrain immune responses at their source, whereas MSCs serve as tissue-resident gatekeepers that swiftly extinguish excessive inflammation and generate a pro-regenerative microenvironment. Concurrent failure of these complementary elements may drive autoimmune pathology, whereas excessive immunosuppression may allow tumors to evade immune surveillance. The central role of MSCs in peripheral immune tolerance reinforces the earlier suggestion that they be renamed "master signaling cells". In addition, the potent immunomodulatory capacity of MSCs and their ability to promote tissue repair render MSC-based interventions promising strategies for treating autoimmune diseases and tissue injury. In conclusion, my model acknowledges the roles of Tregs and MSCs in peripheral immune tolerance and highlights their contributions to ensuring that the immune system is powerful enough to eradicate pathogens, yet sufficiently restrained to safeguard the host.

Use of AI and AI-assisted technologies

Not applicable.

ORCID iDs

Phuc Van Pham https://orcid.org/0000-0001-7254-0717

References

1. Nobel Prize Organisation. Nober Prize 2025 in Physiology or Medicine: Press release. Stockholm, Sweden: Nobel Prize Organisation; 2025. https://www.nobelprize.org/prizes/medicine/2025/press-release. Accessed January 12, 2026.
2. Feng J, Mantesso A, De Bari C, Nishiyama A, Sharpe PT. Dual origin of mesenchymal stem cells contributing to organ growth and repair. *Proc Natl Acad Sci U S A*. 2011;108(16):6503–6508. doi:10.1073/pnas.1015449108
3. Friedenstein AJ, Chailakhyan RK, Latsinik NV, Panasyuk AF, Keiliss-Borok IV. Stromal cells responsible for transferring the microenvironment of the hemopoietic tissues: Cloning in vitro and retransplantation in vivo. *Transplantation*. 1974;17(4):331–340. doi:10.1097/00007890-197404000-00001
4. Caplan AI. Mesenchymal stem cells. *J Orthop Res*. 1991;9(5):641–650. doi:10.1002/jor.1100090504
5. Pittenger MF, Mackay AM, Beck SC, et al. Multilineage potential of adult human mesenchymal stem cells. *Science*. 1999;284(5411):143–147. doi:10.1126/science.284.5411.143
6. Zuk PA, Zhu M, Ashjian P, et al. Human adipose tissue is a source of multipotent stem cells. *Mol Biol Cell*. 2002;13(12):4279–4295. doi:10.1091/mbc.e02-02-0105
7. Toma JG, Akhavan M, Fernandes KJL, et al. Isolation of multipotent adult stem cells from the dermis of mammalian skin. *Nat Cell Biol*. 2001;3(9):778–784. doi:10.1038/ncb0901-778
8. Huang Y, Wu Q, Tam PKH. Immunomodulatory mechanisms of mesenchymal stem cells and their potential clinical applications. *Int J Mol Sci*. 2022;23(17):10023. doi:10.3390/ijms231710023
9. Sarsenova M, Kim Y, Raziyeva K, Kazybay B, Ogay V, Saparov A. Recent advances to enhance the immunomodulatory potential of mesenchymal stem cells. *Front Immunol*. 2022;13:1010399. doi:10.3389/fimmu.2022.1010399
10. Taşlı PN, Bozkurt BT, Kırbaş OK, Deniz-Hızlı AA, Şahin F. Immunomodulatory behavior of mesenchymal stem cells. In: Turksen K, ed. *Cell Biology and Translational Medicine*. Vol. 4. Advances in Experimental Medicine and Biology. Cham, Switzerland: Springer International Publishing; 2018:73–84. doi:10.1007/5584_2018_255
11. El-Sayed M, El-Feky MA, El-Amir MI, et al. Immunomodulatory effect of mesenchymal stem cells: Cell origin and cell quality variations. *Mol Biol Rep*. 2019;46(1):1157–1165. doi:10.1007/s11033-018-04582-w
12. Thaler MS, Klausner RD, Cohen HJ. *Medical Immunology*. Philadelphia, USA: Lippincott; 1977. ISBN:978-0-397-52081-7.
13. Paul WE, ed. *Fundamental Immunology*. 7th ed. Philadelphia, USA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2013. ISBN:978-1-4511-1783-7.
14. Sakaguchi S, Sakaguchi N, Asano M, Itoh M, Toda M. Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor α-chains (CD25). Breakdown of a single mechanism of self-tolerance causes various autoimmune diseases. *J Immunol*. 1995;155(3):1151–1164. doi:10.4049/jimmunol.155.3.1151
15. Sakaguchi S, Takahashi T, Nishizuka Y. Study on cellular events in postthymectomy autoimmune oophoritis in mice: I. Requirement of Lyt-1 effector cells for oocytes damage after adoptive transfer. *J Exp Med*. 1982;156(6):1565–1576. doi:10.1084/jem.156.6.1565
16. Brunkow ME, Jeffery EW, Hjerrild KA, et al. Disruption of a new forkhead/winged-helix protein, scurfin, results in the fatal lymphoproliferative disorder of the scurfy mouse. *Nat Genet*. 2001;27(1):68–73. doi:10.1038/83784
17. Bennett CL, Christie J, Ramsdell F, et al. The immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) is caused by mutations of FOXP3. *Nat Genet*. 2001;27(1):20–21. doi:10.1038/83713
18. Wildin RS, Ramsdell F, Peake J, et al. X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is the human equivalent of mouse scurfy. *Nat Genet*. 2001;27(1):18–20. doi:10.1038/83707
19. Sakaguchi S. Regulatory T cells. *Cell*. 2000;101(5):455–458. doi:10.1016/S0092-8674(00)80856-9
20. Itoh M, Takahashi T, Sakaguchi N, et al. Thymus and autoimmunity: Production of $CD25^+CD4^+$ naturally anergic and suppressive T cells as a key function of the thymus in maintaining immunologic self-tolerance. *J Immunol*. 1999;162(9):5317–5326. doi:10.4049/jimmunol.162.9.5317
21. Wan YY. Regulatory T cells: Immune suppression and beyond. *Cell Mol Immunol*. 2010;7(3):204–210. doi:10.1038/cmi.2010.20
22. Sakaguchi S, Yamaguchi T, Nomura T, Ono M. Regulatory T cells and immune tolerance. *Cell*. 2008;133(5):775–787. doi:10.1016/j.cell.2008.05.009
23. Tian L, Humblet-Baron S, Liston A. Immune tolerance: Are regulatory T cell subsets needed to explain suppression of autoimmunity? *BioEssays*. 2012;34(7):569–575. doi:10.1002/bies.201100180
24. Pham PV. MSCs, but not mesenchymal stem cells. *Biomed Res Ther*. 2024;11(9):6797–6800. doi:10.15419/bmrat.v11i9.924
25. Lee OK, Kuo TK, Chen WM, Lee KD, Hsieh SL, Chen TH. Isolation of multipotent mesenchymal stem cells from umbilical cord blood. *Blood*. 2004;103(5):1669–1675. doi:10.1182/blood-2003-05-1670
26. Weiss ML, Medicetty S, Bledsoe AR, et al. Human umbilical cord matrix stem cells: Preliminary characterization and effect of transplantation in a rodent model of Parkinson's disease. *Stem Cells*. 2006;24(3):781–792. doi:10.1634/stemcells.2005-0330
27. Li CD, Zhang WY, Li HL, et al. Mesenchymal stem cells derived from human placenta suppress allogeneic umbilical cord blood lymphocyte proliferation. *Cell Res*. 2005;15(7):539–547. doi:10.1038/sj.cr.7290323
28. Gronthos S, Mankani M, Brahim J, Robey PG, Shi S. Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. *Proc Natl Acad Sci U S A*. 2000;97(25):13625–13630. doi:10.1073/pnas.240309797
29. Sellheyer K, Krahl D. Skin mesenchymal stem cells: Prospects for clinical dermatology. *J Am Acad Dermatol*. 2010;63(5):859–865. doi:10.1016/j.jaad.2009.09.022
30. Gentile P, Scioli MG, Bielli A, Orlandi A, Cervelli V. Stem cells from human hair follicles: First mechanical isolation for immediate autologous clinical use in androgenetic alopecia and hair loss. *Stem Cell Investig*. 2017;4(7):58. doi:10.21037/sci.2017.06.04
31. Dominici M, Le Blanc K, Mueller I, et al. Minimal criteria for defining multipotent mesenchymal stromal cells: The International Society for Cellular Therapy position statement. *Cytotherapy*. 2006;8(4):315–317. doi:10.1080/14653240600855905

32. Kurtzberg J, Abdel-Azim H, Carpenter P, et al. A phase 3, single-arm, prospective study of remestemcel-L, ex vivo culture-expanded adult human mesenchymal stromal cells for the treatment of pediatric patients who failed to respond to steroid treatment for acute graft-versus-host disease. *Biol Blood Marrow Transplant*. 2020;26(5):845–854. doi:10.1016/j.bbmt.2020.01.018
33. Konishi A, Sakushima K, Isobe S, Sato D. First approval of regenerative medical products under the PMD Act in Japan. *Cell Stem Cell*. 2016;18(4):434–435. doi:10.1016/j.stem.2016.03.011
34. Etra A, Ferrara JLM, Levine JE. Remestemcel-L-rknd (Ryoncil): The first approved cellular therapy for steroid-refractory acute GVHD. *Blood*. 2025;146(16):1897–1901. doi:10.1182/blood.2025028553
35. Park YB, Ha CW, Lee CH, Yoon YC, Park YG. Cartilage regeneration in osteoarthritic patients by a composite of allogeneic umbilical cord blood-derived mesenchymal stem cells and hyaluronate hydrogel: Results from a clinical trial for safety and proof-of-concept with 7 years of extended follow-up. *Stem Cell Transl Med*. 2017;6(2):613–621. doi:10.5966/sctm.2016-0157
36. Gupta A. StemOneTM/Stempeucel®: CDSCO approved, adult human bone marrow-derived, cultured, pooled, allogenic mesenchymal stem cells for knee osteoarthritis. *Biomedicines*. 2023;11(11):2894. doi:10.3390/biomedicines11112894
37. López-García L, Castro-Manrreza ME. TNF-α and IFN-γ participate in improving the immunoregulatory capacity of mesenchymal stem/stromal cells: Importance of cell–cell contact and extracellular vesicles. *Int J Mol Sci*. 2021;22(17):9531. doi:10.3390/ijms22179531
38. Faghih M, Moshiri M, Mazrouei Arani N, et al. Evaluation of TNF-α and IFN-γ primed conditioned medium of mesenchymal stem cell in acetic acid-induced mouse model of acute colitis. *Cell Immunol*. 2024;405–406:104876. doi:10.1016/j.cellimm.2024.104876
39. Jiang W, Xu J. Immune modulation by mesenchymal stem cells. *Cell Prolif*. 2020;53(1):e12712. doi:10.1111/cpr.12712
40. Yi T, Song SU. Immunomodulatory properties of mesenchymal stem cells and their therapeutic applications. *Arch Pharm Res*. 2012;35(2):213–221. doi:10.1007/s12272-012-0202-z
41. Yarygin KN, Lupatov AYu, Sukhikh GT. Modulation of immune responses by mesenchymal stromal cells. *Bull Exp Biol Med*. 2016;161(4):561–565. doi:10.1007/s10517-016-3461-8
42. Castro-Manrreza ME, Montesinos JJ. Immunoregulation by mesenchymal stem cells: Biological aspects and clinical applications. *J Immunol Res*. 2015;2015:394917. doi:10.1155/2015/394917
43. Coulson-Thomas VJ, Coulson-Thomas YM, Gesteira TF, Kao WWY. Extrinsic and intrinsic mechanisms by which mesenchymal stem cells suppress the immune system. *Ocul Surf*. 2016;14(2):121–134. doi:10.1016/j.jtos.2015.11.004
44. Reddy BY, Xu DS, Hantash BM. Mesenchymal stem cells as immunomodulator therapies for immune-mediated systemic dermatoses. *Stem Cells Dev*. 2012;21(3):352–362. doi:10.1089/scd.2011.0404
45. El-Badri NS, Maheshwari A, Sanberg PR. Mesenchymal stem cells in autoimmune disease. *Stem Cells Dev*. 2004;13(5):463–472. doi:10.1089/scd.2004.13.463
46. Li A, Guo F, Pan Q, et al. Mesenchymal stem cell therapy: Hope for patients with systemic lupus erythematosus. *Front Immunol*. 2021;12:728190. doi:10.3389/fimmu.2021.728190
47. Zaripova LN, Midgley A, Christmas SE, et al. Mesenchymal stem cells in the pathogenesis and therapy of autoimmune and autoinflammatory diseases. *Int J Mol Sci*. 2023;24(22):16040. doi:10.3390/ijms242216040