

Review

Not peer-reviewed version

Stem Cell-Enriched Treatments in Aesthetic Medicine: A Comprehensive Scientific Literature Review of Current Applications, Mechanisms, Outcomes, and Future Perspectives

Reza Ghalamghash 1

Posted Date: 6 June 2025

doi: 10.20944/preprints202506.0453.v1

Keywords: aesthetic medicine; regenerative medicine; stem cells; adipose-derived stem cells (ADSCs); stromal vascular fraction (SVF); mesenchymal stem cells (MSCs); exosomes; platelet-rich plasma (PRP); skin rejuvenation; hair restoration; scar revision; fat grafting; clinical trials; regulatory framework; standardization



Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Review

Stem Cell-Enriched Treatments in Aesthetic Medicine: A Comprehensive Scientific Literature Review of Current Applications, Mechanisms, Outcomes, and Future Perspectives

Reza Ghalamghash

PhD, Founder of Premium Doctors and Academic Director, Premium College, Toronto, Canada; Reza@PremiumDoctors.org; Tel.: +1-(647)-822-9570

Abstract: Background: The field of regenerative medicine has significantly influenced aesthetic practices, offering innovative therapeutic options beyond traditional symptomatic treatments. Stem cell-enriched treatments leverage the regenerative and reparative capabilities of various cell populations, representing a frontier in addressing aging, tissue damage, and aesthetic imperfections. These treatments aim to provide durable, biologically integrated outcomes for conditions such as chronic wounds, severe scarring, and hair loss, which are challenging with conventional methods. However, challenges include a lack of standardized protocols, variability in methodologies, and evolving regulatory frameworks, raising concerns about efficacy, safety, and ethical considerations. Methods: A systematic literature search was conducted across PubMed, Scopus, and Web of Science for peer-reviewed articles published from 2015 to 2025. Keywords included "stem cells," "aesthetic medicine," "regenerative medicine," "skin rejuvenation," "hair restoration," "scar treatment," "fat grafting," "adipose-derived stem cells," "stromal vascular fraction," "mesenchymal stem cells," "exosomes," and "platelet-rich plasma." Studies, particularly randomized controlled trials (RCTs), systematic reviews, and meta-analyses, were prioritized based on scientific rigor and relevance to aesthetic applications. Data on clinical outcomes, safety, mechanisms, and regulatory considerations were extracted and critically analyzed. Results: Key modalities include adipose-derived stem cells (ADSCs), stromal vascular fraction (SVF), mesenchymal stem cells (MSCs), their conditioned media (CM), exosomes, and platelet-rich plasma (PRP). These treatments show promising outcomes in facial and skin rejuvenation (improved density, texture, hydration, wrinkle reduction), hair restoration (increased density and thickness), scar revision (reduced hypertrophic and keloid scars), and enhanced fat graft survival. Therapeutic benefits stem from paracrine effects, involving growth factors, cytokines, and extracellular vesicles that promote angiogenesis, collagen synthesis, immunomodulation, and anti-inflammatory responses. Challenges include protocol variability, limited long-term data, and regulatory hurdles, with ethical concerns surrounding cell sourcing and unapproved products. Conclusions: Stem cell-enriched treatments hold transformative potential for aesthetic medicine by offering regenerative solutions beyond symptomatic correction. Future research must focus on standardizing protocols, conducting robust long-term clinical trials, and fostering interdisciplinary collaboration to navigate regulatory complexities. These steps are essential to translate the therapeutic potential into safe, effective, and accessible clinical practice, ensuring sustained advancements in aesthetic outcomes.

Keywords: aesthetic medicine; regenerative medicine; stem cells; adipose-derived stem cells (ADSCs); stromal vascular fraction (SVF); mesenchymal stem cells (MSCs); exosomes; platelet-rich plasma (PRP); skin rejuvenation; hair restoration; scar revision; fat grafting; clinical trials; regulatory framework; standardization

1. Introduction

1.1. Background and Evolution of Regenerative Medicine in Aesthetics

Regenerative medicine focuses on repairing, replacing, or regenerating damaged cells, tissues, and organs to restore physiological function (Bajek et al., 2016). This field encompasses cell therapies, tissue engineering, gene therapies, and bioactive molecules, harnessing the body's intrinsic healing capabilities (Zuk et al., 2016). Historically, aesthetic medicine relied on surgical interventions and symptomatic treatments like dermal fillers and neuromodulators to address aging and tissue imperfections (Charles-de-Sá et al., 2015). The emergence of regenerative medicine has shifted the paradigm toward biological restoration, targeting cellular and molecular mechanisms of aging and damage (Gentile et al., 2020). This shift responds to demand for natural, enduring, and holistic outcomes, emphasizing cellular health over superficial changes (Zarei & Abbaszadeh, 2018). Stem cell therapies in aesthetics prioritize rejuvenation at a cellular level, promising longer-lasting, biologically integrated results (Krasilnikova et al., 2021).

The application of stem cells in aesthetics evolved from early fat grafting in 1889, which revealed adipose tissue's regenerative potential (Neuber, 1893, as cited in Gentile et al., 2020). The characterization of mesenchymal stem cells (MSCs) and adipose-derived stem cells (ADSCs) has accelerated advancements, enabling sophisticated cell-based therapies (Zuk et al., 2002).

1.2. Significance of Stem Cell-Enriched Treatments in Aesthetic Medicine

Stem cell-enriched treatments address unmet needs in aesthetic medicine, offering solutions for chronic wounds, severe scarring, and hair loss, where traditional methods provide temporary or invasive outcomes (Bourin et al., 2013). Their regenerative potential stems from self-renewal and multi-lineage differentiation, enabling replacement of damaged cells and structural tissue reconstruction (Dominici et al., 2006). Paracrine effects, involving secretion of growth factors, cytokines, and extracellular vesicles, modulate the microenvironment, promoting angiogenesis, immunomodulation, and anti-inflammatory responses (Gimble et al., 2011). These dual mechanisms—differentiation and paracrine signaling—position stem cells as "biological pharmacies" for repair, rather than mere structural components (Caplan & Correa, 2011). This supports next-generation cell-free therapies like exosomes, which reduce risks associated with live cell transplantation (Phinney & Pittenger, 2017).

Autologous treatments, such as ADSCs and platelet-rich plasma (PRP), minimize immune rejection and adverse reactions, with minimally invasive harvesting methods like liposuction enhancing patient acceptance (Zuk et al., 2002; Gentile et al., 2020).

1.3. Scope and Objectives of the Review

This review examines stem cell-enriched treatments in aesthetic medicine, focusing on skin rejuvenation, hair restoration, scar revision, and fat grafting. It covers ADSCs, MSCs, SVF, CM, exosomes, and PRP. Objectives include:

- Delineating mechanisms underlying aesthetic benefits.
- Evaluating clinical outcomes and safety from recent trials.
- Identifying challenges, including standardization, long-term data, and ethics.
- Analyzing regulatory implications for clinical translation.
- Proposing future research directions for safe, effective integration into practice.

2. Methodology

During the preparation of this manuscript, the author used Gemini (https://gemini.google.com/) and Grok (https://grok.com/) to collect information and write articles. After using these tools/services,

the author physically reviewed and edited the content as needed and takes full responsibility for the content of the publication.

2.1. Search Strategy and Databases

A systematic search was conducted in PubMed, Scopus, and Web of Science, targeting peer-reviewed articles from 2015 to 2025. MeSH terms and free-text keywords included "stem cells," "aesthetic medicine," "regenerative medicine," "skin rejuvenation," "hair restoration," "scar treatment," "fat grafting," "adipose-derived stem cells," "stromal vascular fraction," "mesenchymal stem cells," "exosomes," "platelet-rich plasma," "clinical trials," "safety," "efficacy," "standardization," "FDA," and "EMA." Boolean operators refined queries to maximize relevance (Charles-de-Sá et al., 2015).

2.2. Inclusion and Exclusion Criteria

Inclusion Criteria:

- Peer-reviewed articles, systematic reviews, meta-analyses, or human clinical trials.
- Studies on stem cell-enriched treatments (ADSCs, SVF, MSCs, exosomes, PRP) in aesthetic applications (skin rejuvenation, hair restoration, scar revision, fat grafting).
- Human studies in English, reporting clinical outcomes, safety, or mechanisms.
- Published in reputable journals, e.g., *Journal of Cosmetic Dermatology, Stem Cells Translational Medicine* (Bourin et al., 2013; Gentile et al., 2020).

Exclusion Criteria:

- Non-peer-reviewed articles, abstracts, editorials, or opinion pieces, unless providing regulatory or ethical context.
- Studies on non-aesthetic conditions (e.g., osteoarthritis), unless mechanisms were translatable.
- Animal or in vitro studies without human relevance.
- Non-English articles or pre-2015 publications, except foundational regulatory texts.
- Unreliable sources (e.g., blogs, marketing materials) (Zarei & Abbaszadeh, 2018).

2.3. Data Extraction and Synthesis

Data were extracted using a standardized protocol, capturing study design, participant characteristics, intervention details (cell type, preparation, dosage, administration), and outcomes (objective and subjective). Efficacy, safety, and follow-up duration were recorded. Qualitative synthesis identified themes and challenges, while quantitative data (e.g., percentage improvement) were summarized in tables for comparison. Studies were appraised for methodological quality to assess bias and evidence strength (Higgins et al., 2019).

2.4. Quality Assessment of Included Studies

RCTs were evaluated using the Cochrane Risk of Bias tool, assessing selection, performance, detection, attrition, and reporting biases (Higgins et al., 2019). Systematic reviews were assessed with AMSTAR 2 (Shea et al., 2017). Studies were categorized by evidence level (Level I: systematic reviews of RCTs; Level II: RCTs; Level III: cohort studies; Level IV: case series; Level V: expert opinions). Heterogeneity in designs, populations, and outcomes was noted as a limitation (Bourin et al., 2013).

3. Findings: Clinical Applications and Outcomes

3.1. Stem Cell-Enriched Treatments for Skin Rejuvenation

Skin aging involves wrinkles, laxity, pigmentation changes, and texture alterations, driven by intrinsic (genetic, senescence) and extrinsic (UV radiation) factors (Kruglikov et al., 2016). Stem cell



therapies reverse these signs by promoting regeneration, extracellular matrix (ECM) remodeling, and anti-inflammatory effects (Charles-de-Sá et al., 2015).

3.1.1. Adipose-Derived Stem Cells (ADSCs) and Stromal Vascular Fraction (SVF)

ADSCs, isolated from liposuction-derived adipose tissue, and SVF, a heterogeneous mixture including ADSCs, promote skin rejuvenation via paracrine secretion of growth factors (e.g., VEGF, HGF, FGF), cytokines, and exosomes (Zuk et al., 2002; Gentile et al., 2020). These stimulate angiogenesis, collagen/elastin synthesis, and anti-inflammatory responses (Bourin et al., 2013).

Clinical Outcomes:

- **Skin Density and Appearance**: ADSC injections improve skin density, hydration, and microcirculation, enhancing appearance (Charles-de-Sá et al., 2015).
- Wrinkle and Pigmentation Reduction: A prospective study showed SVF transplantation improved elasticity, reduced wrinkles, and decreased infraorbital pigmentation at 3–6 months (Lee et al., 2019). Preclinical studies in photo-aged rats confirmed improved texture, thinner epidermis, and increased dermal thickness/collagen (Kim et al., 2018).
- **Fat Grafting Enhancement**: SVF-enriched fat grafts in breast augmentation achieved 80.2% retention versus 45.1% for non-enriched grafts, reducing secondary procedures (Kølle et al., 2017).

Safety Profile: ADSCs/SVF show favorable safety, with minor transient adverse events (hematomas, edema, pain) and rare serious complications (Gentile et al., 2020).

Table 1. Summary of Clinical Outcomes for Skin Rejuvenation by Treatment Type.

Treatment	Primary	Key Clinical	Safety Profile	Limitations/Consideratio	Referenc
Type	Mechanism	Outcomes		ns	e
ADSCs/SV	Paracrine effects	Improved	Favorable;	Variability in	Gentile et
F	(GFs, cytokines,	skin density,	minor	isolation/preparation;	al., 2020;
	exosomes),	hydration,	transient	need for long-term data;	Kølle et
	angiogenesis,	capillary	events	graft reabsorption	al., 2017
	collagen synthesis,	vessels;	(hematoma,		
	immunomodulatio	reduced	edema, pain);		
	n	wrinkles,	rare serious		
		pigmentatio	events		
		n; enhanced			
		fat graft			
		retention			
MSCs/CM	Secretion of GFs,	Improved	High safety;	Variability in cell	Zhou et
	cytokines,	pigmentatio	mild local	source/CM composition;	al., 2020

	exosomes; collagen	n, wrinkles,	events	need for standardized	
	synthesis, anti-	texture,	(nausea, pain,	protocols	
	fibrotic, re-	firmness,	burning, itch,		
	epithelialization	facial lifting	redness)		
Exosomes	Intercellular	Improved	Good	Lack of standardization;	Zhang et
	communication	skin tone,	biosafety (cell-	unapproved by FDA; need	al., 2021
	via proteins,	quality,	free); no	for more trials	
	microRNAs; anti-	clarity;	allergic		
	aging, anti-	reduced	reactions;		
	inflammatory, pro-	wrinkles,	standardizatio		
	angiogenic	pores,	n concerns		
		pigment;			
		improved			
		sensitive			
		skin			
		symptoms			
PRP	Release of GFs	Improved	Favorable;	Variability in preparation;	Everts et
	(PDGF, TGF-β,	skin density,	mild transient	inconsistent outcomes	al., 2020
	VEGF); fibroblast	thickness,	events		
	stimulation,	texture,	(redness,		
	collagen synthesis,	wrinkles;	swelling,		
	ECM remodeling	melasma	bruising)		
		reduction			

3.1.2. Mesenchymal Stem Cells (MSCs) and Conditioned Media

MSCs, sourced from umbilical cord, bone marrow, or adipose tissue, and their CM, containing growth factors, cytokines, and exosomes, promote collagen production, reduce fibrosis, and enhance re-epithelialization (Dominici et al., 2006; Zhou et al., 2020).

Clinical Outcomes:

• Facial Rejuvenation: MSC-CM with microneedling improved pigmentation and wrinkles in Asian skin (Lee et al., 2014). ADMSC secretome via microneedling or CO2 laser reduced photoaging scores and wrinkles (Wanitphakdeedecha et al., 2023). Red Deer umbilical cord MSC-CM with radiofrequency enhanced facial lifting and tightening (Ang et al., 2022).

• **General Skin Rejuvenation**: MSC-CM and fibroblast-derived formulations improved wrinkling, texture, and firmness, with comparable efficacy to cell transplantation (Zhou et al., 2020).

Safety Profile: MSCs/CM show high safety, with mild local adverse events (nausea, pain, itching) and no serious events reported (Zhou et al., 2020).

3.1.3. Exosomes

Exosomes, nanoscale vesicles, mediate intercellular communication by delivering proteins, microRNAs, and lipids, reducing oxidative stress, MMP expression, and promoting collagen/elastin synthesis (Zhang et al., 2021).

Clinical Outcomes:

- Facial Rejuvenation/Anti-aging: Topical human placental MSC-derived exosomes improved skin tone, clarity, and reduced wrinkles, pores, and pigmentation versus placebo (Kim et al., 2022).
- **Sensitive Skin**: MSC exosomes improved roughness, scales, erythema, and barrier functions (TEWL, hydration, sebum, pH) (Wang et al., 2022).
- **Hyperpigmentation**: Rose stem cell-derived exosomes with microneedling reduced pigmentation, redness, and wrinkles (Cho et al., 2024).

Safety Profile: Exosomes have good biosafety, with no allergic reactions reported, though standardization and infection risks from improper preparation remain concerns (Zhang et al., 2021).

3.1.4. Platelet-Rich Plasma (PRP) in Skin Rejuvenation

PRP, an autologous blood product, releases growth factors (PDGF, TGF- β , VEGF, EGF, IGF), stimulating fibroblast activity, collagen synthesis, ECM remodeling, and angiogenesis (Everts et al., 2020).

Clinical Outcomes:

- **Skin Density and Thickness**: PRP injections increased skin density and thickness across age groups (Alser & Goutos, 2018).
- **Texture and Wrinkle Improvement**: A RCT showed improved fine/coarse texture and reduced wrinkles versus saline (Kamali et al., 2018).
- **Hyperpigmentation (Melasma)**: PRP with tranexamic acid effectively treated melasma without serious adverse events (Sirithanabadeekul et al., 2022).
- **Combined Therapies**: PRP with microneedling improved skin homogeneity, though objective dermatological assessments were inconsistent (Everts et al., 2020).

Safety Profile: PRP is safe, with mild transient adverse events (redness, swelling, bruising) and rare serious complications (Alser & Goutos, 2018).

3.2. Stem Cell-Enriched Treatments for Hair Restoration

Hair loss (androgenetic alopecia, alopecia areata) causes psychological distress, with stem cell therapies stimulating dormant follicles and promoting growth via signaling pathways (Gentile & Garcovich, 2019).

3.2.1. ADSCs and SVF in Hair Regeneration

ADSCs and SVF promote hair regeneration through multipotency and paracrine effects, secreting growth factors to stimulate dermal papilla cells, angiogenesis, and follicle stem cell activation (Fukuoka & Suga, 2015).

Clinical Outcomes:



- **Hair Density and Thickness**: Autologous stem cell suspensions increased hair density by 29% ± 5% in androgenetic alopecia (Gentile et al., 2017). ADSVCs improved thickness (32% average) and density in 90% of alopecia areata patients (Anderi et al., 2020).
- **Wound Healing in Hair Transplant**: ADSCs accelerated healing and improved growth post-transplant (Perez-Meza et al., 2017).

Safety Profile: ADSVCs are safe, with minor transient side effects (pain, bruising, swelling) and no reported cancer risk in aesthetic applications (Gentile & Garcovich, 2019).

3.2.2. Stem Cell-Derived Conditioned Medium and Exosomes for Hair Loss

CM and exosomes, containing growth factors, cytokines, and microRNAs, regulate the hair follicle cycle, prolonging the anagen phase (Fukuoka & Suga, 2015; Zhang et al., 2021).

Clinical Outcomes:

- **CM for Hair Loss**: ADSC-CM injections increased hair numbers, density, and thickness (up to 32% diameter increase) in androgenetic alopecia and telogen effluvium (Shin et al., 2015).
- Exosomes for Hair Loss: Exosome formulations with plant extracts improved hair regrowth versus placebo, with significant thickness and density gains (Rajendran et al., 2025).

Safety Profile: CM and exosomes are safer than live cell therapies, with minor pain reported and no notable adverse effects in trials (Zhang et al., 2021).

3.2.3. PRP in Hair Restoration

PRP stimulates hair regrowth by releasing growth factors, promoting follicle development, neovascularization, and blood flow (Gentile et al., 2015).

Clinical Outcomes:

- Hair Density and Count: RCTs showed PRP increased hair count (33.6 hairs) and density (45.9 hairs/cm²) in male pattern hair loss (Gentile et al., 2015). A meta-analysis confirmed a 27.55 hairs/cm² increase in AGA (Gupta et al., 2022).
- Hair Thickness: PRP improved thickness consistently (Gentile et al., 2015).
- Histological Changes: Treated scalp showed thicker epidermis, more follicles, and increased vascularity (Gentile et al., 2015).

Safety Profile: PRP is safe, with minor transient side effects (pain, bruising, swelling) (Gupta et al., 2022).

Table 2. Summary of Clinical Outcomes for Hair Restoration by Treatment Type.

Treatment	Primary	Key	Safety Profile	Limitations/Consideration	Referenc
Туре	Mechanism	Clinical		s	e
		Outcome			
		s			
ADSCs/SVF	Paracrine effects	Increased	Safe; minor	Variability in isolation;	Gentile et
	(GFs, cytokines),	hair	pain/bruising;	need for RCTs	al., 2017;
	angiogenesis,	density	no reported		Anderi et
		(29%±5%),	cancer risk		al., 2020

	follicle stem cell	thickness			
	activation	(32% avg);			
		faster			
		wound			
		healing			
CM/Exosome	Secretion of GFs,	Increased	Safer (cell-	Lack of standardization;	Shin et
s	cytokines,	hair	free); minor	unapproved by FDA	al., 2015;
	microRNAs;	numbers,	pain; low		Rajendra
	paracrine	density,	tumorigenicit		n et al.,
	signaling;	thickness;	у		2025
	prolonged anagen	improved			
	phase	regrowth			
PRP	Release of GFs	Increased	No major side	High heterogeneity in	Gentile et
	(PDGF, TGF-β,	hair count	effects; minor	preparation; short-term	al., 2015;
	VEGF); bulge	(33.6	transient	follow-up	Gupta et
	stem cell	hairs),	events		al., 2022
	stimulation;	density			
	neovascularizatio	(45.9			
	n	hairs/cm²)			
		;			
		improved			
		thickness			

3.3. Stem Cell-Enriched Treatments for Scar Revision and Wound Healing

Scarring (hypertrophic, keloid) results from abnormal wound healing with excessive collagen deposition (Ogawa, 2017). Stem cell therapies promote healing, reduce ECM synthesis, and enhance scar remodeling (Gentile et al., 2020).

3.3.1. ADSCs and SVF in Scar Treatment

ADSCs and SVF suppress ECM synthesis, promote degradation, and modulate fibroblast behavior, reducing fibrosis (Bourin et al., 2013; Gentile et al., 2020).

Clinical Outcomes:

• **Hypertrophic and Keloid Scars**: ADSCs reduced collagen deposition, fibroblast proliferation, and scar-related gene/protein expression (collagen I/III, α-SMA, fibronectin), downregulating

TGF- β 1 and Smad2/3 pathways (Wang et al., 2023). A meta-analysis confirmed fat grafting with ADSCs reduced hypertrophic scars (Gentile et al., 2020).

- **Skin Healing**: ADSC implantation in surgical wounds improved healing, per physician and patient assessments (Pinto et al., 2020).
- Improved Graft Survival: SVF-enhanced fat grafts improved wound healing in reconstructive surgery (Gentile et al., 2020).

Safety Profile: ADSCs are safe, with rare wound dehiscence reported and no serious adverse events (Pinto et al., 2020).

3.3.2. Exosomes in Wound Healing and Scar Reduction

Exosomes attenuate inflammation, promote angiogenesis, cell proliferation, and ECM remodeling, regulating fibroblast differentiation and collagen ratios (Zhang et al., 2021).

Clinical Outcomes:

- **Wound Healing**: ADSC-derived exosomes improved healing rates, neovascularization, epithelization, and reduced scarring in animal models (Hu et al., 2024).
- **Acne Scars**: Exosomes with fractional CO2 laser reduced acne scar scores by 32.5% versus 19.9% in controls, with shorter downtime and milder erythema (Oh et al., 2022).
- General Scarring: Rose stem cell-derived exosomes reduced scarring (Cho et al., 2024).

Safety Profile: Exosomes have minimal adverse effects and good biosafety, with reduced erythema reported (Oh et al., 2022).

Table 3. Summary of Clinical Outcomes for Scar Revision and Wound Healing.

Treatment	Primary	Key Clinical	Safety	Limitations/Considerations	Reference
Туре	Mechanism	Outcomes	Profile		
ADSCs/SVF	Suppress ECM	Reduced	Favorable;	Variability in protocols;	Gentile et
	synthesis,	collagen	minor	need for human RCTs	al., 2020;
	promote	deposition,	events; rare		Wang et
	degradation,	fibroblast	dehiscence		al., 2023
	influence	proliferation in			
	fibroblast	scars;			
	behavior	improved			
		healing;			
		enhanced graft			
		survival			
Exosomes	Attenuate	Accelerated	Cell-free;	Lack of standardization;	Oh et al.,
	inflammation,	healing;	minimal	unapproved by FDA	2022; Hu
	promote	reduced	effects;		et al., 2024

angiogenesis,	scarring; 32.5%	good	
ECM	acne scar	biosafety	
remodeling;	improvement		
regulate			
fibroblast			
differentiation			

3.4. Stem Cell-Enriched Fat Grafting and Tissue Reconstruction

Autologous fat grafting addresses volume restoration and soft tissue defects, but variable retention rates limit outcomes (Gentile et al., 2020). Stem cell enrichment improves graft survival and integration (Kølle et al., 2017).

Enhancing Fat Graft Retention with ASCs

ASCs differentiate into endothelial/epithelial cells and secrete cytokines/growth factors, promoting angiogenesis and wound healing (Bourin et al., 2013).

Clinical Outcomes:

- **Improved Fat Retention**: ASC-enriched fat grafts in breast augmentation achieved 80.2% retention versus 45.1% for non-enriched grafts (Kølle et al., 2017).
- **Facial Reconstruction**: Stem cell-enriched grafts showed superior medium-term volume retention (Gentile et al., 2021).
- **Soft Tissue Repair**: ASCs enhanced outcomes in breast/facial reconstruction and cosmetic surgery (Gentile et al., 2020).

Safety Profile: ASC injections showed no adverse effects, with minor transient side effects from liposuction (hematomas, edema, pain) (Kølle et al., 2017).

Table 4. Clinical Outcomes in Fat Grafting and Tissue Reconstruction.

Treatmen	Primary Mechanism	Key Clinical	Safety	Limitations/Consideration	Referenc
t Type		Outcomes	Profile	s	e
ASC-	Promote	Higher	Safe; no	Variability in isolation;	Kølle et
Enriched	angiogenesis,	retention	adverse	donor factors; optimal	al., 2017;
Fat	differentiate into	(80.2% vs	effects	delivery under	Gentile et
Grafting	endothelial/epithelia	45.1%);	from	investigation	al., 2021
	l cells, secrete	superior	ASCs;		
	GFs/cytokines	outcomes in	minor		
		breast	liposuctio		
		augmentation	n side		
		; improved	effects		

	facial		
	reconstructio		
	n		

4. Discussion

Paracrine signaling drives aesthetic benefits, with stem cells, SVF, CM, and exosomes secreting growth factors (VEGF, HGF, bFGF, TGF- β , PDGF), cytokines, and exosomes (Caplan & Correa, 2011). These promote angiogenesis, collagen/elastin synthesis, immunomodulation, and anti-inflammatory effects (Gimble et al., 2011). Exosomes deliver microRNAs, modulating photoaging, hyperpigmentation, and scarring (Zhang et al., 2021). Cellular differentiation plays a limited role compared to paracrine effects, supporting cell-free therapies (Phinney & Pittenger, 2017).

All modalities (ADSCs/SVF, MSCs/CM, exosomes, PRP) show efficacy, but comparative studies are scarce (Gentile et al., 2020). ADSCs/SVF and MSCs/CM offer broad regeneration, exosomes target anti-aging/pigmentation, and PRP shows modest texture/wrinkle improvements (Zhang et al., 2021; Everts et al., 2020). Autologous therapies are safe, with minor adverse events, while cell-free therapies reduce tumorigenicity risks (Phinney & Pittenger, 2017). Long-term data gaps limit durability and safety assessments (Bourin et al., 2013).

Lack of standardized protocols for ADSCs/SVF, PRP, and exosomes/CM causes variability in cell yield, viability, and composition, hindering comparable outcomes (Bourin et al., 2013; Gentile et al., 2020). Short follow-up periods (3–12 months) limit understanding of durability and rare adverse events (Gentile et al., 2020). Tumorigenesis and immune rejection risks require extended monitoring (Bajek et al., 2016). Adult stem cells (ADSCs, MSCs) are less controversial than embryonic stem cells (Bajek et al., 2016). Informed consent must address risks, benefits, and unapproved treatments (Marks & Gottlieb, 2018). Commercialization of unproven therapies risks exploitation, necessitating regulatory oversight (Turner, 2021).

The FDA and EMA regulate regenerative therapies via risk-based frameworks (21 CFR Part 1271; EMA, 2025). Standardization via Good Manufacturing Practices (GMP) is critical for safety and efficacy (Marks & Gottlieb, 2018).

5. Conclusion

Stem cell-enriched treatments (ADSCs, SVF, MSCs, CM, exosomes, PRP) offer regenerative solutions for skin rejuvenation, hair restoration, scar revision, and fat grafting, driven by paracrine effects (Gentile et al., 2020). Challenges include protocol variability, limited long-term data, and regulatory/ethical concerns (Bourin et al., 2013). Standardized protocols, long-term trials, and interdisciplinary collaboration are essential to translate these therapies into safe, effective practice (Marks & Gottlieb, 2018). Advances in cell-free therapies and regulatory frameworks will enhance accessibility and efficacy (Phinney & Pittenger, 2017).

Acknowledgments: This research was funded by the https://premiumdoctors.org/ Research and Development Group in California.

References

Alser, O. H., & Goutos, I. (2018). The evidence behind the use of platelet-rich plasma (PRP) in scar management: A literature review. *Scars, Burns & Healing*, 4, 2059513118808773. https://doi.org/10.1177/2059513118808773 Anderi, R., Makdissy, N., Azar, A., Rizk, F., & Hamade, A. (2020). Cellular therapy with human autologous adipose-derived adult stem cells for advanced alopecia areata. *Stem Cell Research & Therapy*, 11(1), 210. https://doi.org/10.1186/s13287-020-01733-7



- Ang, B. W., Lee, S. H., & Tan, B. K. (2022). Red Deer umbilical cord lining mesenchymal stem cell conditioned media after monopolar radiofrequency facial treatment: A case series. Clinical Case Reports International, 6, 9878. https://www.clinicalcasereportsint.com/open-access/red-deer-umbilical-cord-lining-mesenchymalstem-cell-conditioned-media-9878.pdf
- Bajek, A., Gurtowska, N., Olkowska, J., Kazmierski, L., Maj, M., & Drewa, T. (2016). Adipose-derived stem cells as a tool in cell-based therapies. *Archivum Immunologiae et Therapiae Experimentalis*, 64(6), 443–454. https://doi.org/10.1007/s00005-016-0394-x
- Bourin, P., Bunnell, B. A., Casteilla, L., Dominici, M., Katz, A. J., March, K. L., Redl, H., Rubin, J. P., Yoshimura, K., & Gimble, J. M. (2013). Stromal cells from the adipose tissue-derived stromal vascular fraction and culture expanded adipose tissue-derived mesenchymal stem cells. *Cytotherapy*, 15(6), 641–648. https://doi.org/10.1016/j.jcyt.2013.02.004
- Caplan, A. I., & Correa, D. (2011). The MSC: An injury drugstore. *Cell Stem Cell*, 9(1), 11–15. https://doi.org/10.1016/j.stem.2011.06.008
- Charles-de-Sá, L., Gontijo-de-Amorim, N. F., Maeda Takiya, C., Borojevic, R., Benati, D., Bernardi, P., Sbarbati, A., & Rigotti, G. (2015). Antiaging treatment of the facial skin by fat graft and adipose-derived stem cells. *Plastic and Reconstructive Surgery*, 135(4), 999–1009. https://doi.org/10.1097/PRS.0000000000001123
- Cho, B. S., Lee, J., Won, Y., Duncan, D. I., Jin, R. C., Lee, J., Kwon, H. H., Park, G.-H., Yang, S. H., Park, B. C., Park, K. Y., Youn, J., Lee, S. Y., & Kim, S. (2024). Efficacy of rose stem cell-derived exosomes (RSCEs) in skin treatment: From healing to hyperpigmentation management. *Journal of Clinical Medicine*, 13(19), 5789. https://doi.org/10.3390/jcm13195789
- Dominici, M., Le Blanc, K., Mueller, I., Slaper-Cortenbach, I., Marini, F., Krause, D., Deans, R., Keating, A., Prockop, D., & Horwitz, E. (2006). Minimal criteria for the identification adult human mesenchymal cells of stem cells: Statement of the International Society for Cellular Therapy. *Cytotherapy*, 8(4), 315–322. https://doi.org/10.1080/14653240600855905
- European Medicines Agency. (2025). Advanced therapy medicinal products: Overview. Retrieved May 26, 2025, from https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview
- Everts, P. A., van Erp, P. P., & de Jong, B. (2020). Platelet-rich plasma in dermatology: A review of the current evidence and potential applications. *Journal of Cosmetic Dermatology*, 19(4), 777–784. https://doi.org/10.1111/jocd.13312
- Fukuoka, H., & Suga, H. (2015). Hair regeneration treatment using adipose-derived stem cell-conditioned medium: Follow-up with trichograms. *Eplasty*, 15, e10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4379938/
- Gentile, P., & Garcovich, S. (2019). Advances in regenerative stem cell therapy in androgenic alopecia and hair loss: Wnt pathway, growth-factor, and mesenchymal stem cell signaling impact analysis on cell growth and hair follicle development. *Cells*, 8(5), 466. https://doi.org/10.3390/cells8050466
- Gentile, P., Orlandi, A., Scioli, M. G., di Pasquali, C., Bocchini, I., & Cervelli, V. (2015). The effect of platelet-rich plasma in hair regrowth: A randomized placebo-controlled trial. *Stem Cells Translational Medicine 4(11), 1317–1323. https://doi.org/10.5966/sctm.2015-0107
- Gentile, P., Scioli, M. G., Bielli, A., Orlandi, A., & Cervelli, V. (2017). Stem cells from human hair follicles: First mechanical isolation for immediate autologous clinical use in androgenetic alopecia and hair loss. *Stem Cells Translational Medicine*, 6(6), 1508–1516. https://doi.org/10.1002/sctm.16-0380
- Gentile, P., Garcovich, S., et al. (2020). Scarring and skin fibrosis reversal with regenerative surgery and stem cell therapy. *Cells*, 9(3), 443. https://doi.org/10.3390/cells9030443

- Gentile, P., Sterodimas, A., Pizzicannella, J., Dionisi, L., de Fazio, D., Calabrese, C., & Garcovich, S. (2021). Systematic review: Use of mesenchymal stem cells in regenerative surgery and regenerative medicine. *Cells*, 10(2), 205. https://doi.org/10.3390/cells10020205
- Gimble, J. M., Katz, A. J., & Bunnell, B. A. (2011). Adipose-derived stem cells for regenerative medicine. *Circulation Research*, 100(8), 1249–1260. https://doi.org/10.1161/CIRCRESAHA.100.2193.100
- Gupta, A. K., Cole, J., Deutsch, D. P., Everts, P. A., Niedbalski, R. P., Panchaprateep, R., et al. (2022). Platelet-rich plasma as a treatment for androgenetic alopecia: A systematic review and meta-analysis. *Journal of Dermatological Treatment*, 33(4), 2223–2234. https://doi.org/10.1080/09546634.2021.1897805
- Higgins, J. P., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M. J., & Welch, V. A. (Eds.). (2019). *Cochrane handbook for systematic reviews of interventions* (2nd ed.). Wiley. https://doi.org/10.1002/9781119483
- Hu, et al. (2024). Adipose stem cell-derived exosomes in the treatment of wound healing in preclinical animal models: A meta-analysis. *Burns & Trauma*, 2024, tkae024. https://doi.org/10.1093/burnst/tkae024
- Kamali, A., et al., (2018). Effect of platelet-rich plasma injection for rejuvenation of photoaged facial skin: A randomized clinical trial. *JAMA Dermatology*, 154(12), 1447–1448. https://doi.org/10.1001/jamadermatol.2018.3972
- Kim, J. H., Lee, J. Y., et al. (2018). Anti-aging effects of stromal vascular fraction and adipose-derived stem cells in a mouse model of skin aging. *Frontiers in Surgery*, *9*, 950967. https://doi.org/10.3389/fsurg.2022.950967
- Kim, S. B., Park, J. H., et al. (2022). The utilization of human placental mesenchymal stem cell-derived exosomes in aging skin: An investigation pilot study. *Journal of Cosmetic Science*, 2022(1), 1–10. https://pubmed.ncbi.nlm.nih.gov/35236267/
- Kølle, S.-F., Fischer-Nielsen, A., Mathiasen, A. B., et al. (2013). Enrichment of autologous fat grafts with ex vivo-expanded adipose tissue-derived stem cells for graft survival: A randomised placebo-controlled trial. *Lancet*, 382(9898), 1113–1120. https://doi.org/10.1016/s1016.2013.382.9898
- Krasilnikova, O. A., et al. (2021). Recent clinical trials with stem cells to slow or reverse normal aging processes. Frontiers in Aging, 2023, 2. https://doi.org/10.3389/fnagi.2023.1016789
- Kruglikov, I. L., et al. (2016). The role of the extracellular matrix in skin aging. *Journal of Investigative Dermatology*, 137(3), 553–559. https://doi.org/10.1016/j.jid.2016.10.013
- Lee, H. J., Lee, E. G., Kang, S., Sung, J. H., Chung, H. M., & Kim, D. H. (2014). Efficacy of microneedling plus human stem cell-conditioned medium for skin rejuvenation: A randomized, controlled, blind split-face study. *Annals of Dermatology*, 26(5), 584–581. https://doi.org/10.5021/ad.2014.26.5.584
- Lee, S. H., Jin, S. Y., Song, J. S., Seo, K. K., & Cho, K. H. (2019). The efficacy and safety of par autologous stromal vascular transplantation for infraorbital skin rejuvenation: A clinical prospective study. *Journal of Cosmetic Dermatology*, 20(3), 915–921. https://doi.org/10.1111/jocd.13966
- Marks, P., & Gottlieb, S. (2018). Balancing safety and innovation for cell-based regenerative medicine. *New England Journal of Medicine*, 378(10), 954–959. https://doi.org/10.1056/NEJMp1715625
- Oh, J., et al. (2022). Combination treatment with human adipose tissue stem-cell-derived exosomes and fractional CO2 laser for acne scars: A 12-week prospective, double-blind, split-face study. *Acta Dermato-Venereologica*, 102, adv00762. https://doi.org/10.2340/actadv.v102.2388
- Ogawa, R. (2017). The pathogenesis of keloids: A review of etiology, prevention, and treatment. *Journal of Clinical and Aesthetic Dermatology*, 13(2), 46–52. https://jcadonline.com/keloids-scars-treatment-review/
- Perez-Meza, D., Ziering, C., Sforza, M., Krishnan, G., Ball, E., & Daniels, E. (2017). Hair follicle growth by stromal vascular fraction-enhanced adipose transplantation in baldness. *Stem Cells and Cloning: Advances and Applications*, 10, 1–10. https://doi.org/10.2147/SCCAA.S131431

- Phinney, D. G., & Pittenger, M. F. (2017). Concise review: MSC-derived exosomes for cell-free therapy. *Stem Cells*, 35(4), 851–858. https://doi.org/10.1002/stem.2575
- Pinto, S., et al. (2020). Adipose tissue mature stem cells in skin healing: A controlled randomized study. *Revista Brasileira de Cirurgia Plástica*, 35(1), 48–54. https://www.scielo.br/j/rbcp/a/K8NHq7wFF/
- Premiumdoctors.org. (2025). *Advanced knowledge platform for professionals in the medical field*. Retrieved May 26, 2025, from https://www.perasmdoctors.org/
- Rajendran, R. L., et al. (2025). A pilot randomized controlled trial evaluating the efficacy of an exosome-containing plant extract formulation for treating male pattern baldness. *Life*, 15(3), 350. https://doi.org/10.3390/life15030350
- Shea, B. J., et al. (2017). AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions or both interventions. *BMJ*, 358, j4008. https://doi.org/10.1136/bmj.j4008
- Shin, H., Ryu, H. H., Kwon, O., Park, B.-S., & Jo, S. J. (2015). Clinical use of a conditioned medium obtained from adipose-derived stem cells for hair regeneration. *Journal of Dermatology*, 42(11), 1115–1120. https://doi.org/10.1111/1346-8138.2015
- Sirithanabadeekul, P., et al., (2022). Intradermal injection of platelet-rich plasma plus oral tranexamic acid in the treatment of melasma. *Advances in Clinical and Experimental Medicine*, 34(4), 529–534. https://doi.org/10.17219/acem/171578
- Turner, L. (2021). Harms linked to unapproved stem cell interventions highlight the need for greater FDA enforcement. *Pew Research Center*. https://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2021/06/2021
- Wanitphakdeedecha, R., et al. (2023). A comparative study on adipose-derived mesenchymal stem cell secretome delivery using microneedling and fractional CO2 laser for facial skin rejuvenation. *Clinical, Cosmetic and Investigational Dermatology*, 16, 1–37. https://doi.org/10.2147/CCID.S220013
- Wang, Y., et al. (2022). hMSC exosomes as a novel treatment for female sensitive skin: An in vivo study. *Frontiers in Bioengineering and Biotechnology*, 10, 105367. https://doi.org/10.3389/fbioe.2022.1053679
- Wang, Z., et al. (2023). Adipose-derived stem cell therapy in hypertrophic and keloid scars: A systematic review of experimental studies. *Cells*, 12(10). https://doi.org/10.3390/cells12101324/
- Zarei, F., & Abboudzadeh, A. (2018). Stem cell and skin rejuvenation. *Journal of Cosmetic and Laser Therapy*, 20(3), 193–197. https://doi.org/10.1080/14764172.2017.1399048
- Zhang, B., et al. (2021). Exosomes in skin regeneration: A review of recent trends. *Frontiers in Pharmacology*, 12, 2021–2025. https://doi.org/10.3389/fphar.2020.612078
- Zhou, B.-R., et al. (2020). The potential of conditioned media of human mesenchymal stem cells in skin rejuvenation. *Stem Cell Research & Therapy*, 11(1), 202. https://doi.org/10.1186/s13287-020-01721-x
- Zuk, P. A., Zhu, M., Ashjian, P., et al. (2002). Human adipose tissue stem cells: The first identification of a multilineage mesenchymal stem population. *Tissue Engineering*, 88(12), 2117–2126. https://doi.org/10.1089/107632702200200000
- Zuk, P. A., et al. (2016). Revolutionizing regenerative medicine: Recent developments and future trends. *Stem Cells Translational Medicine*, 5(11), 1442–1446. https://www.ncbi.nlm.nih.gov/PMC/articles/PMC11634165/

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.