Journal of Regenerative Aesthetic Medicine

ISSUE 2
May 2025

The *Future* of Polynucleotides

Introducing The RAM Institute

Understanding **Exosomes**

Peptides in your Protocols

As part of the RAMI Regenerative Aesthetic Medicine Institute

JRAM Journal of Regenerative Aesthetic Medicine

Welcome to the Journal of Regenerative Aesthetic Medicine

As we enter an exciting new chapter in regenerative medicine, we are thrilled to announce the launch of The Regenerative Aesthetic Medicine Institute (RAMI) - a global hub dedicated to advancing research, education, and clinical excellence in our evolving field.

With this milestone, the Journal of Regenerative Aesthetics (JRAM) begins its journey as the official publication of the Institute, reflecting its mission to elevate and expand the impact of regenerative science in aesthetic practice.

For our first issue under the Insititute, JRAM is proud to present a forward-looking issue that captures the pulse of innovation and insight driving our field.

We explore the exciting future of polynucleotides, shedding light on their demand across the globe and what developments we can expect to see over the coming years. We also examine the environment's impact on telomere health, offering a nuanced view of how external factors shape cellular ageing and vitality. Our comprehensive overview of hair loss gives you a starting point for introducing regenerative hair treatments to your practice, while compelling pieces on peptides and PRP provide invaluable guidance that will steer you towards more effective, personalised, and scientifically grounded treatment strategies.

Additionally, we're honored to feature a profile on Dr Tingsong Lim, a global leader in regenerative aesthetics, whose pioneering work continues to influence both practice and philosophy.

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The Team

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RAMI Regenerative Aesthetic Medicine Institute

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Meet our Scientific Committee

Steering the education of The RAM Institute

Our Scientific Committee plays a crucial role in the success and credibility of The RAM Institute. Members oversee all JRAM content and curate the RAMCE programme to ensure everything we produce is cutting-edge and scientifically sound.

Professor Maurizio Cavallini

Professor Maurizio Cavallini is the Chief Medical Advisor at Monteverdi Tuscany in Italy. He graduated in medicine from the University of Milan, and holds postgraduate qualifications in plastic surgery, microsurgery and experimental surgery. A frequent writer and lecturer, Professor Cavallini has authored more than 130 pieces in notable national and international medical journals, as well as publishing books and speaking globally on plastic surgery and aesthetic medicine. He is also the President of the Italian Scientific Society of Aesthetic Medicine - Agora and adjunct professor in the University of Genova in Italy, along with being a fellow of many scientific societies in plastic surgery and aesthetic medicine.

Mr George Christopoulos

Mr George Christopoulos is a plastic surgeon and Assistant Professor of Aesthetic Medicine at the College of Medicine & Dentistry at Ulster University. He has a Master's in Health Care Management and a PhD (Distinction) in the surgical treatment of cancer from the University of Athens. Since relocating to the UK in 2015, Mr Christopoulos has completed a second Master's in Reconstructive Microsurgery (Distinction), and held roles in burns and plastics throughout the UK.

Dr Kate Goldie

With more than 15 years of global experience, Dr Kate Goldie is recognised as one of the leading figures in aesthetic medicine. Having trained more than 7,000 practitioners worldwide, her innovative approach and commitment to excellence have made her a sought-after educator and speaker. Beyond her extensive teaching, Dr Goldie is a respected thought leader, regularly sharing the stage with industry pioneers and contributing to groundbreaking research. Dr Goldie is deeply passionate about advancing the field of regenerative aesthetics and is at the forefront of new developments and innovations.

Dr Lee Walker

Dr Lee Walker is Director and Clinical Lead at the award-winning BCity Clinics in Liverpool, with extensive experience in medical aesthetics since 2001. He chairs the Complications in Medical Aesthetics Collaborative (CMAC) UK and has published widely on blindness, vascular occlusion, facial ageing, anatomy and injection technique. A member of the Royal College of Surgeons in both Scotland and England, he also holds postgraduate qualifications in clinical education. Dr Walker is part of Teoxane's international faculty and serves as an educational consultant for Revance USA.

Get in touch with the committee

Email **info@ram-institute.com** to discuss ideas and receive more information.

Journal abstract submission

Conference abstract submission

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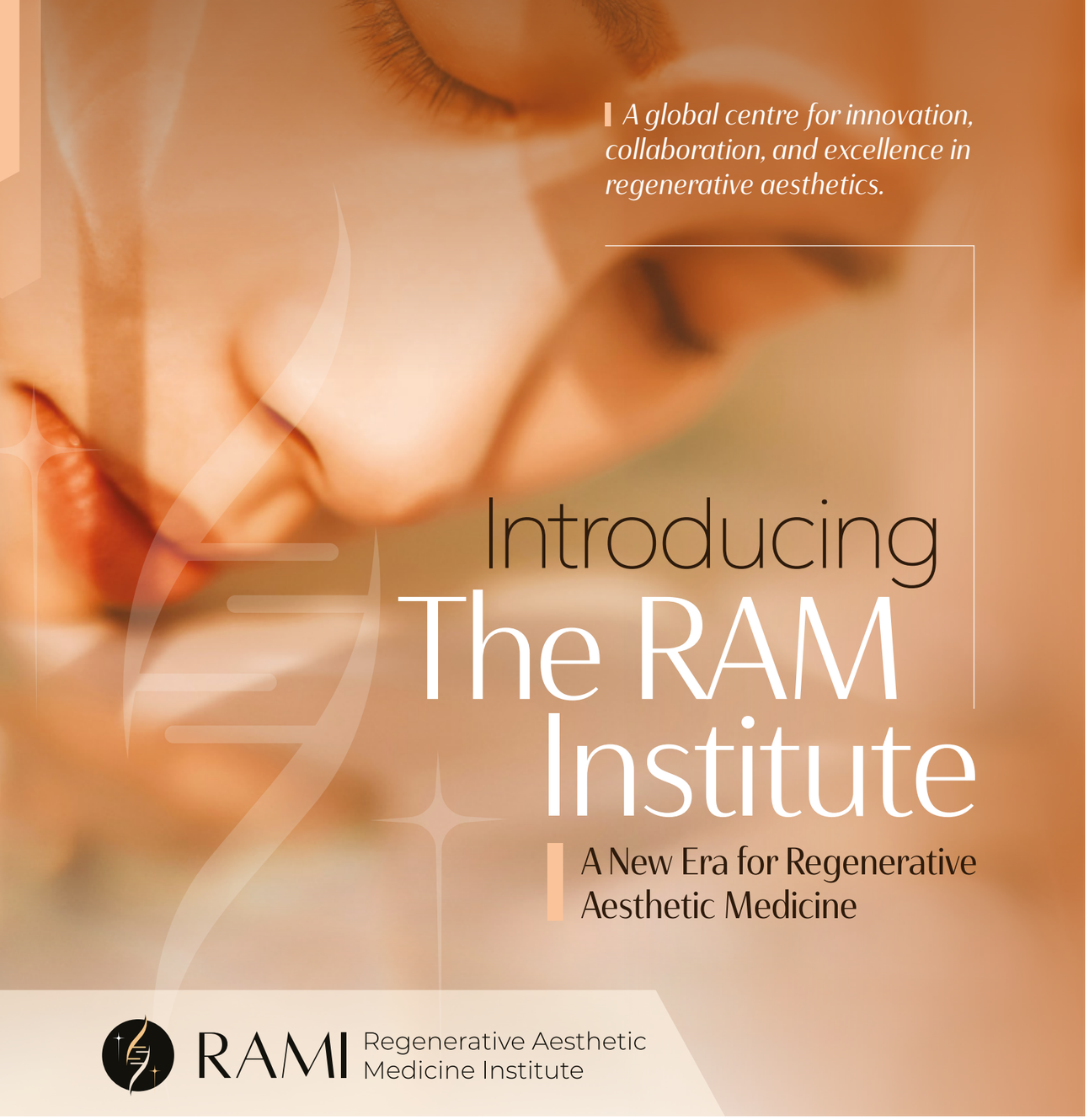


A global centre for innovation, collaboration, and excellence in regenerative aesthetics.

Introducing The RAM Institute

A New Era for Regenerative Aesthetic Medicine

RAMI Regenerative Aesthetic Medicine Institute

It is with great enthusiasm that we at the Journal of Regenerative Aesthetic Medicine (JRAM), announce a defining moment in the evolution of our field: the launch of **The Regenerative Aesthetic Medicine Institute (RAMI)** - a global centre for innovation, collaboration, and excellence in regenerative aesthetics.

What began as a single, focused initiative - the inaugural Regenerative Aesthetic Medicine Conference and Exhibition (RAMCE) in 2023 - has rapidly evolved into something much greater. With two successful conferences behind us and a growing international community of pioneers, 2025 marks the formal establishment of The RAM Institute as a multi-dimensional platform dedicated to advancing the science and practice of regenerative aesthetic medicine.

A vision grounded in science, elevated by community

The RAM Institute exists to cultivate a vibrant, global network of clinicians, researchers, educators, and industry leaders. Its mission is ambitious yet essential: To elevate clinical standards, accelerate innovation, and improve patient outcomes through transformative education, collaboration, and research.

At JRAM, we are proud to be a cornerstone of this mission - documenting and disseminating the research, insights, and case studies that drive our field forward.

Our **core values**

The RAM Institute is guided by four fundamental values that shape every aspect of its work:

- **Innovation:** Advancing techniques and technologies grounded in scientific evidence.
- **Collaboration:** Uniting disciplines to share knowledge and catalyse progress.
- **Excellence:** Setting and upholding the highest standards in clinical and academic practice.
- **Integrity:** Maintaining transparency, ethics, and trust in everything we do.

JRAM reflects these principles in our editorial policy, Scientific Committee review process, and commitment to publishing meaningful, impactful work.

Three pillars of advancement

The RAM Institute empowers the regenerative aesthetics community through three flagship initiatives:

1 **JRAM** (this journal)

Published quarterly in February, May, August, and November - JRAM is a scientifically-led journal inviting submissions in original research, clinical case studies, and thought leadership. We welcome new authors and ideas that contribute to the scientific foundation of regenerative aesthetic practice.

Interested in publishing?
Scan the QR Code here.

2 **RAMCE** (conference and exhibition)

Now entering its third year, RAMCE returns on November 8, 2025, at the Pullman Hotel, London. This annual gathering of global thought leaders serves as a platform for bold ideas, cutting-edge science, and meaningful clinical discussion.

Want to speak at RAMCE 2025?
Submit your abstract by scanning the QR Code.

3 E-learning platform

A comprehensive digital education hub is currently in development. Designed for the modern regenerative aesthetic practitioner, this platform will deliver flexible, evidence-based professional development, anytime, anywhere.

Scientific leadership

At the heart of The RAM Institute is its Scientific Committee, composed of internationally respected experts who guide and uphold our academic and clinical standards. You can read about their individual experiences and expertise on the next page.

The Scientific Committee's oversight ensures that all our initiatives - from editorial reviews to event programming- are grounded in rigorous, ethical, and clinically relevant science.

A Message to Our Community

Let's shape the future of aesthetic medicine - together

A movement for elevating standards, inspiring innovation, and driving meaningful change in how we think about beauty, health, and regenerative care.

We invite you to be a part of it.

Explore. Collaborate. Lead.
Welcome to the RAM Institute.

The JRAM News Brief

Essential reading on advancements in regenerative science and aesthetic practice

Market Growth and Infrastructure Development

Cell Therapy Market Size Projected to Reach USD 33.93 Billion by 2033

In eight years, the global cell therapy market is set to grow from USD 6.86 billion in 2025 to USD 33.93 billion.

This expected growth, at a CAGR of 22.12%, is as a result of rapid advances in stem cell research, according to Straits Research.

The market intelligence company highlights that a continuing availability of grants from government and corporate funding sources to support clinical trials into cell therapy treatments is driving the market.

Straits Research said, "Rapid advances in stem cell research offer the potential to address unmet disease management requirements in the pharmaceutical, biotech, and medical industries... Furthermore, the rising desire for personalised treatment and public knowledge of the benefits of cell therapy is expected to provide new business opportunities in the field."

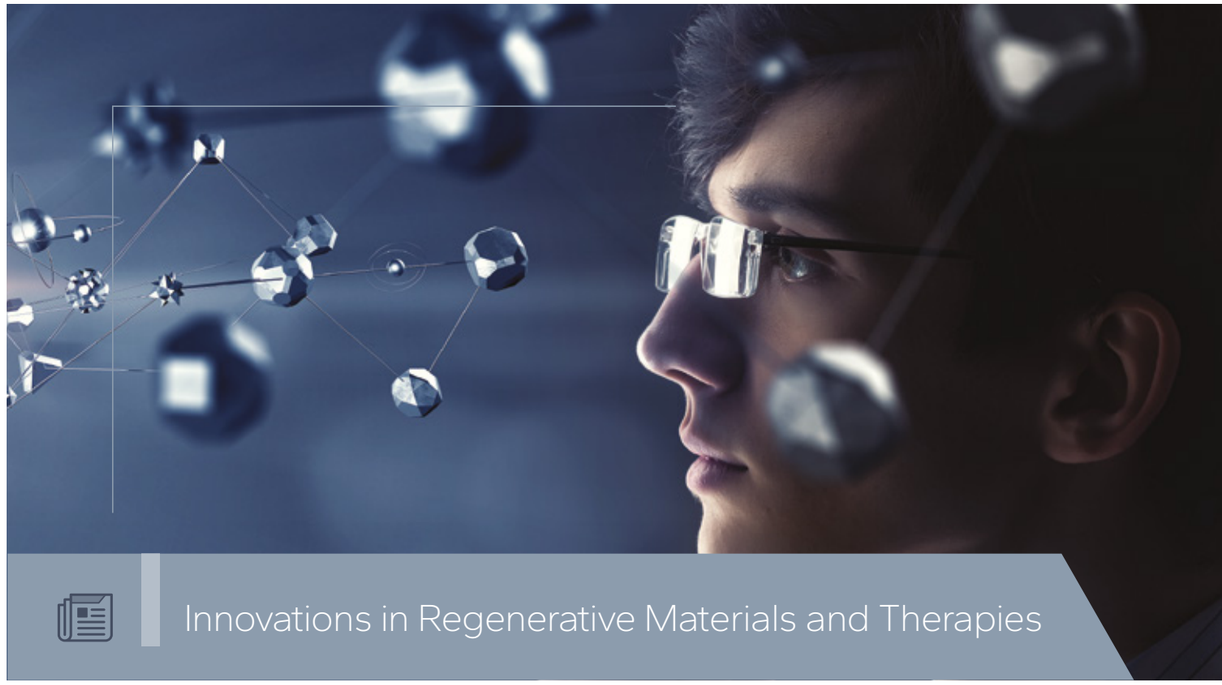
Statistics suggest that North America is the most significant global cell therapy market shareholder, with an estimated CAGR of 14.8% over the forecast period.

Stem Cell Research Centre Opens in the UAE

The United Arab Emirates University has opened a stem cell research centre dedicated to addressing the increasing global demand for regenerative treatments.

According to the University, this is the first of its kind in the academic world in the UAE. As well as supporting research, the centre aims to enhance manufacturing capabilities and establish international partnerships to support the stem cell market in the Middle East.

Professor Fatma Al Jasmi, Acting Dean of the College of Medicine and Health Sciences at the UAEU, said, "The opening of the Stem Cell Research Centre is a significant achievement that reflects the university's vision to promote research innovation and build national capacities in medical sciences. Through this centre, we aim to prepare a new generation of Emirati scientists capable of offering advanced medical solutions and solidifying the UAE's position as a global leader in regenerative medicine."



Innovations in Regenerative Materials and Therapies

FDA clears new tissue regeneration treatment

The Food and Drug Administration (FDA) has cleared Cohealyx - a collagen-based dermal matrix designed for tissue integration and revascularation.

According to AVITA Medical, the company which co-developed the product alongside Regenity Biosciences, Cohealyx consists of an advanced bovine collagen-based design that facilitates cellular migration and blood vessel formation. The company said, "Preclinical studies in porcine models demonstrated that Cohealyx generated robust tissue capable of consistently supporting a split-thickness skin graft in a two-stage procedure earlier than leading dermal matrices in the study."

The product's capabilities will next be evaluated in real-world settings, focusing on clinical efficacy and cost savings in treating full thickness wounds and burns.

'Living' gel created to mimic human tissue healing

Researchers from Pennslyvania State University have outlined how they have developed a material that can mimic the behaviour of the extra-cellular matrix (ECM) to heal wounds after tissue damage.

Published in *Material Horizons* in February 2025, the authors explain how they aimed to develop acellular nanocomposite living hydrogels with nonlinear mechanics and self-healing properties.

They said, "Inspired by the mechanical behavior of ECMs, we develop acellular nanocomposite living hydrogels (LivGels), comprising network-forming biopolymers and anisotropic hairy nanoparticle linkers that mimic the dynamic mechanical properties of living counterparts.

We show that a bifunctional dynamic linker nanoparticle (nLinker), bearing semi-flexible aldehyde- and carboxylate-modified cellulose chains

attached to rigid cellulose nanocrystals converts bulk hydrogels to ECM-like analogues via ionic and dynamic covalent hydrazone bonds. The nLinker not only enables the manipulation of nonlinear mechanics and stiffness within the biological window, but also imparts self-healing to the LivGels."

While previous synthetic alternatives raised concerns about biocompatibility, these hydrogels have avoided synthetic polymers entirely. Additionally, testing has shown that they can quickly recover their structure after experiencing high strain. The researchers believe these gels could be used across medicine - potentially acting as scaffolds for tissue repair in regenerative medicine and providing a more realistic model for testing new medications in drug development.

Co-researcher on the study Amir Sheikhi said, "Our next steps include optimising LivGels for specific tissue types, exploring in-vivo applications for regenerative medicine, integrating LivGels with 3D bioprinting platforms and investigating potential in dynamic wearable or implantable devices."

E-skin patch heals wounds and grows hair using the body's own stress signals

Researchers in China have developed an electronic skin patch that aims to revolutionise the treatment of chronic wounds. Published in *Advanced Functional Materials* in February 2025, Multimodal Antibacterial E-Skin Patch Driven by Oxidative Stress for Real-Time Wound-Status Monitoring and Integrated Treatment of Chronic Wounds, details the outcome of studies on the e-skin patch known as TENG-gel.

The patch is constructed using a combination of polydimethylsiloxane/polytetrafluoroethylene (PDMS/PTFE) film, eutectic gallium-indium (E-GaIn), and a composite hydrogel made from quaternary chitosan, polyacrylamide, sodium alginate, and molybdenum disulfide (MoS_2) nanosheets.

According to the researchers, this layered assembly enables the patch to harness the body's oxidative stress to power itself, eliminating the need for external energy sources. One of the standout features of the TENG-gel is its multimodal antibacterial capability. It integrates peroxidase-like activity, photothermal therapy, and a nano-knife effect, achieving a bacterial elimination rate exceeding 95% against both Gram-positive and Gram-negative bacteria. This approach aims to prevent infections in chronic wounds, promoting a more conducive environment for healing.

The TENG-gel's ability to generate electrical stimulation also facilitates the migration of fibroblasts by activating specific signalling pathways. Additionally, it accelerates vascularisation by promoting the secretion of growth factors such as CD31, VEGF, and TGF-β. These actions were found to collectively enhance tissue regeneration, leading to a 1.6-fold increase in new hair follicle formation and a 2.4-fold increase in collagen deposition compared to control groups.

The patch also boasts dual temperature and strain-sensing capabilities, allowing for real-time monitoring of the wound environment and providing alerts to potential external threats. The researchers note that this feature ensures clinicians can provide timely interventions and tailored treatment strategies, aligning with the principles of personalised medicine.

Study suggests enhanced skin regeneration with nutrient-enriched calcium hydroxyapatite dilution

An in vitro study published in the journal *Cureus* in March 2025 has suggested that a nutrient-rich dilution of calcium hydroxyapatite (CaHA) may significantly boost the compound's regenerative potential.

Researchers conducted a comparative in vitro analysis using Stiim®, a commercial CaHA product, diluted with either standard saline or a custom poly-micronutrient solution containing essential vitamins, amino acids, and minerals. Microscopic imaging and cell culture assays were used to evaluate how each formulation interacted with fibroblasts.

The poly-micronutrient mix appeared to outperform the saline-diluted formulation, showing improved cell viability, increased fibroblast activation, and greater collagen synthesis markers.

"The key finding is that the micronutrient solution may act synergistically with CaHA to enhance its effects at a cellular level," the authors said, noting, "This could potentially translate into longer-lasting and more natural rejuvenation outcomes in clinical use."

There were no signs of destabilisation in the poly-micronutrient mixture, indicating the solution could be safe for future clinical testing. Clinical trials are necessary to confirm the findings in real-world applications and to determine optimal concentrations for safety and efficacy.

Research indicates positive results for PRF stretch mark treatment

Researchers have found that combining microneedling with autologous platelet-rich fibrin (PRF) may deliver better outcomes than traditional platelet-rich plasma (PRP) treatments in reducing abdominal stretch marks, also known as striae distensae. The findings come from a randomised comparative study published in the *Archives of Dermatological Research* in March 2025.

PRP and PRF are both blood-derived treatments used in regenerative medicine and aesthetics, but they differ in composition and performance. PRP is a liquid concentrate of platelets obtained using anticoagulants and high-speed centrifugation, leading to a rapid but short-lived release of growth factors.

In contrast, PRF is prepared without additives using slower centrifugation, resulting in a fibrin-rich gel that releases growth factors more gradually over several days. PRF also contains white blood cells and provides a natural scaffold that supports longer-lasting tissue regeneration.

The study involved 30 participants who received treatments on both sides of their abdomens using a split-method approach.

One side was treated with microneedling combined with PRF, while the other side received microneedling with PRP. Over the course of 3 sessions, spaced one month apart, researchers monitored skin improvement using clinical photography, measurement tools, patient feedback, and skin biopsies.

While both treatment types led to significant visible improvements in stretch mark appearance, PRF appeared to slightly outperform PRP in terms of skin texture and patient satisfaction - though the differences weren't statistically significant.

"Platelet-rich fibrin may offer a more natural and longer-lasting release of growth factors compared to PRP," the researchers noted, pointing to its ease of preparation and cost-effectiveness as additional benefits.

Cold plasma-activated solutions show promise in healing chronic wounds

Research published in *Biomedicine & Pharmacology* has discussed a novel approach to treating chronic wounds using plasma-activated media (PAM). The authors explore the therapeutic potential of cold atmospheric plasma (CAP) to enhance wound healing processes.

CAP is a partially ionised gas that, when applied to biological solutions, generates reactive oxygen and nitrogen species (RONS). These reactive species are known for their antimicrobial properties and ability to promote tissue regeneration. The research investigates how CAP-treated solutions can be utilised to accelerate skin wound healing, particularly by stimulating re-epithelialisation in preclinical in vivo models involving rats and mice.

Key findings indicate that PAM exhibits significant antimicrobial activity against common wound pathogens and can stimulate cellular responses beneficial for tissue repair. The research suggests that PAM could serve as an effective adjunct or alternative to traditional wound care methods, especially in managing chronic wounds that are resistant to conventional treatments.

This contributes to the growing body of evidence supporting the biomedical applications of cold plasma technologies, highlighting their potential in developing advanced therapies for wound management.

Further research is needed to standardise how plasma is generated and applied, as current methods vary widely. Additionally, robust clinical trials are essential to confirm the safety, effectiveness, and optimal use of plasma-activated solutions in human patients.

A novel approach to treating chronic wounds using plasma-activated media (PAM)

Advanced imaging technology reveals structural diversity of small extracellular vesicles

A pioneering study from Kanazawa University's Nano Life Science Institute (WPI-NanoLSI) has unveiled a novel application of high-speed atomic force microscopy (HS-AFM) videography to visualise small extracellular vesicles (sEVs) in unprecedented detail.

These nanoscale particles, crucial for intercellular communication, have been challenging to study due to their minute size and dynamic nature.

Led by researchers Keesiang Lim and Richard W. Wong, the team employed HS-AFM to capture real-time, nanometer-resolution images of sEVs derived from HEK293T cells. This technique allowed them to observe the vesicles' surface structures and interactions under near-physiological conditions without the need for extensive sample preparation.

The study revealed two distinct sEV subpopulations: smaller vesicles (≤100 nm) exhibited greater membrane rigidity and higher concentrations of exosomal markers like CD63 and CD81, suggesting an endosomal origin. In contrast, larger vesicles (>100 nm) showed more structural variability, indicating a different biogenesis pathway.

"By leveraging HS-AFM videography, we can now directly observe the dynamic interactions of surface markers on individual sEVs, paving the way for the development of high-precision EV-based biomarkers," said Wong.

The researchers suggest that the method could contribute to advancements in targeted drug delivery and regenerative medicine by enabling more precise characterisation of therapeutic EVs.

The full study is available in the *Journal of Extracellular Vesicles.*

Genetic & Cellular Insights into Regeneration

Research indicates genetic explanation for regeneration

A team of international researchers suggests that tissue regeneration may be more widespread in mammals than previously believed.

In a study on a group of African rodents called brush-furred mice, it was discovered that they could regrow musculoskeletal tissue instead of healing injuries with scar tissue. Brush-furred mice are part of the deomyinae subfamily of rodents, of which there are 42 species.

According to the University of Kentucky, this is also the case for spiny mice, another species in the deomyinae subfamily, which can regrow lost skin, restore function to a severed spinal cord and repair damaged heart tissue.

This is unlike nondeomyinae rodents, which are found to heal injuries via fibrotic repair with scar tissue.

A team of international researchers suggests that tissue regeneration may be more widespread in mammals than previously believed

In a paper published in the *Proceedings of the National Academy of Sciences of the United States of America (PNAS)*, the researchers stated, "These data reveal a phylogenetic signal for enhanced regenerative ability in deomyinae which is key to testing evolutionary hypotheses about the emergence of regenerative ability in mammals."

Of note, Stephen Kiama, Ph.D., who took part in the research, said, "This study provides yet another animal model for scar-free wound healing."

Fellow researcher Ashley W. Seifert, Ph.D, added, "Importantly, this study provides the foundation to test the degree to which specific cellular, genetic and physiological features are or are not correlated with regenerative ability, which will pave the way for subsequent studies."

New study reveals insights into human skin regeneration using xenografts

A recent study published in *Cells* in March 2025 has provided valuable insights into the regenerative behaviour of human skin when transplanted onto immunodeficient mice. The research focuses on understanding how the epidermal proliferation patterns recover in such xenograft models, offering potential advancements in dermatological treatments and skin transplantation techniques.

Researchers obtained full-thickness human skin samples, including all dermal layers and appendages, from consenting patients undergoing plastic surgeries. These samples were then transplanted onto 8-week-old NOD SCID mice. Biopsies were collected at intervals of 40, 75, and 110 days post-grafting to analyse the restoration process.

The study employed advanced imaging and computational clustering techniques to assess keratinocyte heterogeneity and proliferation dynamics within the epidermal basal layer. Findings indicated that the xenografted human skin successfully restored most skin structures, including hair follicles, sebaceous glands, and sweat glands. Notably, the epidermal stem cell niche structure was also reestablished, underscoring the model's potential to mimic human skin regeneration dynamics effectively.

These results suggest that human skin xenografts can serve as a functional in vivo model for studying human skin behaviour, disease pathologies, and potential treatments. By providing a reliable microenvironment that closely resembles actual human tissue functioning, this model could be instrumental in advancing research on skin regeneration and developing novel therapeutic strategies.

Scientists have identified a vital protein that helps protect hair follicle stem cells (HFSCs) and enables adult hair regeneration

Research highlights key protein that enables hair regrowth

Scientists have identified a vital protein that helps protect hair follicle stem cells (HFSCs) and enables adult hair regeneration.

Published in March 2025 in *Nature Communications*, their research reveals how MCL-1 acts as a 'cellular bodyguard' for activated HFSCs. In this study, the team used mouse models to show that deleting the MCl-1 gene led to rapid death of activated HFSCs and a complete block in hair regrowth after induced hair removal.

Interestingly, quiescent (inactive) HFSCs were unaffected by the absence of MCL-1. It was only when the cells were called into action that they succumbed to stress and died - unless MCL-1 was present.

The researchers also discovered that MCL-1 is regulated by the ERBB signaling pathway, which is known to promote stem cell activation and hair growth. This connection highlights a potential target for future treatment: boosting ERBB signaling or MCL-1 activity could enhance stem cell survival and promote hair regeneration.

Scientists pioneer high-resolution mapping of 3D collagen cell cultures

Researchers have unveiled a cutting-edge approach for analysing 3D cell culture systems composed of type I collagen - one of the most abundant structural proteins in the human body. By combining light and electron microscopy with mass spectrometry imaging (MSI), the researchers performed a multiparametric physicochemical analysis of the 3D matrix, revealing insights into cellular organisation, biochemical environments, and extracellular matrix (ECM) dynamics.

Published in *Scientific Reports* in March 2025, the study introduces a robust methodological framework for examining collagen-based 3D cultures that more closely mimic the complexity of living tissues than traditional 2D models.

The research team used a multimodal imaging strategy that included:

- Light microscopy to visualise the overall distribution and morphology of cells within the collagen gel. Using phase contrast and fluorescence imaging, they could monitor cell viability, matrix remodeling, and structural integrity.
- Transmission and Scanning Electron Microscopy (TEM & SEM) to provide anometer-scale resolution of collagen fibers and cellular interfaces. TEM captured cross-sections of cells and matrix interactions, while SEM detailed the surface topography of the hydrogel and cell protrusions. These observations confirmed how cells adapt to and remodel their 3D surroundings.
- Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) to map the distribution of lipids, amino acids, and other biomolecules within the 3D scaffold. This allowed for spatially resolved chemical profiling - shedding light on how different regions of the matrix may influence or respond to cell behaviour.

By integrating structural and chemical imaging, the researchers achieved a comprehensive physicochemical profile of the 3D collagen model.

In regenerative aesthetics, collagen-based scaffolds are commonly used in dermal fillers, wound healing therapies, and antiaging applications. The ability to precisely analyse how cells behave within these matrices at both structural and molecular levels could lead to the development of more biocompatible, longer lasting, and biologically active aesthetic materials.

Exosomes in Regenerative Medicine

Study identifies extracellular vesicles' ability to modulate pigmentation.
Research conducted in Malaysia and published by the International Journal of Nanomedicine in February 2025 has found that small extracellular vesicles derived from umbilical cord mesenchymal stromal cells (UC-MSC-sEVs) can stimulate human dermal fibroblast proliferation, regulate the skin's extracellular matrix and reduce melanin production.

The study aimed to investigate the impact of UC-MSC-sEVs on in-vitro models. Umbilical cord samples were collected from consenting mothers aged 18-44 who underwent natural or caesarean delivery at full term without pregnancy complications, infection diseases or a history of cancer. Human dermal fibroblasts were obtained from consenting healthy patients aged 18-60 who had undergone abdominoplasty.

Findings revealed a high concentration of UC-MSC-sEVs positively influenced fibroblast proliferation and the regulation of the extracellular matrix. UC-MSC-sEVs did not stimulate human melanoma cell growth, but reduced pigmentation by decreasing melanin synthesis.

Researchers said, "These in-vitro findings highlight the dose-dependent beneficial effects of UC-MSC-sEVs on skin cells, particularly fibroblasts and melanocytes, through different cellular mechanisms. This underscores the importance of considering sEV dose or charge in future studies and suggests a promising approach for addressing hypertrophic scars and hyperpigmentation, offering insights into the field of dermatology."

Review identifies current literature on exosomes for hair loss

A scoping review published in *Cureus* in March 2025 has examined the extent and type of evidence in current literature on the use of exosomes as a treatment for hair loss.

Exosomes are nano-sized extracellular vesicles that play a crucial role in intercellular communication by transporting bioactive molecules such as proteins, lipids, and RNA. They exert their effects on hair follicles by activating dermal papilla cells, modulating pathways to promote hair follicle development, reducing inflammation and enhancing angiogenesis.

The U.S. Food and Drug Administration (FDA) currently classifies exosomes as biological drugs, and no exosome products have received FDA approval for hair loss treatment. The FDA has issued warnings about unapproved exosome therapies due to reports of complications, underscoring the need for rigorous clinical testing and regulatory oversight.

Researchers conducted a broad literature search that yielded 1,087 citations. After removing 284 duplicates, 803 articles were screened for eligibility. Ultimately, 16 studies met the inclusion criteria for the review. These studies investigated exosome applications across various regenerative contexts, including hair follicle regeneration, wound healing, spinal cord injury repair and collagen regeneration.

Exosomes were sourced from mesenchymal stem cells, human adipose-derived stem cells, macrophages and human dermal fibroblasts.

Of note, 14 out of the 16 studies utilised microneedle patches, highlighting a growing consensus around this method's efficiency in localised, minimally invasive delivery. Compared to standard injection or topical methods, microneedle-mediated delivery demonstrated superior tissue penetration and retention.

The review positions microneedle patch delivery of MSC-derived exosomes as the leading candidate for clinical translation in hair restoration therapies. It details how they show promising results in stimulating the anagen phase, improving hair density, and promoting vascularisation around hair follicles.

While definitive large-scale clinical trials are still lacking, the growing body of preclinical and early-phase clinical evidence makes a strong case for further exploration. It should be noted that human-derived exosomes are banned from use under EU and UK regulations.

The Guardian identifies UK clinics offering human-derived exosomes

An investigation by UK-based newspaper The Guardian has found several clinics are offering human-derived exosomes treatment for skin and hair regeneration.

Under UK and EU regulations, human-derived exosomes are banned due to concerns with significant health risks.

According to the newspaper, several clinics were found to be promoting products sourced from human umbilical cord blood stem cells or other human cell sources.

Dr Guillaume van Niel, a research director at the Angers Cancer and Immunology Research Centre in Nantes, France, told The Guardian, "The most dangerous risk would be that viruses are in the product. Viruses have the same size and the same physical properties as exosomes. It's nearly impossible to sort exosomes out of a pool of viruses. If you isolate one, you get the other."

A Department for Business and Trade spokesperson added, "Exosomes of human origin are banned in cosmetics that are sold in the UK. We urge anyone who has concerns about the safety of a product to contact their local trading standards department or Citizens Advice."

New study highlights potential of stem cell-derived exosomes in treating scleroderma skin fibrosis

A recent study published in Scientific Reports in February 2025, reveals that exosomes derived from adipose mesenchymal stem cells (AMSCs) may offer a promising new approach to treating skin fibrosis in systemic sclerosis (SSc), commonly known as scleroderma.

SSc is a chronic autoimmune disease characterised by progressive fibrosis of the skin and internal organs, leading to significant morbidity. Current treatments have limited efficacy, especially in addressing skin fibrosis, which affects over 90% of SSc patients.

The study, led by researchers from Fudan University in Shanghai, investigated whether exosomes - nano-sized vesicles secreted by AMSCs - could replicate the therapeutic effects of the stem cells themselves. In laboratory experiments, both direct and indirect co-cultures of AMSCs with skin fibroblasts from SSc patients resulted in reduced expression of fibrosis markers, including α-SMA, COL1A1, COL3A1, and TGF-β 1.

Further analysis demonstrated that exosomes isolated from AMSCs could be taken up by SSc fibroblasts and similarly inhibit the expression of these fibrosis-related genes and proteins. Notably, the exosomes appeared to exert their anti-fibrotic effects by inhibiting the TGF-β 1/Smad3 signaling pathway, a key regulator of fibrosis.

To validate these findings in vivo, the researchers employed a bleomycin-induced mouse model of skin fibrosis. Mice treated with either AMSCs or their derived exosomes showed significant reductions in skin thickness and collagen deposition compared to untreated controls. Western blot analyses confirmed decreased levels of fibrosis markers and suppression of the TGF-β 1/Smad3 pathway in treated mice.

The authors suggest that AMSC-derived exosomes could serve as a 'cell-free' therapeutic alternative to stem cell transplantation, potentially mitigating risks associated with cell-based therapies, such as immune rejection and tumorigenicity. They conclude that these exosomes may be 'rising star candidates' for the treatment of SSc skin fibrosis.

While these findings are promising, the study acknowledges the need for further research to fully understand the mechanisms involved and to assess the long-term safety and efficacy of exosome-based therapies in clinical settings.

The authors suggest that AMSC-derived exosomes could serve as a 'cell-free' therapeutic alternative to stem cell transplantation

In recent years, we've seen a growing emphasis on skin health and subtle enhancements, driving interest in polynucleotides.

The *Future* of Polynucleotides

Exploring the rise of this revolutionary injectable treatment and its impact across the world

In 2024, the global polynucleotides injectable market was valued at USD 131.05 million, with projections indicating growth to USD 490.68 million by 2033.[1]

This exponential increase, with a CAGR of 14.40%, demonstrates how polynucleotides have evolved from a mere 'buzzword' in regenerative medicine, into a well-established, reliable and popular treatment.[1]

So, what does the future hold? We examine the development of polynucleotides and hear from two experts on what to expect over the next decade.

A brief history of polynucleotides

Polynucleotides are biological molecules comprising a series of monomer units called nucleotides. These nucleotides are made up of a sugar (ribose or deoxyribose), a phosphate group and nitrogenous base. The two main types of polynucleotides are DNA (double-stranded sugar phosphate deoxyribose) and RNA (single-stranded sugar phosphate ribose).[2]

Since the discovery of DNA in 1953, scientists have learnt more about the role of polydeoxyribonucleotides and polynucleotides and used them to contribute to the development of modern medicine. Their therapeutic abilities have meant that they've been used to successfully treat complex wounds and ulcers, inflammatory arthritis, inflammatory bowel diseases, burns and early oestoarthritis.[2]

More recently, polynucleotides have gained traction as a non-invasive aesthetic treatment. Research highlights that their biocompatibility, biodegradability and regenerative properties makes them well suited for skin rejuvenation, revitalisation, pre-treatment priming, scar management and hair growth treatments.[2]

Aesthetic practitioner, dental surgeon, clinical researcher and trainer Dr Souphiyeh Samizadeh has observed this evolution firsthand in the UK and Asia. She explains, "While research initially focused on wound healing, experimental aesthetic applications began in Europe in the mid-2000s with Mastelli's Polynucleotides HPT® technology. Over in South Korea, polynucleotides - particularly Rejuran Healer - gained popularity thanks to their treatment for acne scars and skin rejuvenation as early as 2014."

As we know, the 2020s made way for the mainstream global use of polynucleotides. "This has expanded into under-eye treatment, scar revision and hair restoration, alongside introducing combination therapies," highlights Dr Samizadeh.

Increasing popularity

In a short time, demand for polynucleotides has soared. Data from Rare: Group, a UK-based market intelligence firm specialising in private healthcare, indicates that as of October 2024, polynucleotides treatment had increased by 102%. Ben Pask, founder of Rare: Group, says, "In a six-month period, the polynucleotides market penetration shot from 5 to 10% - a significant jump."[3]

Pask attributes this surge to the growing interest in longevity and wellness. Consumers are increasingly mindful of their health, influenced by brands like ZOE, which offers personalised nutrition plans, and high-profile figures such as Bryan Johnson, who reportedly spends $2 million annually on 'biohacking' to maintain youth.

"Rightly or wrongly, regenerative aesthetics also sits in this space, with many clinicians now going beyond toxins and fillers, and incorporating treatments and services that support overall health, aesthetics, longevity and wellness," explains Pask.

Asia leads the polynucleotides market, holding a 46.5% share in 2024.[1] Dr. Samizadeh cites multiple reasons for this dominance.

"Biotech firms such as Hugel Pharma and Medytox are at the forefront of polynucleotide research and development. Additionally, in South Korea, polynucleotides are classified as Class II medical devices, allowing for faster approvals compared to the EU's stricter regulations," she says. China also operates in a regulatory 'grey zone,' enabling rapid adoption of off-label polynucleotide treatments.

Moreover, Asia's high clinic density (Seoul has one clinic per 500 people) and affordable pricing - ranging from £100-£300 per session in Korea compared to £500-£800 in the UK - make treatments more accessible. "Many clinics offer 'tourist bundles,' packaging polynucleotides with other treatments at discounted rates, attracting international patients," Dr Samizadeh adds.

Cultural attitudes also play a role. "In Asia, there is a strong emphasis on preventative skincare, with many seeking treatments in their 20s and 30s to achieve 'glass skin' -hydrated, smooth, and poreless." She explains how Asian patients tend to adopt a 'skin-first' philosophy where they place a high priority on achieving optimal skin health, with extensive social pressure for a youthful appearance coming from a competitive job market, finding partners and social media influencers.

"This contrasts with Western patients, who traditionally begin aesthetic treatments later to address wrinkles and volume loss. With a more diverse ethnic population, there's also been a higher demand for pigmentation treatments," notes Dr Samizadeh.

However, Western markets are shifting. "In recent years, we've seen a growing emphasis on skin health and subtle enhancements, fuelling interest

As of October 2024, polynucleotides treatment had increased by 102%

in polynucleotides," Dr Samizadeh says. This, combined with increased research specific to aesthetic concerns, will continue to drive their popularity.

Room for future growth or a market cap?

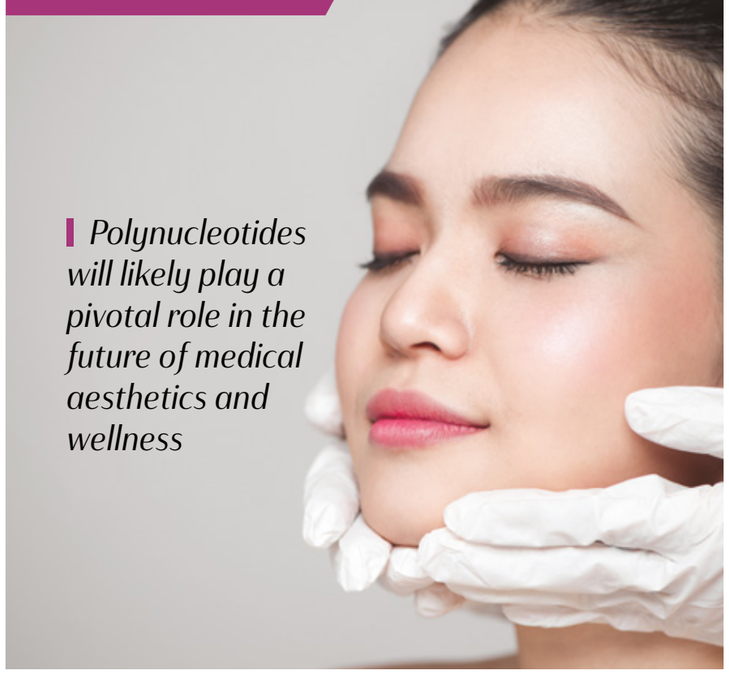
According to Rare: Group, a survey of 957 UK consumers interested in medical aesthetics revealed that only 22% fully understood polynucleotide treatments, while 35% had heard of them but were unclear on their benefits, and 43% were entirely unaware.[4]

Additionally, market penetration remains lower than expected in regions like the Midlands and Wales, suggesting further growth opportunities.

However, challenges remain. Pask notes that some practitioners have raised concerns about discomfort during procedures and the gradual nature of results. "While not an issue for all patients, these factors can be hurdles. Moreover, the aesthetic industry continually sees new innovations, which can create competition," he explains.

Dr Samizadeh predicts further advancements will influence polynucleotide treatments. "Practitioners are already combining polynucleotides with regenerative therapies like exosomes and stem cells for enhanced results," she says, adding that regulatory changes may also impact the market. "I anticipate that the FDA will approve polynucleotides for scar treatment soon, which could expand their global use, while the EU may introduce stricter cross-border sales regulations," she says.

Furthermore, Dr Samizadeh suggests that the introduction of synthetic polynucleotides could also mitigate ethical concerns regarding animal sourcing, potentially driving wider adoption.



Polynucleotides will likely play a pivotal role in the future of medical aesthetics and wellness

"It's likely that AI will also play a role," Dr Samizadeh adds, suggesting that 3D skin mapping could allow for more personalised polynucleotide treatments.

Adapting to the future

To sustain growth, Pask emphasises the importance of equipping practitioners with the right tools. "Education on long-term benefits over quick fixes, alongside techniques to enhance patient comfort, will be crucial," he says.

Dr Samizadeh warns of potential safety risks due to rapid market expansion. "We lack long-term data for some products, with most studies tracking results for under 12 months," she notes. Additionally, with new brands emerging, ensuring product efficacy, DNA extraction standards, purification processes, and ethical sourcing is essential.

She also highlights how there are variable protocols for injection depth, which are worth exploring, as well as a need for standardised training across all polynucleotides' brands.

Polynucleotides have rapidly evolved from a niche concept to a mainstream treatment in aesthetics and regenerative medicine. While challenges exist, including regulatory shifts, patient education, and evolving competition, the market's potential remains strong. With ongoing research, technological advancements, and increasing global awareness, polynucleotides will likely play a pivotal role in the future of medical aesthetics and wellness.

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Words: Chloé Gronow

Topical Drug Reduces Skin Ageing

A look at ABT-263 and its impact on senescent cells

In a study published by *Aging* in December 2024, researchers from the Boston University School of Medicine outlined how a drug called ABT-263 can significantly improve wound healing in ageing skin.[1]

It was found to effectively reduce several senescence markers in the aged skin of mice, as well as accelerating wound healing. Here we share the findings and consider its place in regenerative aesthetics.

Cellular senescence and skin ageing

Senescent cells are dysfunctional cells that have permanently ceased proliferation. Rather than undergoing apoptosis, these cells persist within the body, where they contribute to chronic low-grade inflammation through the secretion of pro-inflammatory cytokines, chemokines, and matrix-degrading enzymes - a process known as the senescence-associated secretory phenotype (SASP).

The accumulation of senescent cells increases with age, exacerbating systemic inflammation and accelerating tissue degeneration. In the context of aesthetics, this process manifests as a decline in skin quality, including reduced elasticity, increased wrinkling, and impaired wound healing.[2]

In aged skin on humans, primates and mice, chronic senescent cells are reported to comprise up to 15% of cells in the epidermis and dermis.[1]

Research approach

The researchers outline in *Aging* that many clinical trials that investigate the use of senolytics - drugs that eliminate senescent cells - are already underway; focusing on ameliorating age-related diseases such as osteoporosis, kidney disease and pulmonary fibrosis. They do not, however, address how senescence-reduction in aged tissues might affect responses to a subsequent injury such as cutaneous wounds.[1]

Additionally, while in-vitro and in-vivo research has indicated some reduction in detectable senescent cells in aged mouse skin, data relating to the impact of their removal on subsequent wound repair is limited.

As such, the researchers chose to specifically examine ABT-263's impact on wound healing. This is a senolytic drug that inhibits the anti-apoptotic proteins BCL-2 and BCL-xL, which are upregulated in senescent cells.

They said, "We selected ABT-263 for this study due to its reported broad-spectrum senolytic activity on multiple cell types. Furthermore, prior studies have utilised ABT-263 with robust effect on skin-specific senescent cell clearance of fibroblasts, myofibroblasts, and melanocytes."

To avoid removing potentially beneficial cells expressing senescence markers, the researchers opted for pre-treatment rather than continuous senolytic treatment. They commented that this strategy could be particularly valuable for elective and reconstructive surgeries in elderly patients who are at higher risk for non-healing wounds and incisional dehiscence.

Methods

Either ABT-263 or a DMSO vehicle alone was applied directly to the skin of 24-month-old male mice daily over a five-day period. A 1cm full-thickness dorsal skin wound was then created five days after the last day of treatment. Wounds were imaged every three days and specific software used to calculate the wound area.

Senescence-associated beta-galactosidase (SA-β-gal) staining was completed, immunohistochemistry and histological assessment undertaken, bulk RNA sequencing and analysis, and statistical analysis were conducted to collate the study's results.

Results

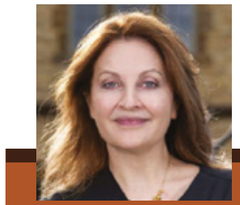
Following treatment with topical ABT-263, aged skin demonstrated decreased gene expression of senescence markers p16 and p21, as well as reductions in SA-β-gal- and p21-positive cells compared to DMSO controls. It should be noted that the treatment also triggered a temporary inflammatory response and macrophage infiltration in the skin.

The study found that 33% of the ABT-263 treated mice had completed healing by day 18, compared to 0% of the DMSO-treated mice. Researchers also commented that the ABT-263 treated mice experienced accelerated wound closure time, which became statistically significant by day 15. Complete healing was noted in 80% of the ABT-263 by day 24, compared to only 56.3% in the DMSO group. This represented a 1.4x fold improvement in the complete healing rate.

Discussion

The researchers highlight that increases in collagen expression following ABT-263 treatment is interesting. They said, "ABT-263 appears to enhance collagen expression and production, potentially improving aged skin structure and function. The removal of senescent cells by ABT-263 may create a more favorable environment for healthy fibroblasts to produce collagen, thereby promoting tissue regeneration and repair."

They also noted how this is in contrast with the impact of ABT-263 on fibrotic skin conditions, where the treatment typically reduces collagen expression: "This difference in collagen response might be due to the distinct cellular environments and pathological processes involved in ageing versus fibrotic conditions. In fibrotic skin, where excessive collagen deposition by myofibroblasts is pathologic, ABT-263 effectively reduces collagen levels, alleviating fibrosis. These contrasting outcomes highlight the context-dependent effects of ABT-263 and suggest its potential for selectively modulating collagen expression based on the specific skin condition being treated."



"Cell senescence plays a key role in soft tissue ageing. The ageing cascades amplified by SASPs result in increasing degradation of structurally competent ECM which in turn further impair cells' function through the loss of youthful mechanotransduction. ABT-263 in this early animal study shows promise not just for wound healing post surgery. or perhaps even lasers, but also for potentially slowing soft tissue degradation or optimising tissue response to injectable biostimulators. The topical administration route used would be practically useful as patients could pre-treat at home. More research is of course required but it could be potentially useful in aesthetics."

Dr Kate Goldie,
RAM Institute Scientific Committee

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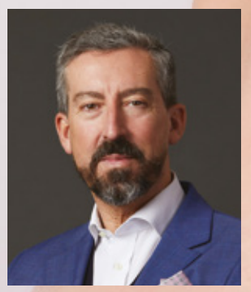
The composition of exosomes allows them to modulate various physiological pathways, from inflammation and cell migration to tissue remodeling and angiogenesis.

Introducing Exosomes

Professor Maurizio Cavallini presents an overview of the biological function, mechanism of action, and clinical applications of extracellular vesicles in skin regeneration



The field of regenerative medicine has seen remarkable advancements in recent years, with exosomes emerging as a promising tool for tissue repair and rejuvenation.

These extracellular vesicles, secreted by various cell types, play a critical role in intercellular communication, modulating physiological processes essential for skin regeneration. This article provides an introductory overview of what they are and how they can be used.

Types of exosomes

Exosomes can be classified based on their origin, which significantly influences their composition and biological activity. They are:

Human-derived exosomes

These are commonly harvested from mesenchymal stem cells (MSCs), fibroblasts, keratinocytes, and immune cells such as dendritic cells. Among these, MSC-derived exosomes are considered ideal for skin regeneration due to their content of:[1,2]

- Growth factors (e.g., EGF, VEGF, TGF-β)
- Anti-inflammatory cytokines
- Regulatory microRNAs (e.g., miR-21, miR-146a)

MSC exosomes have been shown to promote angiogenesis, epithelialisation, and immune modulation.[1,2] Despite this, their use raises important ethical concerns and they are not approved for use in countries such as the UK. Elsewhere, sources such as umbilical cord or placental tissue require strict donor screening and informed consent protocols. There is no universally accepted regulatory framework for the use of human-derived exosomes. This lack of standardisation complicates clinical translation and raises concerns about product consistency, safety, and long-term effects.[3,4]

Animal-derived exosomes

Exosomes from animal sources - especially bovine and porcine - are used for their wound healing capabilities. Bovine milk-derived exosomes have immunomodulatory and antioxidant properties, and are considered for oral and topical formulations due to their natural stability, while porcine-derived exosomes, particularly from adipose tissue or skin fibroblasts, have demonstrated efficacy in tissue regeneration and burn healing models.

While results are promising, some research highlights potential risk of zoonotic transmission and immunogenic reactions. The importance of stringent quality control measures to mitigate risk should not be underestimated.[3]

Plant-derived exosomes

Secreted by plant cells, these nano-vesicles have gained attention due to their low immungenicity, biodegradability and natural abundance. Examples include:

- **Grapes:** Rich in antioxidants and polyphenols; shown to enhance skin barrier repair and reduce oxidative stress.[5]
- **Ginger:** Contains anti-inflammatory molecules; may help in balancing skin microbiota.[6]
- **Aloe vera:** Known for wound healing and skin hydration; exosomes may carry polysaccharides and bioactive lipids.[7]

Again, plant-derived exosomes lack standardisation of isolation and purification methods, with no established regulatory framework. Concerns include the variability of reprodicibility, batch-to-batch consistency, and potential presence of toxic or allergenic plant compounds.[8-10]

Biology of exosomes

Exosomes are nano-sized extracellular vesicles (typically 30-150 nm in diameter) formed via the endosomal pathway. Inside the cell, they originate from the inward budding of the late endosomal membrane, forming multivesicular bodies (MVBs). When MVBs fuse with the plasma membrane, they release exosomes into the extracellular environment.[11]

Once secreted, exosomes act as biological messengers, transferring their cargo to recipient cells via endocytosis, membrane fusion, or receptor-ligand interactions. Their contents reflect the cell of origin and include:[1,2]

- **Proteins:** growth factors, membrane receptors, heat shock proteins
- **Lipids:** sphingomyelin, cholesterol, ceramides (involved in membrane fusion and stability)
- **Nucleic acids:** mRNA, regulatory microRNAs (miRNAs), and sometimes DNA fragments

The composition of exosomes allows them to modulate various physiological pathways, from inflammation and cell migration to tissue remodeling and angiogenesis.[12,13]

Mechanism of action in skin regeneration

Exosomes are intended for topical skin application, usually via microneedling. It should be noted that it is illegal to inject exosomes in Europe. Their regenerative potential comes from their ability to influence multiple skin repair processes at the cellular level:

1. Enhancing cell proliferation and migration:
Exosomes deliver growth factors like EGF and TGF-β directly to keratinocytes and fibroblasts, stimulating proliferation and accelerating re-epithelialisation.[14,15]

2. Promoting collagen synthesis and ECM remodeling:
Fibroblast activation by exosomal cargo, especially miR-21 and matrix-modulating proteins, leads to increased production of type I and III collagen and elastin, improving skin texture and firmness.[2,16]

3. Supporting angiogenesis:
Exosomes stimulate endothelial cells via VEGF and angiogenic miRNAs (e.g., miR-126), encouraging capillary formation essential for nutrient delivery and oxygenation in wound sites.[1,17]

4. Modulating inflammation:
Anti-inflammatory effects are largely mediated by miRNAs such as miR-146a and miR-155, which suppress NF-κB signaling and reduce pro-inflammatory cytokine production (e.g., TNF-κ, IL-6). This contributes to a favorable microenvironment for healing and prevents chronic inflammation.[4,12]

5. Combating oxidative stress:
Many exosomes contain antioxidant enzymes (e.g., superoxide dismutase) and regulatory RNAs that reduce reactive oxygen species (ROS) and lipid peroxidation, protecting skin cells from environmental and age-related oxidative damage.[8,18]

Future directions in research

As exosome science continues to mature, several promising research avenues are emerging that may shape the future of regenerative dermatology and aesthetic medicine.

Engineered and functionalised exosomes

A growing body of research is focused on engineering exosomes to improve their therapeutic efficacy, targeting, and cargo delivery. New strategies include loading exosomes with small molecules, RNA therapeutics, or proteins via electroporation, sonication, and incubation techniques. Surface modifications - such as the attachment of ligands or antibodies - can enhance target specificity, allowing exosomes to selectively interact with damaged or diseased skin cells.[19,20] These advances aim to overcome the limitations of natural exosomes by increasing circulation time, enhancing stability, and improving cargo loading efficiency.[21]

Exosome-mimetic nanovesicles

To address challenges associated with the natural production and scalability of exosomes, researchers have developed exosome-mimetic nanovesicles. These artificially engineered vesicles are designed to replicate the structure and function of natural exosomes. Recent advancements have demonstrated that exosome-mimetic nanovesicles can effectively deliver bioactive molecules to target cells, promoting skin regeneration and repair. For instance, studies have shown that these nanovesicles can enhance collagen synthesis, improve skin elasticity, and reduce the appearance of wrinkles by facilitating the delivery of growth factors and other regenerative agents to dermal fibroblasts.[22]

Moreover, exosome-mimetic nanovesicles have been utilised to accelerate wound healing processes. By mimicking the natural communication pathways of exosomes, these nanovesicles can modulate inflammatory responses, promote angiogenesis, and facilitate tissue remodeling, which are critical steps in effective wound repair.[23] In the context of hair restoration, exosome-mimetic nanovesicles have shown potential in stimulating hair follicle regeneration. By delivering specific signaling molecules to the scalp, these nanovesicles can activate dermal papilla cells, leading to enhanced hair growth and density.[24]

The development of exosome-mimetic nanovesicles addresses several limitations associated with natural exosomes, including low yield and variability in isolation processes. These engineered vesicles offer a scalable and reproducible platform for delivering therapeutic agents, making them highly relevant for applications in regenerative aesthetics.

Integration with omics and personalised medicine

The convergence of exosome research with omics technologies - including genomics, transcriptomics, proteomics, and metabolomics - is paving the way for personalised approaches in skin health and regenerative aesthetics.[25]

By analyzing the RNA, protein, and lipid content of exosomes, researchers can identify specific biomarkers associated with skin ageing, inflammation, and other dermatological conditions. This approach enables the development of liquid biopsies, offering a non-invasive method to monitor skin health and disease progression. Recent studies have demonstrated the potential of multi-omics profiling of extracellular vesicles in early cancer detection, underscoring the applicability of this technology in dermatology.[25]

In regenerative aesthetics, integrating omics data with exosome analysis facilitates the creation of personalised treatment strategies. For instance, a patient's unique exosomal profile can inform the customisation of therapies aimed at enhancing collagen synthesis, modulating inflammatory responses, or reducing oxidative stress. This tailored approach ensures that interventions are specifically designed to address individual molecular deficiencies, thereby optimising aesthetic outcomes.[25]

Standardisation and regulatory frameworks

The field is also seeing efforts to create standardised protocols for exosome isolation, characterisation, and quality control. Initiatives by organisations like the International Society for Extracellular Vesicles (ISEV) are working toward clearer guidelines that can support clinical translation and regulatory approval in the future.[26]

From research to practice

Exosomes are already making their way into real-world aesthetic and regenerative treatments. Their mechanisms are well supported by emerging science: modulating inflammation, enhancing collagen synthesis, and promoting tissue regeneration. Yet, while clinical interest is growing rapidly, the field remains in its early stages in terms of regulation, product consistency, and long-term safety validation.

As research continues to evolve , with hopefully more independent clinical studies and long-term analysis, and more robust frameworks are established, exosomes are poised to become an integral part of personalised, biologically intelligent skincare and regenerative therapies. For clinicians, the focus now shifts to responsible integration - grounded in evidence, aligned with best practice, and guided by the principle of patient-first innovation.

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The impact of air pollution on Telomere Integrity and Skin Health

Insight into how practitioners can leverage new study findings to combat premature ageing

Ageing is a multifaceted process influenced by both intrinsic and extrinsic factors, including environmental exposures. Recent research published in *GeroScience* has established a clear link between air pollution, greenspace exposure, and biological ageing using data from the UK Biobank.[1]

The study published in February 2025, *Associations between environmental air pollution, greenspace and apparent biological ageing*, highlights the impact of environmental pollutants on biological age acceleration, with a particular focus on telomere dynamics. Given the well-documented role of telomere shortening in cellular senescence and ageing, these findings may hold significant value for regenerative aesthetic medicine.

Telomeres and ageing

Before examining the results of the research, it is important to understand what telomeres are and the role they play in ageing.

As the protective nucleotide sequences at the ends of chromosomes, telomeres play a critical role in cellular ageing and replicative capacity. These repetitive DNA sequences act as a buffer, preventing chromosomal deterioration and maintaining genomic stability. However, with each cell division, telomeres naturally shorten due to the limitations of DNA replication. When telomeres become critically short, cells enter a state of replicative senescence or undergo apoptosis, contributing to ageing and tissue degeneration.[2,3]

Excessive telomere shortening is associated with heightened cellular stress, chronic inflammation, and an increased risk of age-related diseases, including cardiovascular disease, neurodegeneration, and metabolic disorders. Oxidative stress, induced by environmental factors such as pollution and UV radiation, accelerates telomere attrition by causing direct DNA damage and impairing telomere maintenance mechanisms.[4] Inflammation further exacerbates telomere shortening by increasing pro-inflammatory cytokine activity, which drives immune cell turnover and stress-induced senescence.[5]

In recent years, telomere length has emerged as a crucial biomarker of biological ageing, with shorter telomeres reflecting an accelerated ageing process.[6] This has profound implications for dermatology and skin ageing, as skin fibroblasts and keratinocytes rely on intact telomeres for optimal function and regenerative capacity.

When telomeres shorten excessively, skin cells lose their ability to divide and repair damage, leading to visible signs of ageing such as thinning, wrinkling, and

reduced elasticity. Additionally, telomere dysfunction has been linked to impaired collagen synthesis and increased susceptibility to environmental damage, further contributing to premature skin ageing.[7]

By understanding the mechanisms behind telomere attrition and its environmental triggers, clinicians can better assess the impact of external stressors on ageing and implement targeted interventions.

The study revealed several significant findings related to the impact of air pollution

Study parameters

The study assessed biological ageing in 156,690 participants using the PhenoAge algorithm, which estimates biological age from clinical biomarkers. The residual between biological and chronological age, termed Phenotypic Age Acceleration (PhenoAgeAccel), served as a marker for ageing beyond expected chronological progression. The study employed linear regression models, adjusting for covariates such as age, sex, smoking status, BMI, and socioeconomic factors, to determine associations between environmental exposures and biological ageing. Additionally, subgroup analysis was conducted to explore variations in susceptibility, with a particular focus on telomere length, lifestyle habits, and demographic differences.

The study examined the impact of five key air pollutants - NO2, NOx, PM2.5, PM10, and PM2.5-1 - as well as greenspace exposure (measured in 300m and 1,000m buffer zones around participants' residential locations).[1]

Key findings

The study revealed several significant findings related to the impact of air pollution and greenspace exposure on biological ageing. Higher levels of air pollution, particularly PM2.5 and NO2, were strongly associated with increased biological ageing, as reflected in greater PhenoAgeAccel values.

Specifically, each 1 μg/m³ increase in PM2.5 was associated with a 0.151-unit increase in PhenoAgeAccel, while each 1 μg/m³ increase in PM10 was linked to a 0.041-unit increase in PhenoAgeAccel. NO2 exposure was also positively correlated, with a 0.007-unit increase in PhenoAgeAccel per 1 μg/m³ increase. These findings suggest that even small increases in pollutant concentrations can significantly accelerate biological ageing at the cellular level.[1]

Conversely, greater greenspace exposure was found to have a modest but statistically significant protective effect, reducing the rate of biological ageing. A 10% increase in greenspace within a 1,000m buffer around a participant's residence was associated with a –0.003 unit decrease in PhenoAgeAccel. Similarly, a 10% increase in natural environment exposure within the same buffer led to a –0.002 unit decrease in PhenoAgeAccel. [1]

Notably, individuals with shorter telomere length were more vulnerable to the ageing effects of pollution, suggesting that telomere integrity plays a crucial role in determining susceptibility. In the shortest telomere length quartile (0-25%), associations between air pollution and accelerated ageing were significantly stronger. For instance, NO_2 exposure was associated with a β = 0.010 increase in PhenoAgeAccel, while those with greenspace within 1000m were associated with a β = –0.004 decrease in PhenoAgeAccel.[1]

These patterns were not observed in quartiles with longer telomeres, indicating that individuals with inherently shorter telomeres may be biologically more vulnerable to the damaging effects of pollution on ageing.

Additionally, lifestyle factors such as smoking and alcohol consumption appeared to modify these associations, further emphasising the complexity of environmental and behavioral influences on ageing.

Clinical implications

The findings of this study have notable implications for understanding and addressing skin ageing, particularly within regenerative aesthetics. As the largest and most environmentally exposed organ, the skin is especially vulnerable to environmental stressors. Fine particulate matter (PM) and nitrogen oxides (NOx), both strongly associated with accelerated biological ageing in the study, contribute to skin ageing through several interlinked pathways:

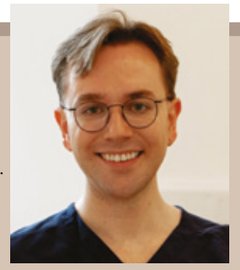
- **Collagen degradation:** Exposure to PM stimulates the expression of matrix metalloproteinases (MMPs), which break down collagen and elastin in the dermis. This leads to visible signs of ageing such as reduced skin elasticity, sagging, and fine lines.[8]
- **Pigmentation irregularities:** NO_2 and PM induce oxidative stress within melanocytes, promoting melanin overproduction and resulting in hyperpigmentation, uneven skin tone, and age spots - frequent concerns among patients in urban settings.[9,10]
- **Loss of barrier function:** Air pollution disrupts the skin's lipid barrier, increasing transepidermal water loss and reducing hydration. This not only accelerates visible ageing but also contributes to sensitivity and inflammatory skin conditions.[8]
- **DNA damage and cellular senescence:** Pollutants cause oxidative DNA damage in dermal fibroblasts, leading to cellular senescence and impaired regenerative capacity. Over time, this results in slower wound healing, dull complexion, and increased vulnerability to environmental insults.[11,12]

These mechanisms are supported by the study's observation that individuals with shorter telomere lengths - markers of systemic ageing - were more susceptible to pollution-related biological ageing, reinforcing the idea that skin health reflects deeper cellular ageing processes.

While the study found that the anti-ageing effect of greenspace exposure was smaller in magnitude than the pro-ageing effects of pollution, its impact remains clinically relevant. Greater exposure to greenspace was associated with a statistically significant reduction in PhenoAgeAccel, suggesting it could serve as a modifiable protective factor. The protective effect of greenspace on biological ageing - and potentially on skin health - may be mediated by several pathways:

- **Air quality improvement:** Trees and vegetation naturally filter airborne pollutants, reducing exposure to harmful PM and NOx that accelerate dermal ageing.[13]
- **Stress reduction:** Time spent in nature has been shown to lower cortisol levels and reduce systemic inflammation, which can otherwise exacerbate inflammatory skin conditions and promote telomere attrition.[14]
- **Encouragement of physical activity:** Greenspaces promote outdoor exercise, which improves circulation, mitochondrial efficiency, and antioxidant capacity - all of which support skin regeneration and reduce oxidative stress.[15]
- Enhanced Microbial Diversity: Exposure to biodiverse environments may strengthen the skin and gut microbiome, bolstering immune response and reducing inflammation, both of which contribute to healthier, more resilient skin.[16]

Collectively, these findings support a holistic approach to antiageing and skin health - one that considers environmental exposures, systemic ageing markers like telomere length, and the value of lifestyle-based interventions.



"This is a significant study for any clinician working in dermatology, aesthetic and regenerative medicine. As clinicians we have seen firsthand the impact of environmental pollutants and lifestyle factors on common aesthetic complaints of our patients and to have data demonstrating a clinical impact of these on telomere shortening is significant. This reinforces the vital importance of a holistic approach to regenerative aesthetic medicine - we must ensure our patients understand the positive impact of reducing stress and environmental aggressors on their cellular ageing."

Dr Ben Taylor-Davies, aesthetic practitioner

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Words: Chloé Gronow

DermaFocus
REGENERATIVE AESTHETICS

Advertorial

In Focus: Purasomes

Your guide to the innovative technology using exosomes and growth factors to reset cellular activity

Earlier this year, DermaFocus added an exciting new range to its product portfolio. Purasomes, manufactured by Dermoaroma in Italy, uses a unique patented technology known as AMPLEX Plus.

Driven by the ambition to discover safe, sustainable and natural skin and hair care solutions, the Dermoaroma research team spent nine years working with top European scientists to create this ground-breaking formula.

Each of the three products within the Purasomes range contains AMPLEX Plus - a patented technology that has been created using secretomes, which combines the action of 20 billion exosomes, 20 growth factors and other beneficial properties from ethically sourced bovine colostrum.

We caught up with DermaFocus executive director Milad Bemana to learn more...

Q. Why did you choose a product that uses growth factors and exosomes harvested from bovine colostrum?

Bovine colostrum has significant and well researched health benefits. It has the richest source of growth factors and a high content of antibodies, antioxidants, cytokines, lactoferrin and lactoperoxidase, which all contribute to effective skin and hair regeneration.

Research suggests that bovine colostrum is the optimal substitute for human colostrum, while also containing less lactose and more proteins.

Q. How does Dermoaroma ensure the bovine colostrum used in AMPLEX Plus is ethically sourced?

The bovine colostrum used in AMPLEX Plus comes from cattle bred in an Organic Certified family-run farm in Italy. The cattle are grass fed and the colostrum is harvested one to five hours after parturition to ensure it is of the best quality.

Before harvesting, significant steps are taken to ensure that no calves are deprived of colostrum that is needed to support their growth and development.

Q. How is AMPLEX Plus created?

Once the bovine colostrum is harvested, it is delivered and processed in specially equipped transport to the Dermoaroma production site within 24 to 48 hours.

When it arrives, the bovine colostrum is purified so only the most potent biologically active elements are utilised. Using a centrifuge, exosomes and growth factors are isolated, allowing impurities such as fat, dead cells and debris to be discarded.

The exosomes and growth factors then go through a reliable dehydrating process, which allows them to be stored at room temperature without comprising their integrity. The end product is a 5ml vial containing 200mg of 20 billion exosomes and 20 of the most potent growth factors ready for use.

Q. How are Purasomes administered?

Purasomes are delivered to the dermis via microneedling. A series of three to five treatments every four weeks is recommended for Purasomes NC150+ Skin Nutri Complex and Purasomes SGC100+ Skin Glow Complex, while the number of sessions for Purasomes HSC50+ Hair & Scalp Complex depends on individual patient requirements.

Q. Can Purasomes be used alongside other products?

As well as being a reliable standalone treatment, Purasomes work as excellent skin primers for energy-based treatments, while also aiding skin recovery if used afterwards. They can also be used alongside Polynucleotides HPT® to fully optimise results.

Q. How safe are Purasomes?

Thanks to the swift harvesting process and meticulous purification system, the AMPLEX Plus technology used in Purasomes has been found to be completely safe and non-toxic.

It contains no artificial components, does not have a risk of transmitting infections and no ethical concerns with its use have been identified.

As lyophilised products, Purasomes can be easily transported and stored.

Q. Are Purasomes suitable for everyone?

Each of the products within the Purasomes range can be used on all skin types. We do not recommend using Purasomes on patients who are pregnant or breastfeeding. We would also recommend being cautious with patients suffering from autoimmune conditions.

As the colostrum used in the AMPLEX Plus is obtained from cattle, Purasomes may be unsuitable for some Vegan patients. AMPLEX Plus is Halal and Kosher certified.

The **products**

Purasomes NC150+ Skin Nutri Complex

TARGET: ***tired and aged skin***

Treatment with this product will:

- Stimulate fibroblasts to repair skin damage
- Increase skin density
- Protect skin from harmful free radicals
- Improve collagen and elastin production
- Moisturise skin and reduce water loss
- Promote formation of new blood vessels to accelerate skin recovery

Purasomes SGC100+ Skin Glow Complex

TARGET: ***dull, damaged and hyperpigmented skin***

This impressive formula can:

- Reduce the appearance of scars and skin lesions
- Minimise pores
- Decrease age spots and post-inflammatory hyperpigmentation
- Improve overall skin tone
- Rebuild a flawless skin complexion
- Revitalise skin for radiance and vitality
- Enhance skin's brightness and luminosity

Purasomes HSC50+ Hair & Scalp Complex

TARGET: ***thin and damaged hair***

Using Purasomes HSC50+ Hair & Scalp Complex will:

- Nourish and moisturise the scalp
- Remodel hair follicles' environment
- Reactivate and regulate hair growth cycle
- Restrict hair loss
- Thicken, strengthen and brighten lack lustre hair

To learn more about Purasomes scan the QR code!

Preserving Function, Not Just Form:

The Regenerative Vision of **Dr Tingsong Lim**

The global speaker, educator, and regenerative aesthetics researcher shares his science-first approach to preserving tissue function and redefining how the skin ages

When you meet Dr Tingsong Lim, you quickly understand why he's become one of the world's most sought-after voices in regenerative aesthetics. Based in Kuala Lumpur but rarely still, Dr Lim travels the globe educating practitioners on how to move beyond surface-level treatments and into the biology of true cellular repair.

With a background in medicine, research, and cross-cultural training in Japan, the US, and Malaysia, Dr Lim brings a uniquely holistic view to modern aesthetics - one deeply rooted in biology and patient wellness.

His work is unified by a single goal: to change the way we understand skin ageing. His focus is on cellular repair, not cover-ups. Regeneration, not replacement.

We sat down with Dr Lim to talk about where it all started, why regenerative approaches matter, and how the field is evolving far beyond surface-level treatments.

"Our field is really about improving quality of life"

"I grew up in Kuala Lumpur, and then went to Japan for medical school," says Dr Lim. "I spent almost 10 years there, then trained in the States before coming back to Malaysia. Aesthetics was really starting to taking off here."

What he saw in aesthetic practice wasn't just about appearances. "I realised aesthetics is an exciting new field of medicine. It's not just about how someone looks - it's about wellness, emotional health, and improving quality of life."

And that emotional wellbeing, he notes, isn't superficial. "When someone feels confident, there's this positive energy. And that affects more than how they feel - it impacts physical health too."

"Speaking different languages opens up different ways of seeing things"

Dr Lim credits much of his global perspective to language - and the years he spent living and studying abroad. "In school we studied English, Malay, and Mandarin," he says. "Then I got a scholarship to Japan for medical school and stayed there about 10 years - that's how I learnt Japanese too."

It's not just about communication, he explains. "Speaking different languages really opens up different ways of seeing things. It helps you understand different cultures, different priorities. I used to be quite introverted, but living abroad trained me to communicate better."

Now, that cross-cultural fluency helps him collaborate with experts around the world - and stay open to new ideas. "It helps me build real friendships with brilliant people. That's how you grow."

"We're not just preserving life. We're preserving function."

Dr Lim's turn toward regenerative aesthetics came from a sense that something was missing in traditional practice.

"In Western medicine, we're often just treating symptoms," he explains. "But there's this big area we don't talk enough about - how to maintain wellness and keep tissue healthy before it starts to break down."

That's where regenerative aesthetics comes in, he says. "We're looking at the microenvironment - how to preserve a healthy internal state so the body stays functional. Not just living longer, but living better."

He adds, "We've moved past just injecting filler. Now it's about preserving tissue. We want the cells and the environment to stay optimal for as long as possible."

"People aren't just afraid of ageing - they're afraid of becoming dependent"

Dr Lim's patients - mainly Asian, from middle to upper-income backgrounds - often come with goals that go beyond vanity.

"A lot of them have already started making healthier choices - eating well, exercising, taking supplements. But there's also fear. Not just of getting old, but of becoming a burden to the people around them."

Over time, Dr Lim began to notice patterns - especially in Southeast Asian skin types. "We see more inflammation, more UV damage. And a lot of aesthetic treatments weren't helping. Overdoing injectables, lasers - it can actually speed up tissue ageing."

"In many cases, we're seeing fibrosis, disrupted skin quality, and 'overfilled syndrome'. Not only do the treated areas age faster, but the surrounding tissues do too. We're damaging the whole ecosystem."

"Polynucleotides are like giving energy back to the DNA"

Dr. Lim's go-to regenerative tool these days? Polynucleotides.

"They're not just injectables. They give back to the fundamental structure of our DNA. Think of DNA as the blueprint for everything - the proteins, the function. And with ageing, we get wear and tear, and the DNA repair mechanisms start to break down."

"When that happens, it's like a hard drive running out of space - it starts throwing away files, and that creates instability. That's where problems like chronic inflammation or cancer can start."

Polynucleotides, he says, are "like a battery for your DNA. They don't just help repair the structure - they also provide the energy for cell function."

Because they're built from nucleotides like adenosine triphosphat (ATP), he explains, they support everything from mitochondrial energy to membrane function. "You get better cell function and communication, better toxin clearance, and a stronger extracellular matrix. That's when the skin starts to really improve."

"We don't always need to inject into the dermis"

Dr Lim recently published a study on polynucleotides in 30 Asian patients - looking at an unconventional technique.

"Everyone assumes you have to inject into the dermis to improve skin. But we injected into the subcutaneous fat, and we saw really interesting results - better matrix quality, less trauma, less inflammation, faster recovery."

"The best way to learn? Find all the experts - and become friends with them"

Dr Lim is a regular on the international speaker circuit, and one of the things that keeps him going is his love of learning.

"I'm just very curious by nature. I always want to understand what's really going on - why something works, or why it doesn't. I think the best way to learn is to find the smartest people around the world... and become friends with them. That's where the real conversations happen."

"Exosomes are the internal fruit of the bigger fruit"

While stem cells sparked early interest, Dr Lim now finds more consistency in exosome-based treatments.

"With stem cells, they're expensive and not always predictable. They need instructions. So, why not use what's inside the cell? That's where exosomes come in."

He describes exosomes as tiny information packages that support communication between cells. "They also help the cell membranes. That's where a lot of signaling happens. If you ask me, polynucleotides are still more fundamental - but when you combine them with exosomes, the effect is stronger."

"I'm researching new materials and new approaches"

Dr Lim is particularly excited about the potential of new regenerative tools like recombinant collagen and electromagnetic stimulation.

"Before, collagen injections could cause problems like granulomas. But now we're using smaller fragments, which help form the base for new collagen and break down into spare parts like useful amino acids."

He's currently working on four more publications, three of which look at the impact of various forms of collagen - from silkworm, equine, and porcine sources.

The fourth is research into using Belotero Revive with glycerol, which has been found to have a regenerative effect on both dermis and the adipose tissue.

Electromagnetic stimulation, known for its use in sports medicine, is another non-invasive method Dr Lim is enthusiastic about. "It recharges the communication between tissues. I always say it's like a pump in a fish tank - if the pump is old, toxins build up, water gets murky. This helps clear out the microenvironment."

I always want to understand what's really going on

"Some of what people call regenerative is actually doing damage"

For practitioners looking to adopt regenerative treatments, Dr Lim's message is clear: stay curious, and stay grounded in the science.

"We really need to go back to the science - not just do what's trendy. Some people are overdoing things in the name of regeneration, but that's not how it works. When we overstimulate tissues, we can reduce their function."

He points again to overfilled syndrome. "It's not just the injected area that suffers. We've seen ageing accelerate in untreated areas too. That tells us the tissue network is all connected - and when we disrupt one part, the others respond."

"Aesthetics has always been regenerative - we just didn't know it"

Dr Lim's philosophy is rooted in repair, not reversal. He emphasises that regenerative aesthetics isn't a trend - it's a shift in how we understand the biology of ageing.

"We're not just making people look better. A lot of the time, we're trying to repair the source of the signs of ageing and preserve tissue function. That's a big deal."

He adds, "And I think now we have more clarity on how this works. Aesthetics has always been regenerative in some way - but now we're understanding the mechanisms. And it's our responsibility to use that knowledge in a way that supports, not overstimulates."

Recent Publications
by Dr Tingsong Lim on Regenerative Aesthetics

Impact of Synchronized RF and HIFES on Midface Rejuvenation
Published: January 2025
This study assessed the combined use of radiofrequency (RF) and high-intensity facial electrical stimulation (HIFES) in 37 participants. After four sessions over 24 weeks, results showed increased midface volume, improved skin displacement, and thickening of the Zygomaticus Major muscle - highlighting the treatment's regenerative potential for midfacial ageing.

Facial Skin Quality Improvement After Treatment With CPM-HA20G: Clinical Experience in Korea
Published: February 2025
This 24-week prospective study evaluated the effectiveness and safety of CPM®HA20G, a hyaluronic acid dermal filler with glycerol, in enhancing facial skin quality among Korean women. The findings indicated significant improvements in skin hydration, elasticity, and overall aesthetic appearance without serious adverse reactions.

Polynucleotides HPT™ for Asian Skin Regeneration and Rejuvenation - The Tridimensional Perspective
Published: February 2024
This study explores the benefits of intradermal Polynucleotides High Purification Technology (PN HPT™) in improving skin tone evenness, surface evenness, firmness, and glow in Asian subjects. The results demonstrated significant enhancements in skin quality with sustained benefits up to six months post-treatment.

Exploring Facial Overfilled Syndrome from the Perspective of Anatomy and the Mismatched Delivery of Fillers
Published: February 2024
This article examines the phenomenon of Facial Overfilled Syndrome (FOS), characterised by excessive use of fillers leading to a distorted appearance. Dr Lim and colleagues analyse the anatomical factors contributing to FOS and propose strategies for prevention and management.

PN-HPT® and Striae Albae–Exploratory Interim Analysis of a Randomised Prospective Study
Published: August 2023
This study investigates the safety and efficacy of Polynucleotides Highly Purified Technology (PN HPT®) as a therapeutic strategy for mature striae albae (white stretch marks), indicating promising results in skin regeneration

Pan-Asian Consensus on Calcium Hydroxyapatite for Skin Biostimulation, Contouring, and Combination Treatments
Published: August 2021
Dr Lim contributed to this consensus paper, which provides strategic guidance on the use of calcium hydroxyapatite (CaHA) fillers for skin biostimulation and contouring in Asian patients. The publication emphasises customised aesthetic strategies to accommodate the heterogeneity of Asian anatomies and cultural preferences.

Clinicians must grasp the mechanisms driving follicular dysfunction across different types of hair loss.

The Science of Hair Loss

Mr George Christopoulos presents a comprehensive overview of hair loss mechanisms and how regenerative therapies may offer targeted, evidence-based solutions

Hair loss (alopecia) presents a multifactorial clinical challenge with significant patient demand for effective and lasting solutions. As regenerative therapies continue to gain traction in both clinical and aesthetic medicine, understanding the underlying pathophysiology of alopecia becomes essential for evidence-based treatment planning. Before integrating modalities such as platelet-rich plasma (PRP), stem cell therapy, polynucleotides, or exosomes, clinicians must grasp the mechanisms driving follicular dysfunction across different types of hair loss.

This article provides an in-depth review of the principal forms of alopecia, elucidates the biological pathways leading to follicular damage, dormancy, or destruction, and examines how both conventional and regenerative interventions modulate these pathways. By establishing a scientific framework, clinicians will be better positioned to stratify patients based on underlying aetiology and integrate regenerative solutions in a rational manner.

Types of **Hair Loss**

Androgenetic Alopecia (Pattern Hair Loss)

Androgenetic alopecia (AGA), also known as male or female pattern hair loss, is the most common form of alopecia, affecting many men by middle age and a substantial proportion of women post-menopause. AGA is characterised by progressive miniaturisation of hair follicles, where terminal hairs are gradually replaced by finer vellus hairs.

The principal driver of AGA is dihydrotestosterone (DHT), a potent androgen derived from testosterone via the enzyme 5-alpha reductase. In genetically predisposed scalp regions - typically the vertex and frontal zones - hair follicles exhibit increased 5-alpha reductase activity and heightened androgen receptor (AR) expression.[1]

DHT binding to ARs initiates signalling cascades that shorten the anagen (growth) phase and reduce follicular size, a process termed follicular miniaturisation. This culminates in decreased hair shaft diameter and density and manifesting as visible thinning. In contrast, the occipital scalp tends to be resistant to DHT due to lower AR and enzymatic activity.[2]

Genetics plays a significant role, with heritability estimated as high as 80% in twin studies.[3] The most robust genetic associations involve polymorphisms in the AR gene on the X chromosome, which partly explains earlier onset and increased prevalence in men.[4] Additional loci implicated in genome-wide association studies include regions on chromosome 20p11 and genes within the Wnt/β-catenin signalling pathway, further underscoring the polygenic nature of .[5]

Emerging evidence also implicates local modulators such as prostaglandin D2 (PGD2), found to be elevated in balding scalps, which acts as a negative regulator of hair growth.[6] Moreover, dysregulation of the Wnt/β-catenin pathway, critical for follicular stem cell activation, has been linked to impaired follicle regeneration.[7]

Alopecia Areata (Autoimmune Hair Loss)

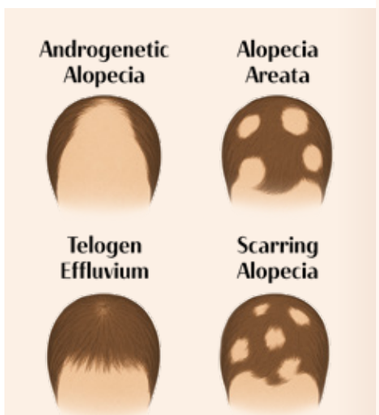
Alopecia areata (AA) is a T-cell mediated autoimmune condition characterised by sudden, patchy, non-scarring hair loss. It may involve the scalp, face, and body, with potential progression to alopecia totalis or universalis.

Clinically, AA presents with smooth, well-demarcated areas of hair loss, often featuring 'exclamation mark' hairs - short, tapered hairs that are narrower at the base and wider at the tip, typically located at the periphery of patches. These hairs are a diagnostic hallmark of active disease, resulting from inflammation that weakens the lower hair shaft, leading to breakage. The disease course is variable, ranging from spontaneous remission to chronic relapsing forms.

AA is associated with a collapse of immune privilege in the anagen hair follicle bulb, where normally low MHC expression protects follicular antigens from immune detection. In AA, CD8+ cytotoxic T cells expressing NKG2D infiltrate the peribulbar area and secrete interferon-gamma (IFN-γ) and other pro-inflammatory cytokines.[10]

Genetic predisposition is supported by associations with HLA class II, AIRE, and CTLA4 genes.[8] Environmental triggers such as infections, psychological stress, or trauma often precipitate disease onset.[9]

Interleukin-15 (IL-15) has emerged as a central cytokine in AA pathogenesis. Its upregulation sustains T-cell activation via the JAK-STAT pathway, providing the rationale for targeted use of JAK inhibitors in severe disease.[11]



Telogen Effluvium (Stress-Induced Shedding)

Telogen effluvium (TE) is a transient, diffuse non-scarring alopecia characterised by an abnormal shift of hair follicles from the anagen to telogen phase. It often follows systemic stressors such as major illness, surgery, childbirth, severe emotional distress, or nutritional deficiencies (e.g., iron, zinc, or protein). Patients present with diffuse hair thinning and increased shedding, typically noticed during washing or brushing. The hair pull test is often positive across all regions of the scalp. Dermoscopy reveals preserved follicular openings and uniform hair shaft diameters.

Under physiologic conditions, 85-90%

of scalp hairs are in anagen and 10-15% in telogen. In TE, synchronised anagen termination causes a disproportionate number of hairs to enter telogen prematurely, resulting in increased shedding approximately two to three months after the inciting event.[15]

Mechanistically, TE involves dysregulation of hair cycle control through neuroendocrine and inflammatory mediators, including elevated cortisol, prolactin, IL-1, and TNF-α.[16] Postpartum TE is attributed to sudden oestrogen withdrawal, which disrupts the anagen-maintaining effects of oestrogens.[17]

Scarring Alopecias (Cicatricial Alopecias)

Scarring, or cicatricial, alopecias encompass a heterogeneous group of disorders marked by irreversible destruction of hair follicles and replacement by fibrotic tissue. Clinical features include patchy hair loss with perifollicular erythema, scale, pain, burning, and loss of follicular ostia.

Key subtypes include:

- **Lichen Planopilaris (LPP):** A lymphocytic condition with perifollicular erythema and scale, often in middle-aged women.[19]
- **Frontal Fibrosing Alopecia (FFA):** A variant of LPP with progressive frontal hairline recession in postmenopausal women.[20]
- **Discoid Lupus Erythematosus (DLE):** Characterised by atrophic, depigmented plaques with follicular plugging.[22]
- **Folliculitis Decalvans:** A neutrophilic condition with pustules, crusts, and tufted folliculitis, often with bacterial involvement.[24]
- **Central Centrifugal Cicatricial Alopecia (CCCA):** Common in women of African descent; recent findings implicate PADI3 gene mutations.[25]

The hallmark of cicatricial alopecias is destruction of the bulge region containing epithelial stem cells. Once these are lost, follicular regeneration is no longer possible. Inflammation may be lymphocytic, neutrophilic, or mixed, and leads to sebaceous gland atrophy and follicular fibrosis.[26-28]

Other Forms of Alopecia

Additional patterns include:

- **Traction Alopecia:** Mechanical damage from chronic tension (e.g., tight hairstyles); reversible if caught early.[29]
- **Trichotillomania:** Compulsive hair-pulling disorder presenting with irregular patches of hair and hairs of varying lengths.[31]
- **Anagen Effluvium:** Rapid diffuse shedding of anagen hairs following chemotherapy or radiation; typically, reversible post-treatment.[33]
- **Congenital Alopecias:** Rare genetic disorders involving abnormal hair follicle development (e.g., atrichia, hypotrichosis simplex).[35]

Treatment Strategies and Regenerative Therapies

Low-level light therapy (LLLT), or LED phototherapy, is a non-invasive treatment shown to promote hair growth by stimulating mitochondrial activity and increasing ATP production within hair follicle cells[43] Wavelengths in the red and near-infrared spectrum (typically 630-670 nm) have demonstrated the ability to prolong the anagen phase and improve follicular vascularisation. LLLT is often used adjunctively with other therapies to enhance outcomes in patients with androgenetic alopecia.

Autologous Micrograft Technology (AMT), such as Regenera Activa, has emerged as a novel regenerative approach for androgenetic alopecia. This technique involves harvesting a small skin biopsy - typically from the occipital scalp - and mechanically disaggregating it into a suspension rich in progenitor cells, extracellular matrix components, and growth factors. The resulting micrograft solution is immediately re-injected into areas of hair thinning. The biological rationale lies in stimulating follicular niche repair, enhancing dermal papilla activity, and promoting angiogenesis through paracrine signalling.

Two other regenerative modalities, polynucleotides and exosomes, have gained increasing attention in hair restoration. Polynucleotides, derived from purified DNA fragments, exert anti-inflammatory, tissue-reparative, and hydration-promoting effects when injected into the scalp, potentially improving the follicular microenvironment. Clinical data suggest they may reduce hair shedding and enhance follicle calibre in patients with AGA.[40-42] Exosomes, nanoscale extracellular vesicles released by stem cells, deliver a complex payload of growth factors, cytokines, and microRNAs that modulate inflammation, support angiogenesis, and stimulate follicular stem cell activity. Recent studies have shown that MSC-derived exosomes can improve hair density and follicular regeneration in androgenetic alopecia.[37-39]

Although both therapies remain investigational, early data and laboratory studies suggest promising outcomes in improving hair quality, density, and cycling when used alone or in conjunction with other treatments.

Topical finasteride and off-label injectable forms of finasteride and dutasteride are increasingly used in AGA treatment protocols. While these approaches offer the advantage of localised DHT suppression with potentially fewer systemic side effects, it is important to note that their use is off-label and current evidence on long-term safety and efficacy remains limited. These methods aim to deliver local DHT suppression while potentially minimising systemic side effects. However, their long-term safety and efficacy require further high-quality studies.

Type of Alopecia	*Conventional Therapies*	*Regenerative Approaches*
Androgenetic Alopecia	Minoxidil, finasteride (oral and topical), dutasteride (oral and off-label injectable), LLLT, microneedling	PRP, polynucleotides, exosomes, autologous micrografts,[44] PRP, polynucleotides, exosomes[41-43]
Alopecia Areata	Intralesional corticosteroids, topical immunotherapy, JAK inhibitors	PRP (focal disease), experimental exosomes/ polynucleotides[47,48]
Telogen Effluvium	Address underlying cause, minoxidil	PRP, polynucleotides, exosomes (chronic TE)[51,52]
Scarring Alopecias	Immunosuppressants, corticosteroids, antibiotics	Limited benefit; early immune modulation via exosomes under study[55,56]

Local Anaesthesia Considerations

For scalp procedures involving injectable therapies, local anaesthesia is critical for patient comfort.

Nerve blocks are particularly useful for longer or more extensive procedures, as they provide targeted and prolonged anaesthesia with minimal distortion of the treatment area, whereas field blocks or topical anaesthesia may suffice for smaller or superficial interventions.

Common approaches include regional nerve blocks such as:

- Supraorbital and Supratrochlear Nerve Blocks: Effective for frontal and mid-scalp regions.
- Auriculotemporal Nerve Block: Useful for temporal areas.
- Greater Occipital Nerve Block: Targets posterior scalp.

These can be supplemented by topical anaesthetics (e.g., lidocaine-prilocaine creams) or field infiltration with buffered lidocaine and epinephrine for enhanced vasoconstriction and prolonged effect.

The Future of Hair Loss Management

Given the expanding toolkit of regenerative interventions, a combined protocol approach offers a practical framework for clinicians aiming to achieve synergistic effects. My proposed two-session protocol outlined below integrates PRP, polynucleotides, microneedling, micrografts, and exosome therapy into a staged treatment strategy that maximises follicular stimulation, anti-inflammatory support, and dermal regeneration.

Appointment	*Step*	*Intervention*
Session 1	Local Anaesthesia *Microneedling* *PRP Injection* *Polynucleotides* *LED Phototherapy* Home Regimen	Topical lidocaine/prilocaine & regional nerve blocks 1.0-1.5 mm depth across affected zones 8-10 mL intradermal 2 mL intradermal Red-light (630-670 nm) LED post-treatment Initiate minoxidil & finasteride topical
Session 2 after 6 weeks	Local Anaesthesia *Microneedling* *Exosome Therapy* *Autologous Micrograft (AMT)* *LED Phototherapy* Home Regimen	Repeat same as session 1 1 mm depth across affected zones 2 mL exosomes applied topically post-microneedling Regenera Activa: 2-3 punch biopsies processed and re-injected Red-light (630-670 nm) LED post-treatment Continue minoxidil & finasteride topical for 6 weeks

As data continue to accumulate, such protocols will evolve to reflect advances in formulation, delivery techniques, and patient stratification, helping position regenerative medicine at the core of evidence-based hair restoration.

Understanding the pathophysiological basis of alopecia is fundamental for selecting effective interventions. Regenerative treatments such as PRP, polynucleotides, and exosomes represent a growing area of therapeutic innovation, offering promising adjuncts to traditional modalities. As mechanistic insights expand and technologies evolve, the future of hair restoration will likely be shaped by personalised, pathway-specific strategies tailored to individual patient profiles.

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In regenerative medicine, peptides are especially exciting because they offer targeted, low-toxicity, and highly versatile tools

From Signal to Solution: Why Peptides Deserve a Place in Your Protocols

Pharmaceutical scientist and biotechnologist Chloé Lortal explores the use of peptides in regenerative aesthetics

The use of peptides in regenerative medicine dates back to the early 1980s, when scientists first began exploring copper peptides for wound healing. One of the pioneers, Dr Loren Pickart discovered that GHK-Cu (glycyl-L-histidyl-L-lysine copper complex) could significantly improve skin repair and reduce inflammation.[1] This discovery became the foundation for decades of peptide research, and since then, the field has exploded.

Thousands of scientific studies have explored their biological activity, from collagen synthesis to antioxidant defence and immune modulation. In regenerative medicine, peptides are especially exciting because they offer

In aesthetics, peptides have evolved from cosmeceutical ingredients into serious regenerative agents

targeted, low-toxicity, and highly versatile tools for influencing cell behaviour, without the complexity or risk of full protein or stem cell therapies.

In aesthetics, peptides have evolved from cosmeceutical ingredients into serious regenerative agents, used in advanced topical formulations and cutting-edge technologies like exosomes. They have the ability to signal, repair and protect, which makes them great allies against skin ageing[2] Indeed, as short chains of amino acids (from 2 to 50), they act as building blocks of proteins and messengers that can stimulate collagen production, improve wound healing, and regulate inflammation.[2]

In the UK, peptides have become an increasingly integral part of medical aesthetic protocols not only in skincare formulations but also in clinic-based treatments designed to support regeneration, healing, and age prevention.[3] As the market continues to shift towards evidence-led, regenerative solutions, practitioners are seeking solutions that deliver more than surface-level improvements. Peptides have emerged as a trusted tool among clinicians aiming to improve outcomes and accelerate recovery. While initially used in topical serums, peptides are now being explored in regenerative therapies, especially alongside other solutions such as exosomes.

With growing demand, the natural supply of peptides is insufficient, leading to the rise of synthetic and biotech-derived alternatives. These engineered peptides offer enhanced stability and can be designed for targeted receptor interactions, resulting in more precise and effective outcomes.

Mechanisms of action of peptides

Type of Peptide	*Mechanism of Action*
Signal Peptides	Stimulate fibroblasts to produce collagen, elastin, and glycosaminoglycans
Carrier Peptides	Bind and deliver trace elements (e.g., copper, manganese) to promote wound healing and tissue repair
Neurotransmitter-Inhibiting Peptides	Act as topical neuromodulators, relaxing facial muscles to soften dynamic wrinkles
Enzyme-Inhibiting Peptides	Prevent breakdown of collagen and elastin by inhibiting matrix metalloproteinases (MMPs)
Antioxidant/ Biofunctional Peptides	Provide photoprotection and support skin repair, often derived from collagen hydrolysates or synthetic sources

In the aesthetic and regenerative dermatology space, peptides are broadly classified based on their mechanism of action, and they play increasingly critical roles in topical and ingestible anti-ageing interventions.[4] Several peptides can penetrate the top layer of the skin and act as accelerators, triggering specific functions: stimulating collagen synthesis, cell proliferation, reducing melanogenesis or eliminating reactive oxygen species (ROS).[2] All of these are biological pathways essential for tissue repair and cellular regeneration. Signal peptides stimulate the synthesis of collagen, elastin, and glycosaminoglycans by activating fibroblasts. For example, *Palmitoyl Pentapeptide-4* (Pal-KTTKS), derived from a collagen fragment, enhances extracellular matrix production and is widely used to improve skin firmness and to reduce wrinkles.[4]

Another type, carrier peptides, bind trace elements such as copper and manganese and deliver them into the skin, where they promote wound healing and tissue regeneration. The GHK-Cu (Copper Tripeptide-1) complex is a carrier peptide.[4]

Neurotransmitter-inhibiting peptides act like topical neuromodulators, relaxing facial muscles to soften dynamic wrinkles. *Acetyl Hexapeptide-8* (Argireline) is a well-known example, mimicking the action of botulinum toxin to reduce wrinkle depth around expression areas.[4]

Enzyme-inhibiting peptides help preserve skin structure by preventing the breakdown of collagen and elastin. For instance, collagen-derived peptides such as Pro-Hyp and Hyp-Gly have been shown to inhibit MMPs (matrix metalloproteinases) and reduce oxidative stress.[4]

Finally, antioxidant and biofunctional peptides (often from collagen hydrolysates or synthetic designs) offer photoprotection and repair benefits.[4]

Overall, these peptides offer multifaceted strategies for treating ageing skin by improving elasticity, hydration, barrier function, pigmentation and structural integrity.

Enzyme-inhibiting peptides help preserve skin structure by preventing the breakdown of collagen and elastin

Delivery of peptides

So of course, peptides have gained attention in aesthetics for their anti-ageing and regenerative properties, but their effectiveness is often limited by delivery challenges.

When applied topically, peptides face poor skin penetration due to their hydrophilic nature and relatively large molecular size. Additionally, they are prone to enzymatic degradation on the skin's surface and possess a short biological half-life, reducing their stability and bioavailability. These barriers significantly hinder their ability to reach deeper skin layers and stimulate meaningful cellular responses.[2]

Biologically derived vesicles like exosomes can protect peptides and facilitate their targeted delivery. Exosomes are small extracellular vesicles (30-150 nm) naturally released by cells to facilitate intercellular communication. They carry a rich cargo of proteins, lipids, RNA, and bioactive peptides, acting as biological messengers that influence the behaviour of recipient cells. Purasomes is an example of a brand including peptides in its formulas, successfully treating skin and hair concerns.[6,7]

Other strategies have emerged to deliver peptides more effectively. Chemical modification, such as conjugating peptides with hydrophobic chains like myristic or palmitic acid, enhances their lipophilicity and membrane permeability. Cyclisation, another widely used technique, improves structural stability by linking amino and carboxy groups within the peptide chain, protecting them from proteolytic enzymes and increasing their biological activity.[8]

Other encapsulation technologies such as one patented innovation uses cationic lipoligopeptides (CLOPs) to form micelles that enhance peptide delivery by over 400%, boosting both efficacy and tolerability. Additionally, when combined with supportive ingredients like antioxidants (e.g. green tea extract), ceramides, or retinol, these technologies significantly enhance the therapeutic potential of peptides, offering a more robust, regenerative approach to skincare.[8]

Future formulations may also be increasingly personalised, using AI-driven diagnostics and DNA testing to tailor peptide combinations to individual skin needs.

Biologically derived vesicles like exosomes can protect peptides and facilitate their targeted delivery

Legalities of peptides

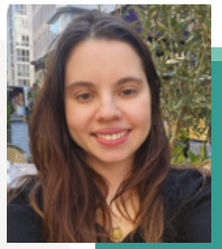
Currently, peptides used in cosmetic formulations are regulated as cosmetic ingredients and can be applied without prescription. However, the UK government is introducing a new licensing scheme for non-surgical cosmetic procedures in England, which may affect how and by whom certain treatments - especially those involving devices or injections - can be administered.

A smart investment

Overall, peptides are rapidly emerging as a building block in regenerative aesthetics and their integration into both skincare and advanced in-clinic treatments reflects their growing credibility and versatility. When combined with smart delivery technologies, peptides amplify outcomes, driving deeper, longer-lasting skin and hair regeneration. Their role extends beyond surface improvement, helping to modulate fibroblast activity, repair oxidative damage, and restore skin density.

For aesthetic clinics aiming to offer high-performance regenerative solutions, investing in clinically backed peptides with effective delivery systems is a forward-thinking strategy to optimise and support long-term results.

Overall, peptides are rapidly emerging as a building block in regenerative aesthetics and their integration reflects their growing credibility and versatility



Chloé Lortal is a biotechnologist and pharmaceutical formulation scientist, currently serving as the Medical Science Liaison at DermaFocus. In her role, she bridges the gap between cutting-edge science and clinical practice in regenerative aesthetic medicine. Passionate about scientific communication and innovation, during her career, Chloé has led numerous educational initiatives for healthcare professionals, ensuring that complex research is translated into practical, real-world applications and has experience supporting clinical outcomes in ageing and longevity through personalised medicine approaches.

Treating Contact Dermatitis

Nurse prescriber Khatra Paterson shares a case study highlighting the regenerative and anti-inflammatory benefits of polynucleotide therapy

Dermatitis is a broad term encompassing inflammatory skin conditions characterised by erythema, pruritus, and barrier dysfunction. Contact dermatitis, in particular, arises from direct exposure to allergens or irritants, leading to localised skin inflammation.[1] Management can be challenging, as identifying the precise trigger is often difficult, and standard treatments, such as topical corticosteroids, may provide only temporary relief. Additionally, corticosteroid use around sensitive areas like the periorbital region is not ideal due to the risk of skin thinning and other adverse effects.[1]

Given these challenges, I sought an alternative therapeutic approach for a patient suffering from contact dermatitis. Polynucleotide injections were considered due to their regenerative and anti-inflammatory properties; they are purified DNA fragments derived from fish gonads that act in the cellular level, enhancing fibroblast activity, promoting tissue repair, and modulating inflammatory mediators.[2] Additionally, the incorporation of LED phototherapy (TriWave) therapy using near infrared light aimed to enhance treatment efficacy by reducing histamine release and further calming inflammation.[3]

Patient profile

A 39-year-old female presented with recurrent contact dermatitis of undetermined aetiology. She reported experiencing episodic skin irritation since moving into her new home three years ago, with the current episode being the most severe. The patient suspected an allergen within the home environment as the trigger. She had previously managed symptoms with hydrocortisone, but flare-ups recurred upon cessation.
My clinical observations noted that her skin was inflamed, erythematous, dry, and scaly, localised around the periorbital region and face. She also reported a burning sensation.

Diagnosis and management

The clinical presentation was consistent with contact dermatitis most likely triggered by an environmental allergen. To determine the specific trigger, the patient was been referred for formal allergy testing.

A steroid-free treatment strategy was pursued due to the periorbital location and history of recurring flare-ups. Polynucleotide therapy (Plinest®) was selected for its regenerative, antioxidant, and anti-inflammatory properties, supporting barrier restoration and reducing oxidative stress.[4]

To further modulate inflammation, near infrared Tri-Wave therapy was introduced as an adjunct, based on its capacity to reduce histamine release and promote tissue healing.[3]
The treatment protocol consisted of:

- Three sessions of Plinest® injections at three-week intervals
- Tri-Wave therapy applied post-treatment on two of the three sessions
- Omitted lidocaine due to concerns of exacerbating irritation
- Small bolus injections administered across inflamed areas

Outcome and follow-up

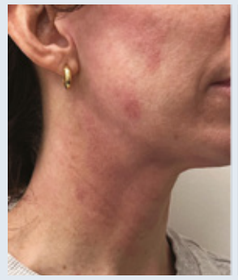
Forty-eight hours after treatment, a marked reduction in inflammation was observed. By the second session, there was noteable restoration of the skin barrier and resolution of clinical signs. For aftercare, the patient was advised to avoid makeup, maintain proper skin hygiene, and use a gentle cleansing routine along with pH Formula Post Recovery Cream and SPF 50. Additionally, antihistamine fexofenadine

"The treatment has allowed me to get on with normal life and not worry about constantly checking what my skin looked like"

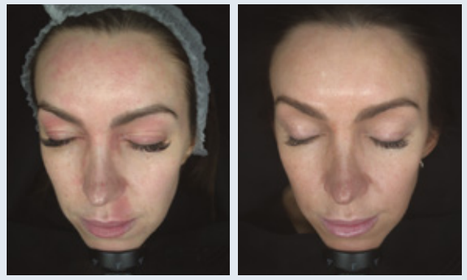
180mg was prescribed once daily, and the patient was advised to abstain from alcohol until the inflammation had completely subsided.
Lifestyle modifications were also discussed, emphasising the benefits of a low-carbohydrate, low-sugar diet to support gut microbiome balance and reduce systemic inflammation.[5]

At the final review, there was no recurrence of skin inflammation. A skin scan confirmed the resolution of acute inflammatory markers. To further reinforce skin integrity, one additional polynucleotide session was planned.

The patient commented, "My skin flare-ups were really affecting my confidence and self-esteem, and I'd tried so many things that just didn't help. After having treatment with Plinest® and Tri-Wave, I noticed a difference after just a couple of days, especially around the eyes. My skin looked healthier and less irritated, while the burning sensation subsided. The treatment even targeted the fine lines around my eyes and on my neck, which was a bonus! I now feel so much more confident facing the world. The treatment has allowed me to get on with normal life and not worry about constantly checking what my skin looked like."

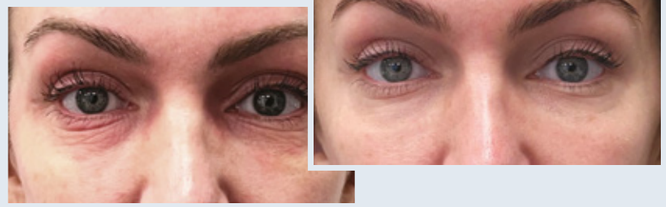


Before and 48 hours after first session of Plinest®



Before and after second session of Plinest®

Before and after Plinest® sessions



Summary
This case highlights the efficacy of polynucleotide therapy combined with adjunctive infrared treatment for refractory contact dermatitis. The rapid response and sustained skin barrier repair underscore its potential as a viable alternative to corticosteroids, particularly in sensitive areas such as the periorbital region. While this single-patient case demonstrates promising results, further controlled studies are needed to evaluate the long-term efficacy and broader applicability of polynucleotide therapy in contact dermatitis. The patient reported high satisfaction, emphasising the need for continued exploration of regenerative dermatological interventions.

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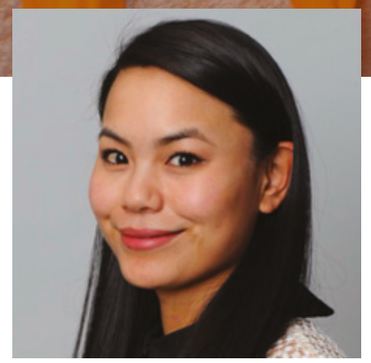
Revolumising the Periorbital Area



Dr Mei-Ying Yeoh discusses the research and techniques for encouraging adipocyte regeneration using polynucleotides

Under-eye concerns, including hollowing, dehydration, skin laxity, and pigmentation, are common presentations in aesthetic practice. While genetic predisposition and thin skin over the orbicularis oculi muscle contribute to these issues, innovative non-surgical approaches have demonstrated promising results in improving skin quality and volume.[1]

In my practice, I often recommend the use of energy-based devices such as radiofrequency microneedling, coupled with exosome treatment, which I have found can successfully address most of these concerns. For noticeable hollows, dermal fillers have been our traditional go-to option. However, an emerging preference in clinical practice is the use of polynucleotides.[2]

Polynucleotides stimulate tissue regeneration, leading to increasing collagen and elastin production, which improves skin elasticity and firmness. They're also able to successfully treat pigmentation, rosacea and scarring.[2]

The standard protocol for use is to inject polynucleotides intradermally to the epidermis.[2] Doing so produces positive results, but I have found that we can enhance outcomes further by adopting a superficial multi-layer injection technique. By injecting polynucleotides in the dermis and subcutaneous layers of the skin, it's possible to enhance adipocyte regeneration, offering subtle but effective volume restoration to under-eye hollows.

Here I will discuss the available research and share my experience.

The **research**

While there is limited research on polynucleotides' impact on adipocyte regeneration, results are promising. A team assessed the effects of polydeoxyribonucleotides (PDRN - a subtype of polynucleotides) on the proliferation and viability of human pre-adipocytes cultured in vitro.[3] Cells at different growth stages (6th and 16th passages) were treated with PDRN at concentrations of 80 µg/mL and 100 µg/mL over various time points to evaluate its impact on cell growth, viability, and senescence.

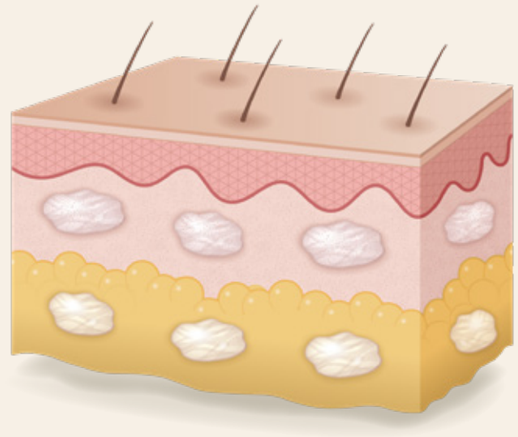
Findings indicated:

- **Enhanced cell proliferation:** PDRN significantly promoted cell growth, particularly in older cells (16th passage). After nine days of treatment, proliferation increased by approximately 30% compared to untreated controls ($p < 0.05$). Growth reached a plateau by day 15.
- **No cytotoxicity:** Viability assays (MTT test) showed that at both 80 µg/mL and 100 µg/mL, PDRN had no toxic effects. At 72 hours, viability remained close to 100% in 6th passage cells and around 92-98% in 16th passage cells.
- **Senescence and growth differences:** β-galactosidase staining revealed that senescent cells increased from 3% at passage 6 to 5.2% at passage 16, indicating progressive ageing. However, PxDRN appeared to counteract this effect by enhancing proliferation.
- **Increased cellular activity:** BrdU staining showed that S-phase cells doubled from 1% (P6) to 2% (P16) with PDRN treatment, suggesting increased DNA synthesis. Additionally, Ki-67 staining confirmed a higher proportion of actively dividing cells in PDRN-treated cultures.

Another study analysed the use of polynucleotide injections as an alternative to traditional dermal fillers for

The patients both reported high satisfaction, with no significant side effects

treating iatrogenic fat atrophy in two patients.[4] The first had localised depression in the left temple due to lipolysis injections and was injected with polynucleotides over a series of six sessions, while the second had depressed scars on her cheek following steroid injections for acne treatment and was treated across four sessions. Polynucleotides were placed to both the intradermal and dermal layers as per the image below.



The patients both reported high satisfaction, with no significant side effects.

The researchers highlighted how the volumising effect obtained through the treatment is likely due to the polynucleotides' stimulation of pre-adipocyte differentiation and tissue regeneration. They noted that larger clinical trials are needed to optimise treatment protocols and confirm efficacy.

The **technique**

I use Plinest® from Mastelli due to its high concentration of Polynucleotides HPT® (20mg per ml) and noteworthy clinical efficacy. Using a cannula allows me to reach all skin layers through one entry port. My cannula of choice is the Precision 32 - the tip, superior polishing and surface lubricant allows for optimum glide. The 27G 40mm is my initial choice for the most superficial delivery, however, if skin quality is very poor, I use the 25G 50mm as there's less risk of bruising and excessive trauma. It's important to highlight that the choice of delivery system is equally important as choosing the best injectable, in order to allow for a controlled and efficient application of polynucleotides. In my experience, the Precision 32 is able to glide through the skin with minimal resistance, allowing placement in from the epidermis to subcutaneous layers, and ensuring comprehensive treatment of the under-eye area.

Most patients tolerate the procedure well, with only a small drop of lidocaine required at the entry point for optimal comfort. In the past, when I've used both a needle and a cannula for multilayering,

patients found it more uncomfortable, so I also used a numbing cream. Having just the one entry point with a single cannula has made managing pain a lot more efficient.

Patient outcomes and considerations

While volume enhancement to under-eye hollows using this multi-layer polynucleotides approach is subtle, it is definitely noticeable - offering a promising alternative for those who do not want or cannot have dermal filler treatment in this area.

Other clinical observations indicate that patients experience:[2]

- Improvements in skin hydration and quality
- Reduction in fine lines and crepiness
- Decrease in hyperpigmentation

This emerging modality has the potential to redefine non-surgical under-eye treatments

The most common side effect is the temporary appearance of superficial product placement, resembling mild swelling or a subdermal 'sausage-like' formation, which typically resolves within three to seven days. Standard contraindications for injectables, including active autoimmune diseases and bleeding disorders, must be considered.

It should be emphasised that a thorough understanding of periorbital anatomy is crucial for safe and effective injections. Superficial injections must account for fine blood vessels to minimise bruising, while deeper injections should be confined to the subcutaneous layer to avoid proximity to the infraorbital neurovascular bundle.[5]

Before and after three sessions (spaced four weeks apart) of Plinest® to the superficial dermis and the superficial subcutaneous layers. Administered with the 25G 50mm Precision 32 cannula.

Future directions and research needs

Polynucleotide injections using a multilayer approach for volume deficits represent an innovative and minimally invasive option for under-eye rejuvenation. Initial patient outcomes suggest improved skin quality and mild volume restoration with minimal discomfort and downtime.

To further validate the efficacy of this technique, more standardised clinical trials are needed. While currently available data suggest potential benefits and clinical observations have found positive results, more robust research with increased cohort numbers will help establish definitive treatment protocols. With careful anatomical consideration and precise technique, this emerging modality has the potential to redefine non-surgical under-eye treatments in regenerative aesthetic medicine.

Dr Mei-Ying Yeoh's career spans general dentistry and hospital-based practice, with extensive experience as a core trainee in maxillofacial surgery. She has managed minor facial injuries and assisted in major surgeries, including jaw reconstruction, gaining deep expertise in head and neck anatomy. Trained by leading experts, Dr Yeoh now focuses exclusively on aesthetic medicine and has been educating medical professionals since 2019.

Disclosure: Dr Mei-Ying Yeoh developed the Precision 32 cannula.

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The Patients' Regenerative Journey

Nurse prescriber Julie Scott shares guidance on creating treatment timelines and building patient trust

The term 'regenerative medicine' was first coined by Dr William Haseltine in 1999. From designing treatment strategies for cancer and AIDS/HIV, to pioneering the development of new drugs based on information from the human genome, Dr Haseltine is a highly respected professor and founder of multiple biotech companies.[1] Conducting extensive research into regenerative techniques, in a 2001 interview he claimed that 'it is conceptually possible to chart a path to human immortality'.[2]

Reading his work is fascinating and inspiring, fuelling my interest in regenerative medicine and its application to aesthetics.

My journey with regenerative medicine

I began working alongside consultant plastic surgeon Mr Peter Butler in 2002. In that year, he set up a clinical research programme in facial transplantation. His work investigated how reprogramming stem cells into specialised cells can replace, repair or regenerate diseased cells.

My career in aesthetics began in 2004. As patients typically present with 'degenerative' consequences of ageing, our approach has historically been focused on reducing the symptoms of ageing, rather than encouraging the body to repair itself and work more effectively in future.

In recent years, the landscape has started changing. With advancements in research and the introduction of regenerative aesthetic treatments, we are able to offer our patients treatments that can help us 'rewind or stop the clock'. While I wholly embrace this transition, it has been important to introduce the concept to patients carefully, so they trust my approach and understand their expected results' timeline.

Understanding our patients = understanding our treatments

To ensure the creation of bespoke treatment plans that meet our patients' expectations, we must take time to thoroughly understand our patients' needs.

To do this successfully, we should identify the intrinsic and extrinsic influences on their ageing concerns, providing advice on adaptions they can make, such as increasing sunscreen use and improving their skincare routines.

We can also use classification tools such as the Glogau scale, which measures the severity of photoageing and wrinkles, and imaging devices to identify the extent of skin conditions such as hyperpigmentation and inflammation.

Gathering this objective data will help inform our treatment plans - whether this involves using treatments in isolation or in combination, to prime skin and/or to boost results.

In my experience, treatment blending is a significant element of my regenerative practice and something I highly advocate for. As an artist will assess and choose the most effective materials to create their masterpiece, we should select technologies that work in harmonisation to deliver optimal outcomes.

Building patient trust

As regenerative treatments will be a new concept for many, it is vital that we translate all the science and technology in a way that is accessible to our patients, while being transparent as to what to expect on their journeys.

I dedciate a full hour to each patient's consultation, showing them before and after photographs, and taking time to explain each concept in layman's terms, talking them through the protocols, potential discomfort and expected side effects.

Equally important is clearly communicating the expected timeline to see results. Many of our patients will be used to seeing the immediate or fairly quick outcome of aesthetic procedures such as hyaluronic acid dermal fillers and botulinum toxin. We now need to highlight the benefits of regenerative results that develop over time - explaining that we're treating from the inside out, and no longer masking the symptoms of ageing.

Looking to the future

The future of regenerative aesthetics is exciting; more research and development into genetics and lifestyle factors of ageing could mean that skincare products and treatments become even more bespoke, further enabling us to 'turn back the clock' on ageing.

As awareness of regenerative tools grows, our patient portfolio may become younger, allowing our 'prevention' clinic menus to become more extensive. This could also mean that our use of toxin and fillers starts to change - perhaps we'll only need to give our first toxin injections for patients aged 40 instead of 30!

It is vital that as our patient demographic shifts, our aesthetic practices adapt to match their needs. I have patients who I have treated for 20 years and the reason they continue to trust me is because I continually modify their plan to match their individually evolving needs, only ever treating what is clinically indicated in each moment along their patient journey. If we as practitioners take the time to develop this trust and invest the time needed to ensure they are informed on their own care, our patients will go on to share this knowledge with their friends, families, and colleagues. This in turn will increase awareness of the power of regenerative aesthetic treatments, creating a reciprocal relationship in which the future of our patients and of regenerative medicine sustain each other.

In the world of regenerative medicine, we have already come a long way and with even more to look forward to. It is fantastic to see aesthetic events creating space for essential education on regenerative treatments, and I'm particularly proud to be a part of RAMCE - the UK's only event dedicated to this exclusively.

Let's continue to share our knowledge and experiences to shape the future of ageing and regeneration for our patients.

Julie Scott is an NMC-registered indepdent nurse prescriber, Level 7 qualifed aesthetic injector and trainer, with more than 30 years' experience in plastics and skin rejuvenation. She established her practice, Facial Aesthetics in 2003, and won Best Clinic South England at the Aesthetics Awards 2023. Julie also won Aesthetic Nurse Practitioner of the Year at the Aesthetics Awards in 2024 and 2022, as well as at the Aesthetic Medicine Awards in 2024. Julie is on the Clinical Advisory Board for the Aesthetics Journal and is a Key Opinion Leader for several leading aesthetic brands.

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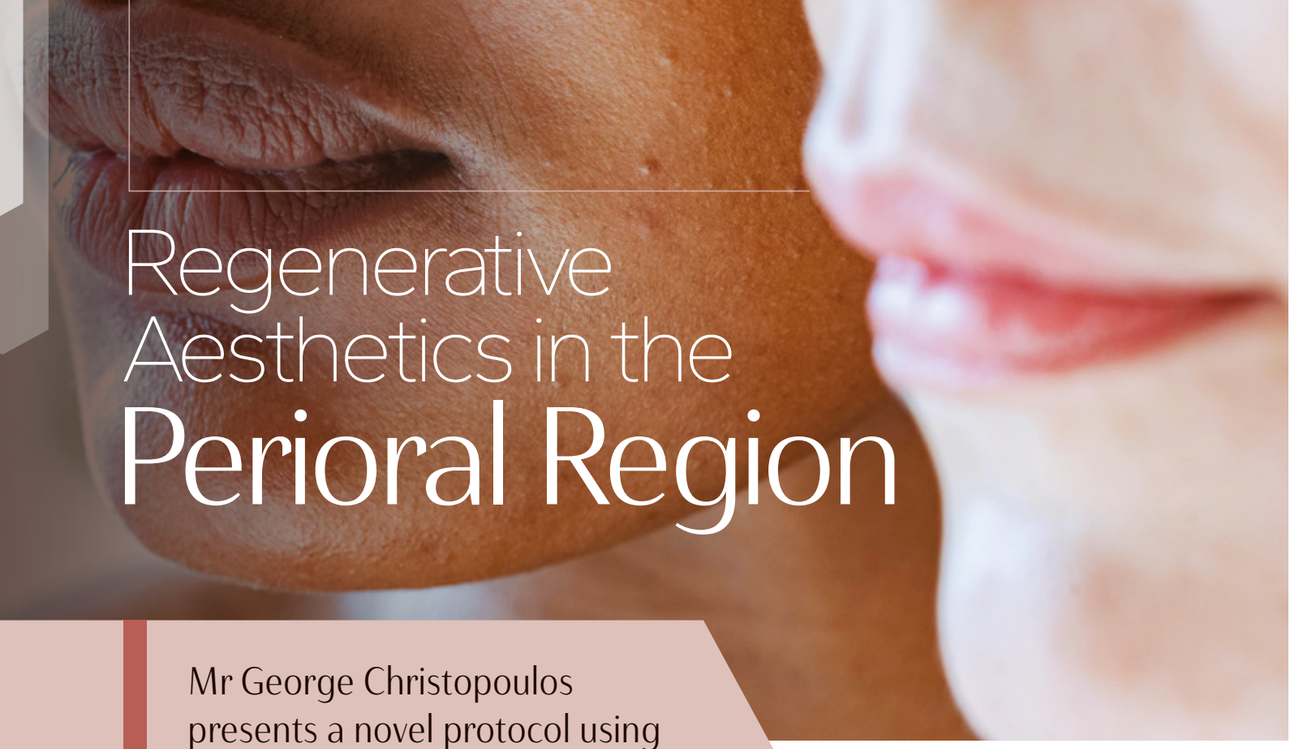


Regenerative Aesthetics in the Perioral Region

Mr George Christopoulos presents a novel protocol using Newest® Polynucleotides HPT®

Abstract

The perioral region remains a challenging area for aesthetic rejuvenation due to the complexity of soft tissue movement and the delicate balance required to maintain natural expression. Historically, the use of conventional injectables in this area has led to a high incidence of complications and unnatural outcomes. In my ongoing efforts to refine regenerative aesthetic approaches, I investigated a novel technique utilising Newest® - a formulation combining polynucleotides and hyaluronic acid - to gently restore skin quality, improve hydration, and address perioral fine lines. This article outlines my protocol and preliminary findings from a prospective clinical trial, which demonstrate the technique's safety, efficacy, and patient satisfaction. Aesthetic practitioner Dr Raquel Amado was recruited to contribute to the research through patient treatment and analysis.

Rationale and objectives

The perioral region is particularly susceptible to signs of ageing, including fine lines, loss of elasticity, and dermal dehydration.[1,2] Traditional use of fillers in this area often results in overcorrection, distortion of natural movement, and a 'perioral overfilled syndrome.'[3-5]

I aimed to develop a safe, standardised, and minimally invasive protocol that could deliver consistent and natural improvements in perioral skin quality. The ideal approach would reduce the reliance on volumising agents, limit complications, and support facial harmonisation through regenerative mechanisms.

Product choice

I chose Newest® as it contains a unique, synergistic blend of polynucleotides and hyaluronic acid (10mg/ml Polynucleotides HPT® and 10mg/ml non-crosslinked HA with mannitol, which is a powerful antioxidant that helps prolong the life of the HA). The patented Polynucleotides HPT® technology, developed by Italian pharmaceutical manufacturer Mastelli, uses DNA fractions obtained from trout bred in fresh water. The DNA fractions go through a stringent purification and sterilisation process, which ensures no proteins or lipids get through to the final product.

Polynucleotides HPT® is clinically proven to promote a trophic and stimulating action on existing fibroblasts, increase collagen synthesis and the viability and number of fibroblasts, as well as improving hydration and scavenging.[6-8]

The addition of hyaluronic acid provides immediate hydration while supporting the polynucleotide-mediated regenerative process. Therefore, this product was selected for its ability to deliver gradual, tissue-friendly rejuvenation without volumising distortion.

The perioral region remains a challenging area for aesthetic rejuvenation

Study design and methods

A total of 20 patients (ages 20-65) were recruited. Inclusion required no perioral treatment for the previous six months. Exclusion criteria included pregnancy, breastfeeding, autoimmune conditions, active infections, or known allergies to treatment components. Standardisation was prioritised throughout:

- Two treatment sessions, spaced four weeks apart
- Follow-up at four weeks post second session
- 3D imaging with integrated skin analysis used pre- and post-treatment
- Validated questionnaires to assess patient satisfaction and perception of results

All procedures were performed under local anaesthesia nerve block or regional infiltration. This minimised patient discomfort and procedural time, with treatments completed in approximately 30 minutes.

Injection technique

A 25G 38mm cannula was employed with a single-entry point per side, located approximately 0.5cm lateral to the corner of the mouth. Five vectors of linear retrograde product application were targeted, with 0.2cc to each (1cc per side in total). These were:

- Towards the nasolabial fold
- Towards the upper lip skin
- Inside the upper vermillion (red part of lip)
- Into the lower vermillion
- Towards the labiomental crease

Remaining in the subcutaneous layer, this technique allowed for comprehensive coverage of the perioral region while reducing trauma and ensuring even product distribution. Both practitioners adhered to the same procedural technique guidelines for the application of one Newest® syringe (2mls).

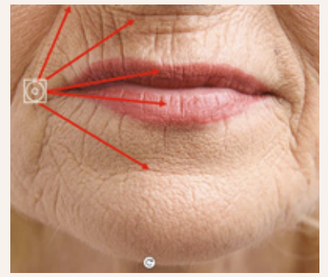


Diagram demonstrates injection point and five vectors for product placement

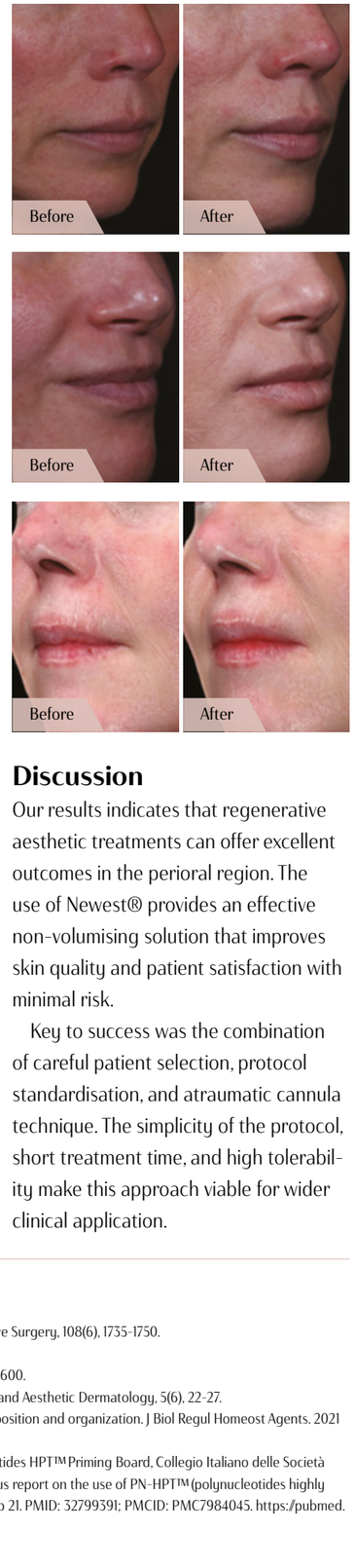
Results

At follow-up, 100% of patients reported satisfaction with their results, with no complications observed; mild swelling was the only post-treatment side effect, aligning with expected outcomes from an injectable procedure.

Significant improvement was noted in:

- Lip hydration
- Skin elasticity
- Appearance of perioral fine lines
- General texture and tone of perioral skin

Photographic documentation and skin analysis corroborated these subjective findings, with measurable improvements in dermal density and surface smoothness.



Discussion

Our results indicates that regenerative aesthetic treatments can offer excellent outcomes in the perioral region. The use of Newest® provides an effective non-volumising solution that improves skin quality and patient satisfaction with minimal risk.

Key to success was the combination of careful patient selection, protocol standardisation, and atraumatic cannula technique. The simplicity of the protocol, short treatment time, and high tolerability make this approach viable for wider clinical application.

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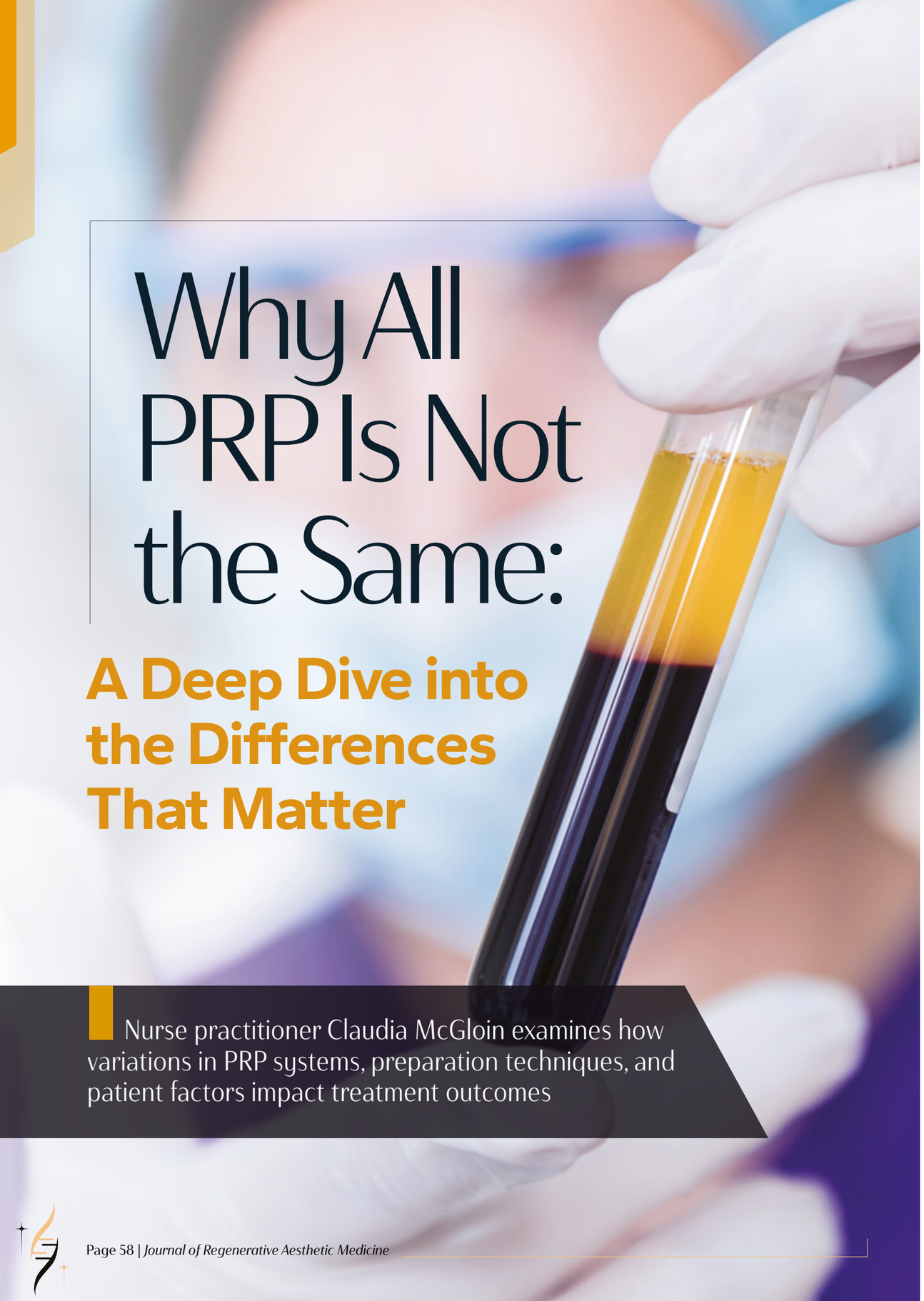

Why All PRP Is Not the Same:

A Deep Dive into the Differences That Matter

Nurse practitioner Claudia McGloin examines how variations in PRP systems, preparation techniques, and patient factors impact treatment outcomes

Platelet Rich Plasma (PRP) has emerged as a powerful tool in regenerative medicine, dermatology, plastic surgery, orthopaedics, and aesthetic treatments due to its ability to accelerate healing and the processes involving tissue repair using the body's own biology. By concentrating platelets and growth factors from a patient's own blood, PRP stimulates tissue repair, reduces inflammation, and promotes regeneration. However, a critical misunderstanding remains widespread among patients and even some healthcare professionals: that all PRP is the same.

In reality, PRP is not a one-size-fits-all treatment. The quality, composition, and clinical effectiveness of PRP can vary greatly depending on how it's prepared, processed, and applied. These differences are influenced by the technology used, the methodology behind the preparation, and even geographic regulatory standards, especially between Europe and the United States.

In this article, I will explore why all PRP is not the same and how these differences can influence treatment outcomes.

What is PRP?

PRP is created by drawing a patient's blood and processing it to isolate a concentrated volume of platelets suspended in plasma. These platelets contain growth factors and cytokines that stimulate healing and regenerative processes. However, not all PRP is the same.[1,2] The end product can differ substantially in terms of:

- Platelet concentration[3]
- Leukocyte (white blood cell) content[4]
- Red blood cell contamination[5]
- Volume of plasma used[6]
- Presence or absence of additives (e.g. anticoagulants)[7]
- Growth factor yield8
- Activation status (activated vs. non-activated)[9]

Each of these variables can drastically alter the way PRP behaves in the body and how effective it is for specific treatments.

The centrifuge process: the key to PRP quality

At the core of PRP therapy lies the centrifuge, a device that spins blood at high speeds to separate its components. The goal is to isolate the PRP from the other components of blood, such as red blood cells, white blood cells, and plasma. The effectiveness of PRP largely depends on how this separation process is carried out.[3,10]

One of the most defining aspects of PRP quality is the centrifuge process used to separate the blood components.

Spin speed & duration

A faster spin may shorten processing time but can also damage platelets or reduce their concentration. A slower, more controlled double-spin process often yields a more potent PRP, with a higher concentration of platelets and less contamination from red and white blood cells.[4,11]

Single vs. **double** spin

Some systems use a single spin, resulting in a basic separation. Double-spin systems further refine the PRP, producing a more purified and platelet-dense product, ideal for precision applications. [6,12]

While certain PRP systems prioritise maximising platelet concentration, others may sacrifice platelet yield for quicker processing or ease of use, impacting the overall effectiveness of the treatment.[7]

Types of PRP: not one-form-fits-all

Different formulations of PRP tailored to specific clinical goals:

- **Pure PRP (P-PRP):** High platelet concentration with low leukocyte content. Ideal for aesthetic procedures and soft tissue repair, where minimal inflammation is preferred.[3,13]
- **Leukocyte-Rich PRP (L-PRP):** Contains higher white blood cell content, which promotes a stronger inflammatory response. This type is beneficial in cases like tendonitis, chronic injuries, and joint degeneration where inflammation aids healing.[4,14]
- **Platelet-Rich Fibrin (PRF):** A variant of PRP processed at slower speeds without anticoagulants, resulting in a fibrin matrix that gradually releases growth factors. PRF is increasingly used in bone regeneration, dentistry, and chronic wound healing.[15,16]

Activated vs. Non-Activated PRP: timing the healing response

An important factor that can influence the success of PRP therapy is whether the platelets are activated before injection. Activation refers to the process of stimulating platelets to release their growth factors by adding substances like calcium chloride or thrombin.[6,17]

Platelets can be 'activated' to release their healing factors before injection, or left in their natural state to activate

gradually in the body:

Activated PRP: Mixed with calcium chloride or thrombin to release growth factors immediately. Used for acute injuries or aesthetic treatments requiring rapid action.[1,18]

Non-Activated PRP: Injected as is, allowing for a slow, sustained release of growth factors over time - ideal for bone regeneration or long-term healing of chronic injuries.[3,19]

Choosing whether or not to activate PRP depends on the specific injury or condition being treated. While activated PRP can yield faster results, non-activated PRP may be more appropriate for long-term regeneration[7]

PRP system variability: brand and technology matter

The technology behind PRP systems can significantly influence the composition, quality, and clinical effectiveness of the final product. Different systems vary in several key aspects:[6,12]

- **Platelet Concentration:** Some systems are engineered to produce highly concentrated PRP, while others yield lower potency preparations that may be less effective for certain treatments.[11]
- **Additives and Anticoagulants:** Many devices introduce anticoagulants like citrate to prevent clotting, which can affect platelet behavior and healing outcomes. In contrast, systems like PRF avoid additives to preserve a more natural platelet environment.[8,9]
- **Filtration Methods:** Certain brands employ advanced filters to remove red blood cells and leukocytes, while others leave more cellular debris, which may impact the therapeutic quality.[5]

The use of additives, filtration techniques, and the degree of platelet concentration can all influence how the body responds to PRP therapy and the effectiveness of tissue healing.[7]

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PRP differences across regions: US vs. Europe

Geographical regulations also influence PRP system availability and standardisation:

United States: The FDA categorises PRP as a medical procedure, not a drug. PRP systems must be 510(k)-cleared, meaning they are substantially equivalent to already-approved devices. This tightens the range of available systems but ensures a degree of regulatory oversight.[20,21]

Europe: The European Union's Medical Device Regulation (MDR) requires CE marking but has more lenient requirements for clinical evidence. This allows a broader range of PRP systems to be marketed but can result in significant variation in quality and clinical efficacy.[22,23]

This regulatory divergence means patients in Europe may encounter more diversity in available PRP systems, but not necessarily higher quality.[6,12]

Individual biology: the patient factor

While the type and preparation of PRP are critical, individual factors also play a significant role in determining the success of PRP therapy. Age, overall health, diet, and medical conditions can all influence how effectively PRP works.[24,25]

Even with a high-quality PRP system, results can still vary based on individual patient factors:

- **Age:** Older individuals may have fewer or less active platelets, potentially diminishing the regenerative effects.[26,27]
- **Health status:** Conditions like diabetes, autoimmune diseases, metabolic diseases, or poor circulation can impair the body's healing response.[28,29]
- **Nutrition:** Deficiencies in key nutrients (like Vitamin C, zinc, and amino acids) can reduce the body's ability to regenerate tissue, even when growth factors are present.[30,31]

A comprehensive approach considers not just the PRP system, but also patient readiness, overall health, and lifestyle factors that support healing. Since PRP relies on the patient's own blood, tailoring the treatment to their specific health profile is critical to achieving the best possible results.[32]

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Efficiency and affordability: what to consider

PRP systems can differ significantly in both cost and usability. Some brands offer ready-to-use kits designed to streamline the process for medical professionals, while others require more complex preparation steps that demand additional time and training.

Costs also vary widely. High-end systems tend to be more expensive, reflecting their advanced technology, greater precision, and potentially superior clinical outcomes. Choosing the right PRP system often involves balancing budget considerations with the desired level of convenience and performance.

The Bottom Line: PRP is a technique-dependent therapy

PRP therapy has revolutionised the way we approach healing and regeneration across both medical and aesthetic fields. Yet, despite its growing popularity, PRP is far from a standardised treatment. The reality is that not all PRP is created equal, and understanding the nuances between different systems, preparation methods, and patient factors is essential to achieving optimal outcomes.

Practitioners - know your tools. Understand the strengths and limitations of your PRP system and avoid assuming that one method works for every case.

From centrifuge design and platelet concentration to leukocyte content, activation methods, and other system-specific features, several key variables influence how effective a PRP treatment will be. These are not just technicalities - they can significantly shape the healing response and the results your patient experiences.

PRP therapy is inherently technique-dependent. Critical factors such as the type of PRP used (Pure vs. Leukocyte-Rich), the centrifugation method (single-spin vs. double-spin), activation timing (immediate vs. gradual), and the patient's own biology all play pivotal roles. It's not simply about drawing blood and injecting platelets - it's about customising the process for each individual and each condition.

It is important to underline that the clinical outcomes of PRP treatments are not solely determined by the quality of the PRP itself, but also by the precision and technique of its administration. In aesthetic applications, intradermal delivery of PRP is particularly critical, as the dermis is the anatomical layer rich in fibroblasts, the key cells responsible for collagen synthesis, tissue repair, and modulation of the extracellular matrix (ECM). Accurate injections of PRP within this layer ensures that growth factors and bioactive molecules interact directly with target cells, thereby maximising their regenerative effects. In addition, injecting at all depths will benefit the patient and enhance the treatment giving optimal results. Therefore, mastering the injection techniques is as essential as understanding the biology of PRP itself in achieving predictable and reproducible aesthetic results.

Specific injection techniques commonly used include microbolus, injecting a series of small papules and linear threading or retrograde technique for more diffuse delivery. Using fine-gauge needles or mesotherapy devices can improve precision and patient comfort. Mastering these techniques, along with an understanding of facial anatomy, is essential to optimise the bioavailability of PRP at the cellular level and achieve consistent, high-quality aesthetic results.

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aesthetic results.

Whether treating musculoskeletal injuries, managing chronic conditions, or pursuing skin rejuvenation, choosing the right PRP system and matching it to the patient's specific needs is crucial. A personalised approach unlocks PRP's full regenerative potential.

Ultimately, success with PRP therapy lies in the details - and in the expertise behind every step of the process.

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