



Lasers as Epigenetic Modulators: Reprogramming Skin Biology Toward Regeneration and Longevity – EADV 2025

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LASERS have transformed dermatology by offering effective treatments for photo-ageing, scars, and pigmentary disorders. Traditionally, their benefits were attributed to thermal injury and subsequent collagen remodelling. However, recent advances suggest that lasers exert deeper biological effects by modulating the skin's epigenetic architecture. Epigenetics, through DNA methylation, histone modifications, and non-coding RNAs, governs cutaneous repair, ageing, and plasticity. Emerging evidence indicates that laser therapy reprogrammes these pathways, rejuvenating fibroblast function, reducing senescence, and normalising aberrant signalling. This feature, based on the Société Française des Lasers en Dermatologie (SFLD) session through the European Academy of Dermatology and Venereology (EADV), explores how lasers act as epigenetic modulators, the translational implications for personalised dermatology, and future opportunities to integrate biomarkers and AI into clinical practice.¹ By reframing lasers as molecular reprogramming tools, dermatology is entering a new era of regenerative and longevity-focused care. These insights from the EADV Congress highlight a paradigm shift, positioning lasers not only as aesthetic instruments but also as drivers of regenerative dermatology and cutaneous longevity.

INTRODUCTION

Dermatology is rapidly evolving from symptomatic repair to regenerative and preventive strategies. Central to this transformation is the growing recognition of the role of epigenetics, the heritable yet reversible modifications in gene expression that do not alter the DNA sequence. Epigenetic mechanisms, including DNA methylation, histone modifications, and non-coding RNAs, shape how the skin responds to intrinsic ageing and extrinsic exposures such as UV radiation, pollution, and diet. The concept of an 'epigenetic clock', reflecting biological rather than chronological age, has emerged as a

powerful biomarker of tissue health and longevity.²



Lasers exert effects far deeper than the dermis; they may directly reshape the epigenetic programming of skin cells



In parallel, lasers have become a cornerstone of dermatology, widely used for photo-ageing, scars, vascular and pigmentary disorders, and, more recently, functional rejuvenation. Historically, their

efficacy was explained by controlled injury leading to wound healing and neocollagenesis. Yet, accumulating data suggest that lasers exert effects far deeper than the dermis; they may directly reshape the epigenetic programming of skin cells, rejuvenating their function and shifting their molecular trajectory.³

This commentary examines the interplay between lasers and epigenetics, highlighting evidence of molecular reprogramming, the broader translational implications for dermatology, and future perspectives on integrating biomarkers and AI into clinical practice.

THE EPIGENETIC LANDSCAPE OF SKIN

The skin is one of the most epigenetically dynamic organs, constantly adapting to environmental stimuli. Its regenerative capacity and ageing trajectory are determined not only by genetic predisposition but also by epigenetic regulation.⁴

- **DNA methylation:** Methylation at cytosine-phosphate-guanine islands silences transcription. With age, methylation patterns become irregular, a process known as epigenetic drift. Genes involved in collagen synthesis,

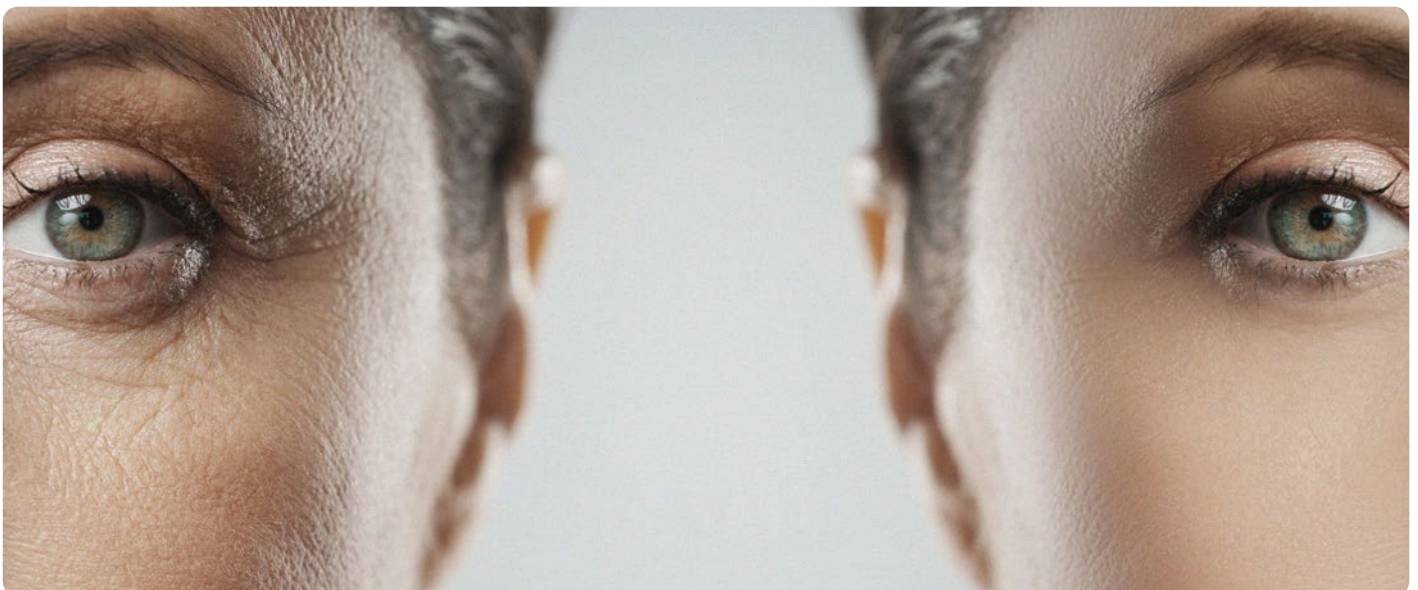
elastogenesis, and antioxidant defense are progressively silenced, while pro-inflammatory pathways are activated.⁵

- **Histone modifications:** Post-translational modifications such as acetylation and methylation influence chromatin accessibility. Open chromatin promotes repair and regeneration, whereas closed conformations inhibit these functions. Altered histone states contribute to dermal thinning and impaired wound healing.⁶
- **Non-coding RNAs:** MicroRNAs (miRNA) and long non-coding RNAs regulate mRNA translation. Dysregulated miRNAs, such as upregulation of fibrotic miR-21 or downregulation of antifibrotic miR-29, drive pathological processes including scarring, pigmentation disorders, and chronic inflammation.²

Taken together, these mechanisms make the skin's epigenome both a record of environmental exposures and a determinant of its regenerative capacity.

Laser-Induced Epigenetic Modifications

Lasers deliver energy that induces microthermal injury, stimulating controlled wound healing. The novelty lies in evidence that this process is mediated by epigenetic reprogramming rather than mere collagen contraction.^{7,8}



DNA Methylation

Fractional CO₂ lasers have been shown to reduce hypermethylation of promoters controlling extracellular matrix (ECM)-related genes, thereby reactivating collagen and elastin production. In fibroblasts from aged skin, post-laser treatment correlates with decreased 'epigenetic age', aligning cellular behaviour with a more youthful profile.⁹

Histone Remodelling

Laser-induced stress activates histone acetyltransferases, leading to chromatin relaxation and increased transcription of pro-regenerative genes. Conversely, fibrotic genes undergo repressive histone modifications, decreasing pathological collagen deposition and improving scar remodelling.¹⁰

Non-coding RNAs

Several studies have demonstrated changes in miRNA profiles post-laser therapy. miR-21, which promotes angiogenesis and fibroblast migration, is upregulated, while miR-29, an inhibitor of collagen synthesis, is downregulated. These coordinated shifts favour balanced ECM remodelling and tissue regeneration.¹¹

Cellular Senescence

Markers of senescence, such as p16^{INK4a} and β-galactosidase, decrease after fractional laser treatment. By modulating senescence-associated secretory phenotype pathways, lasers not only rejuvenate fibroblasts but also reduce chronic inflammation, creating a more favourable regenerative microenvironment.¹²

Transcriptomic Insights

Transcriptome analyses post-laser reveal upregulation of growth factors, angiogenic mediators, and ECM regulators, many under epigenetic control. These findings support the hypothesis that lasers function as molecular reset devices, orchestrating global gene expression changes via epigenetic remodelling.¹³

“These findings support the hypothesis that lasers function as molecular reset devices”

TRANSLATIONAL IMPLICATIONS

The discovery that lasers modulate skin epigenome reframes their role in clinical dermatology.^{8,14} Several translational consequences follow:

- **Objective biomarkers of efficacy:** Current outcome measures rely heavily on subjective grading or patient-reported improvement. Epigenetic profiling, such as changes in DNA methylation age or miRNA signatures, could provide objective, quantifiable biomarkers, enabling clinicians to measure biological as well as aesthetic outcomes.
- **Patient stratification:** Not all patients respond equally to laser therapy. Baseline epigenetic signatures could predict treatment response, guiding personalised protocols. For instance, patients with accelerated epigenetic ageing may require more intensive regimens, while those with youthful profiles might benefit from gentler approaches.
- **Durability of results:** The persistence of improvements after fractional laser therapy may be explained by long-lasting epigenetic remodelling, in contrast to the transient effects of wound healing. This suggests that lasers can achieve semi-permanent molecular resets, explaining why some patients maintain benefits for years.
- **Integration with preventive dermatology:** If lasers can slow or reverse epigenetic ageing, they could be integrated into preventive dermatology programmes, much like sunscreens are used to prevent photo-ageing. This concept of 'epigenetic dermatology' positions lasers as tools not only for correction, but also for long-term preservation of skin health.

- **Aesthetic and longevity medicine convergence:** By demonstrating measurable effects on biological age, lasers could bridge the gap between aesthetic dermatology and longevity medicine. This positions them not merely as cosmetic enhancers but as regenerative therapies aligned with systemic health strategies.

FUTURE DIRECTIONS AND CHALLENGES

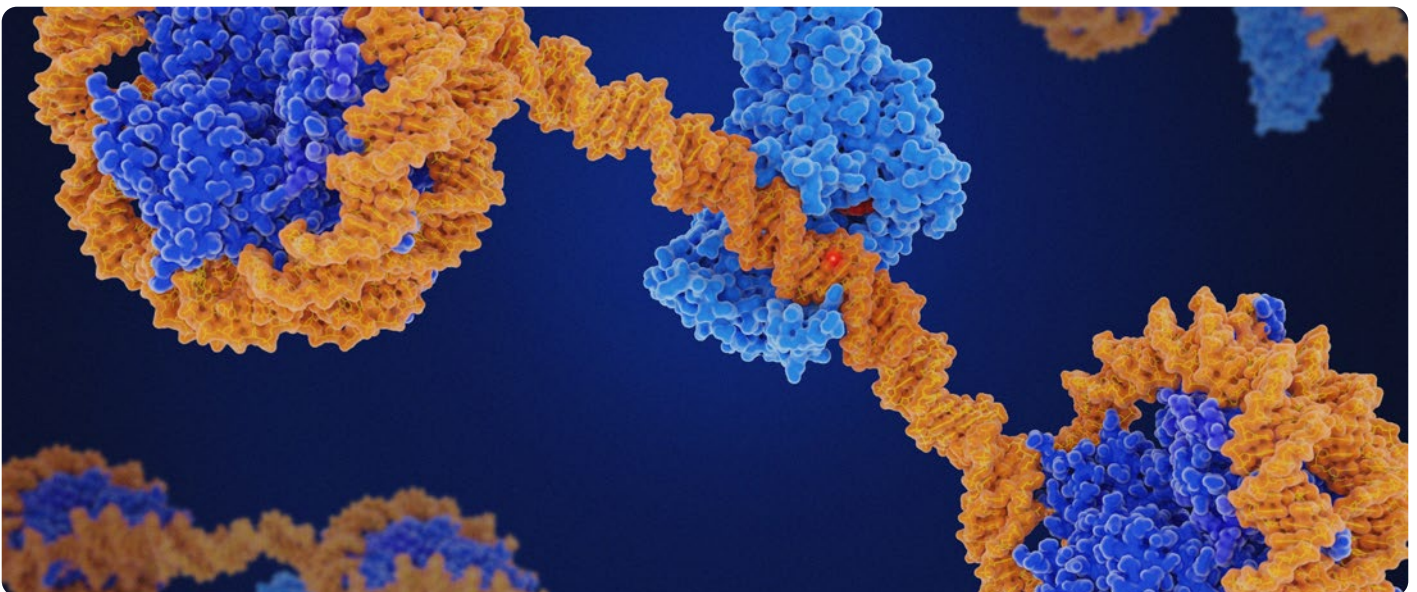
While the interplay between lasers and epigenetics is promising, several challenges must be addressed:

- **Evidence gap:** Current studies are small and often preclinical. Large-scale, controlled trials integrating molecular endpoints are essential to validate the epigenetic effects of lasers.
- **Standardisation:** Consensus is needed on which epigenetic markers (e.g., DNA methylation clocks, specific miRNAs, histone states) best reflect clinical improvement.
- **Longevity focus:** Whether lasers truly reset the epigenetic clock or merely induce temporary changes remains unresolved. Longitudinal studies tracking patients' epigenetic age pre- and post-laser are required.
- **Combination therapies:** The synergy between lasers and epigenetic modulators, such as exosomes and sirtuin activators, should be investigated as potential next-generation protocols.
- **Ethical and regulatory considerations:** As lasers evolve into tools of molecular reprogramming, regulatory frameworks may need to redefine them as regenerative devices rather than purely cosmetic instruments.

FURTHER USES OF MEDICAL LASERS

Beyond their emerging role as epigenetic modulators, lasers continue to demonstrate remarkable versatility across a wide spectrum of dermatologic and surgical applications. The session illustrated how medical lasers are increasingly integrated into both functional and aesthetic indications, extending benefits beyond rejuvenation and resurfacing.

- **Laser treatment of ingrown nails (onychocryptosis):** Laser-assisted management of ingrown nails using CO₂ systems offers precise matrix ablation with minimal postoperative pain and a reduced recurrence rate. The technique enables controlled excision of the affected nail fold, promoting faster healing and superior cosmetic outcomes compared to traditional surgical methods.
- **Laser therapy for adult bruises:** The use of vascular lasers has proven effective in accelerating the resolution of post-



procedural bruises and vascular lesions in adults. Targeted photothermolysis of haemoglobin-rich areas enhances clearance, shortens downtime, and improves overall skin appearance. This approach highlights how lasers can refine recovery and patient satisfaction following aesthetic or medical interventions.

- **Improving scars in children:** Fractional ablative and non-ablative laser technologies have shown significant benefits in the treatment of paediatric scars. Careful adjustment of parameters allows effective remodelling of texture and pigmentation while preserving safety in developing skin. These interventions contribute meaningfully to improving the quality of life and self-esteem of younger patients.

Collectively, these applications underscore the multidimensional value of medical lasers, from restoring function to enhancing appearance, emphasising their place at the intersection of dermatology, surgery, and regenerative medicine.

CONCLUSION

Lasers are no longer simply devices of ablation or resurfacing; they emerge as epigenetic modulators capable of reprogramming skin biology. By influencing DNA methylation, histone states, and non-coding RNAs, lasers induce long-lasting molecular shifts that underlie their regenerative effects.

The implications are profound: lasers may one day be guided by epigenetic biomarkers, optimised by AI, and combined with adjunctive molecular therapies to deliver personalised, preventive, and regenerative outcomes. This convergence of epigenetics and laser dermatology redefines the specialty's role in both aesthetics and longevity medicine.

In this new paradigm, lasers should be recognised not only as instruments of cosmetic enhancement, but also as catalysts of cutaneous longevity.

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