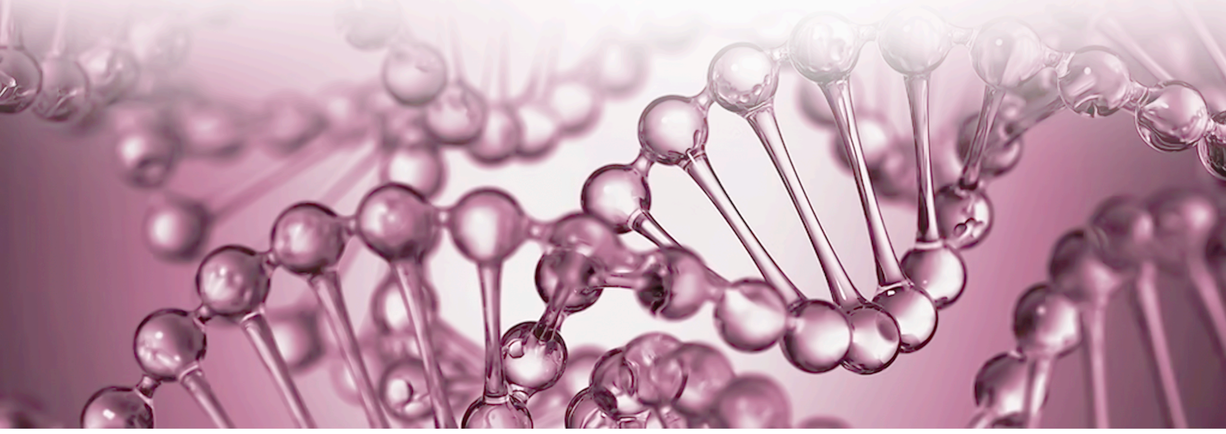
MESOTEN

COMBO DNA

AKRADEX

THE ESSENCE OF COMBO DNA

Synergy of PDRN and PN polynucleotides



At the heart of **Mesoten** Combo **DNA** lies a unique fusion of PDRN and PN, creating a dual-action approach to rapid regeneration and enduring structural improvement.

Sourced from premium French ingredients, this innovative advanced complex revitalizes the skin at a cellular level, restoring elasticity, enhancing density, and ensuring long-lasting results.

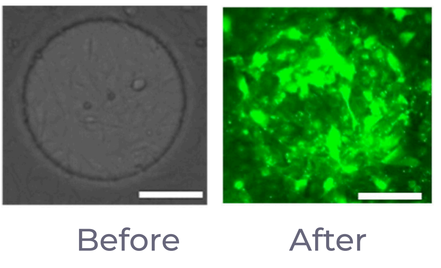
DUAL DNA TECHNOLOGY

Dual DNA Technology is an innovative approach developed by AKRADEX, which for the first time in Korea **combines PDRN and polynucleotides within a single formula.**

	Middle Molecular Weight PDRN	Polynucleotide
Hydration power		
Size	50-1500 kDa	≥1500 kDa
Administration route	Epidermal/ dermal injection	Epidermal/ dermal injection
Advantages	Skin regeneration	Skin regeneration Prolonged Action Increased skin hydration
Formulation	Liquid solution	Hydrogel

PDRN and PN polynucleotides share a similar mechanism of action but **differ in chain length and depth of penetration.** Working in synergy, they stimulate regeneration at multiple layers of the skin, enhancing its firmness and delivering a visible rejuvenating effect.

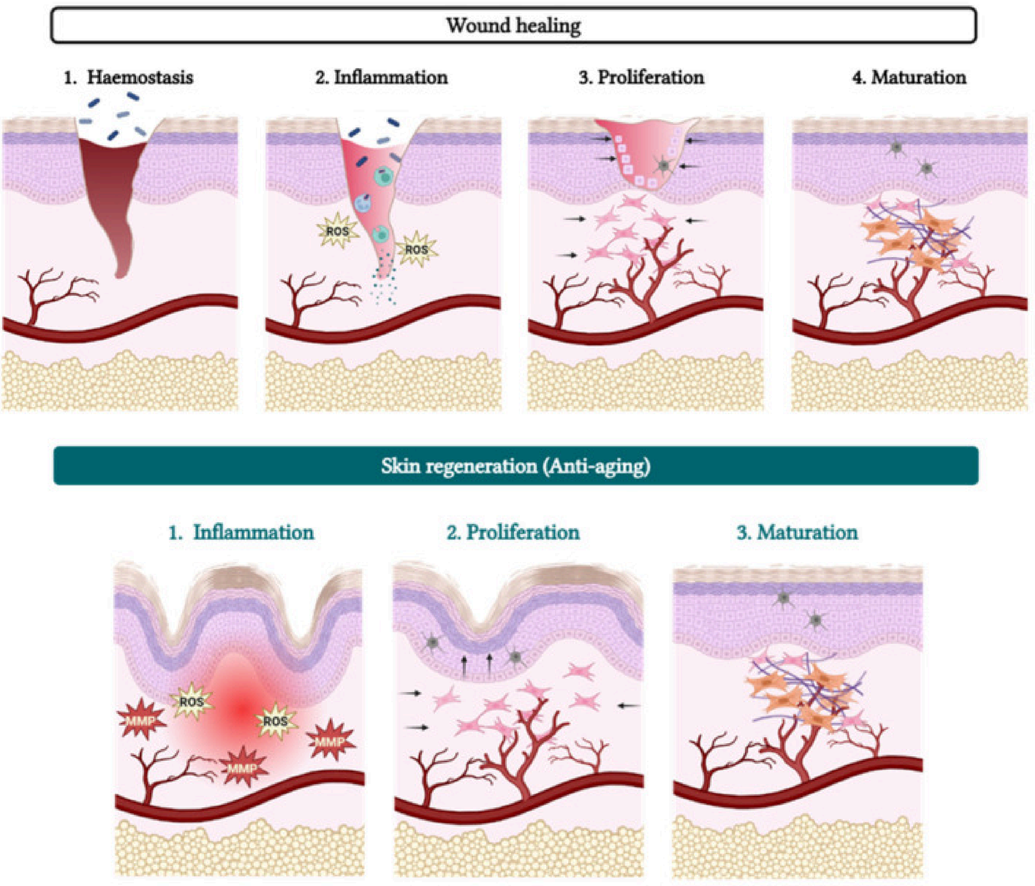
- Wrinkles reduced by 34%
- Skin texture improved by 45%
- Facial contour lifted by 26%
- Results observed within 48 hours after treatment



Before After

INGREDIENTS EFFICACY DATA

Middle molecular weight PDRN (50–1500 kDa) focuses on stimulating regeneration in the epidermal and dermal layers, ensuring effective repair of skin tissues and wound healing.



Polynucleotides (≥1500 kDa), on the other hand, provide deeper and longer-lasting regeneration, while delivering powerful hydration, which also contributes to anti-aging outcomes.

AKRADEX

MDPI

Review

From Polydeoxyribonucleotides (PDRNs) to Polynucleotides (PNs): Bridging the Gap Between Scientific Definitions, Molecular Insights, and Clinical Applications of Multifunctional Biomolecules

Cíntia Marques [1], Alexandre Porcello [1], Marco Cerrano [2], Farid Hadjab [3], Michèle Chemali [4], Kelly Lourenço [1], Basste Hadjab [5], Wassim Raffoul [6], Lee Ann Applegate [7,8,9] and Alexis E. Laurent [7,10,11,*]

1 Development Department, LOUNA REGENERATIVE SA, CH-1207 Geneva, Switzerland; c.marques@louna-aesthetics.com (C.M.); a.porcello@louna-aesthetics.com (A.P.); k.lourenco@louna-aesthetics.com (K.L.)
2 Aesthetic Surgery Department, Clinique Entourage, CH-1003 Lausanne, Switzerland; m.cerrano@entourage.ch
3 Development Department, Albomed GmbH, D-90592 Schwarzenbruck, Germany; f.hadjab@albomed.eu
4 Plastic and Aesthetic Surgery Service, Centre Médical Lausanne Ouest, CH-1008 Prilly, Switzerland; m.chemali@cmlo.ch
5 Independent Consultant Office, F-74330 Poisy, France; abde@basste@yahoo.fr
6 Plastic and Reconstructive Surgery Service, Ensemble Hospitalier de la Côte, CH-1110 Morges, Switzerland; wassim.raffoul@ehc.vd.ch
7 Regenerative Therapy Unit, Lausanne University Hospital, University of Lausanne, CH-1066 Epalinges, Switzerland; lee.laurent-applegate@chuv.ch
8 Center for Applied Biotechnology and Molecular Medicine, University of Zurich, CH-8057 Zurich, Switzerland
9 Oxford OSCAR Suzhou Center, Oxford University, Suzhou 215123, China
10 Manufacturing Department, LAM Biotechnologies SA, CH-1066 Epalinges, Switzerland
11 Manufacturing Department, TEC-PHARMA SA, CH-1038 Bercher, Switzerland
* Correspondence: alexis.laurent@lambiotechnologies.com

check for updates

Academic Editors: Hiroyuki Iijima and Muhammad Shafiq

Received: 13 December 2024
Revised: 13 January 2025
Accepted: 15 January 2025
Published: 19 January 2025

Citation: Marques, C.; Porcello, A.; Cerrano, M.; Hadjab, F.; Chemali, M.; Lourenço, K.; Hadjab, B.; Raffoul, W.; Applegate, L.A.; Laurent, A.E. From Polydeoxyribonucleotides (PDRNs) to Polynucleotides (PNs): Bridging the Gap Between Scientific Definitions, Molecular Insights, and Clinical Applications of Multifunctional Biomolecules. *Biomolecules* **2025**, *15*, 148. https://doi.org/10.3390/biom15010148

Abstract: Polydeoxyribonucleotides (PDRNs) and polynucleotides (PNs) are similar DNA-derived biopolymers that have garnered significant scientific attention since the 1990s for their potential applications in wound healing and skin rejuvenation. These biopolymers exhibit a broad molecular weight (MW) range, typically spanning from 50 to 1500 kDa. However, recent studies have expanded this range to encompass fragments as small as 1 kDa and as large as 10,000 kDa. Clinically, PDRN/PN formulations, commercially available in various galenic forms (gels, creams, serums, masks, and injectables), have demonstrated promising effects in significantly promoting skin regeneration, reducing inflammation, improving skin texture, preventing scar formation, and mitigating wrinkles. Importantly, despite their widespread use in cosmetology and aesthetic dermatology, the interchangeable use of the terms "PDRN" and "PN" in the scientific literature (to describe polymers of varying lengths) has led to considerable confusion within the medical and scientific communities. To specifically address this PDRN/PN ambiguity, this narrative review proposes a standardized structure-based nomenclature for these DNA-derived polymers, the "Marques Polynucleotide Cutoff", set at 1500 kDa. Thus, we propose that the term "PDRN" should be exclusively reserved for small- and medium-chain polymers (MW < 1500 kDa), while the term "PN" should specifically be used to denote longer-chain polymers (MW ≥ 1500 kDa). In a broader perspective, this classification is based on the distinct physicochemical properties and therapeutic effects of these DNA fragments of various MWs, which are comprehensively discussed in the present review.

DNA fragments of interest, as modern methods enable us to obtain longer chains and to better control the fragment MW distributions (see Section 4). In parallel, these evolutions were accompanied by new formulations, namely PN-based hydrogels, which have been widely used clinically, and will be further discussed in Section 6.

It is of the highest importance to note that, for aesthetic or cosmetic purposes, both the names "PDRN" and "PN" always refer to a chain of deoxyribonucleotides, meaning that the polymer is always of DNA origin. As stated before and for the sake of clarity, the term "PDRN" is going to be used in this review to describe small and medium chains of deoxyribonucleotides (i.e., MW < 1500 kDa) and the term "PN" is going to be used to refer to long chains of deoxyribonucleotides (i.e., MW ≥ 1500 kDa; see Section 5), in accordance with the defined "Marques Polynucleotide Cutoff" value of 1500 kDa.

3. PDRN/PN and Skin Regeneration

Due to their potent wound healing stimulation properties [26–33], PDRNs/PNs have been extensively applied for skin regeneration as cosmeceutical ingredients [5] and for medicalized aesthetic purposes. Of note, cutaneous aging processes involve similar dynamics to those of skin wounds and the related repair processes [34]. Therefore, the cellular pathways stimulated by PDRN/PN in wound healing also play a role in reversing the skin aging process, with the potential to regenerate cutaneous tissue that has already been lost

The three main activities mediated by PDRN/PN via A_{2A} receptor binding, as illustrated in Figure 3, may be summarized as follows:

- Inflammation resolution: The resulting cascade reaction leads to a decrease in the levels of pro-inflammatory cytokines (e.g., TNF-α, IL-6, IL-8) [7] and an increase in their anti-inflammatory counterparts (e.g., IL-10), decreasing the overall inflammatory status. The cascade also notably inhibits the synthesis and secretion of collagenase by synovial fibroblasts [7].
- Proliferation: Nucleotides stimulate the secretion of VEGF, which stimulates the formation of new blood vessels (i.e., neo-angiogenesis), as well as growth factors that stimulate cell migration and growth (i.e., fibroblasts and endothelial cells) [6,7,19,33,35,36].
- Remodeling: With decreased inflammation, increased blood support, and cell growth stimulation, the cells (e.g., fibroblasts) are surrounded by optimal conditions to produce collagen (i.e., types I and III) [37–39], elastin, and fibrinogen [18,33]. Those proteins then contribute to form the ECM, providing mechanical and structural support to fibroblasts, generating new tissue [27].

the same patient, an HA-PN filler was effectively used to address these skin laxity issues (i.e., resulting from the polymethyl-methacrylate filler sequelae). Overall, it may thus be set forth herein, based on the available scientific and clinical evidence, that PDRNs/PNs not only serve as biostimulators, but mediate global tissular regeneration, including the formation of blood vessels, cell growth, and protein production.

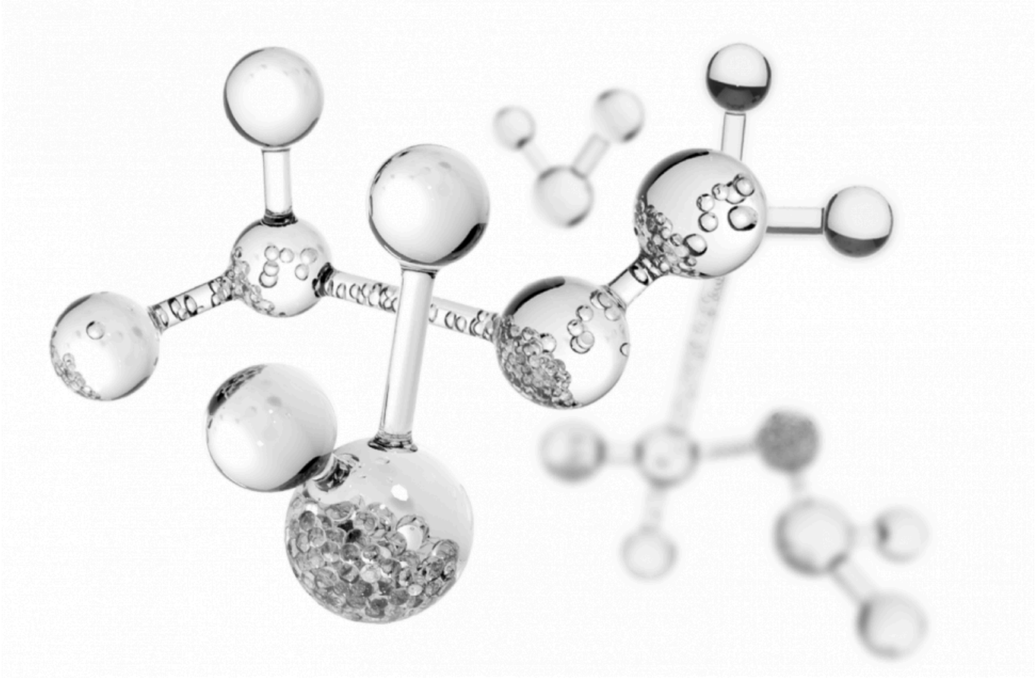
Combo F DUAL DNA concentration 1%

PDRN 300–500 kDa	boosts cell turnover, healing, and inflammation reduction
PN 1400–2000 kDa	delivers long-lasting support for collagen synthesis and skin density

Combo I DUAL DNA concentration 0,5%

PDRN 250–350 kDa	promotes gentle tissue regeneration and reduces inflammation
PN 1000 kDa	supports structural integrity and skin tone in delicate areas

Combo DNA F — an advanced formula with PDRN and PN that stimulates cellular renewal and boosts collagen synthesis, visibly improving skin elasticity and firmness.



Enhanced with glutathione and niacinamide, it evens **out skin tone, provides a healthy glow, and strengthens antioxidant protection.**

Skin becomes denser, deeply hydrated, and visibly rejuvenated, with improved tone and restored barrier function.

An ideal choice for **anti-aging protocols and revitalizing dull, tired, or dehydrated skin.**

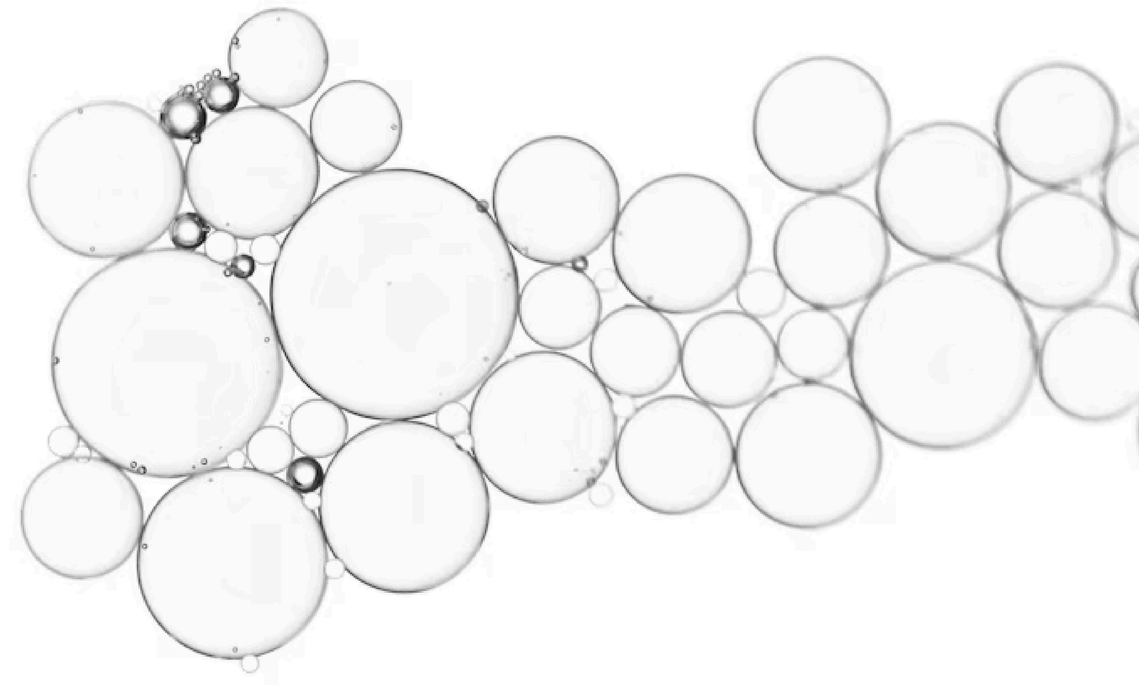
COMBO DNA F INGREDIENTS

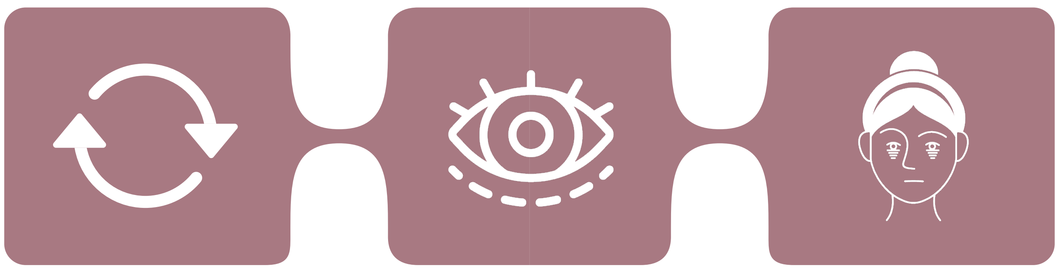
- dual dna technology pdrn+pn
- niacinamide
- glutathione
- hyaluronic acid

EFFECTS

- rejuvenation
- restoration
- brightening and evening of skin tone
- reduction of pigmentation
- radiance
- strengthening of the skin barrier
- hydration

Combo DNA I — Targeted Anti-Age Solution for Delicate Zones.
Next-generation formula combining PN, PDRN, and biomimetic peptides to promote intensive regeneration and wrinkle reduction.





Succinic acid enhances **microcirculation, reduces puffiness, and lightens dark areas.**

Suitable for: periocular area, perioral wrinkles and localized aging areas.

Perfect for focused anti-aging treatments where precision, potency, and visible results are essential - without overcorrecting or adding bulk.

COMBO DNA I INGREDIENTS

- dual dna technology: pdrn+ pn
- succinic acid
- collagen-stimulating peptides: sh-polypeptide-123
- sh-polypeptide-47

EFFECTS

- anti-wrinkle
- improved skin elasticity
- reduction of puffiness
- reduction of dark circles
- stimulation of microcirculation
- restored freshness and expressiveness of the eyes

APPLICATION PROTOCOL COMBO DNA I

APPLICATION AREA

Periorbital Area
needle: 33g-34g, 1.5mm/2.5mm
injection depth: 1.5-2 mm
layer: epidermis/dermis
technique: cleopatra mask micro-papular
*excluding the upper mobile eyelid area

Perioral Wrinkles
needle: 30g–32g
technique: papular
injection depth: 2-3 mm

Recommended
3 procedures at 10-14 day intervals

Maintenance Treatment
every 3-6 months

TECHNIQUE «CLEOPATRA MASK»

AKRADEX specialists have developed a new application method for **Combo DNA i**, called the **“Cleopatra Mask”**.

METHOD OVERVIEW

The technique is named after its distinctive injection pattern: the product is applied to the zones around the eyes and temples, creating a “mask” effect. this ensures even distribution of polynucleotides and PDRN, stimulating tissue regeneration and rejuvenation.

TREATMENT AREA

- Periorbital area (under-eye, crow’s feet, lower eyelid)

Do not inject into the movable upper eyelid!

- Temple area

APPLICATION PROTOCOL COMBO DNA F

- needle 30g–32g, 4/6/12 mm
- **technique:** deep papular

APPLICATION AREA

Face
injection depth: 3-5 mm
layer: dermis/hypodermis

Neck/Hands
injection depth: 2–3 mm
*papules may persist for 2–4 days

Decollete
injection depth: 3-5 mm
layer: dermis/hypodermis

Recommended
3 procedures at 10-14 day intervals

Maintenance Treatment
every 3-6 months

Combo DNA F		Combo DNA I
	**PRODUCT**	
face, neck, decollete, hands	**APPLICATION AREA**	periorbital/ perioral wrinkles
PDRN + PN 5mg	**MAIN INGREDIENTS**	PDRN + PN 2mg
niacinamide, glutathione, hyaluronic acid 2%	**ADDITIONAL INGREDIENTS**	sh-Polypeptide-123, sh-Polypeptide-47, succinic acid
2,5 ml 2 syringes	**VOLUME** **UNITS**	1,1 ml 1 syringe

CONTRADICTIONS

- Diabetes
- Epilepsy
- Persons under the age of 18
- Pregnancy and lactation
- Known hypersensitivity or individual intolerance to product components
- Autoimmune diseases
- Oncological diseases (active or recent within 5 years)
- Acute infectious or inflammatory diseases (including colds, flu, herpes)
- Open wounds, ulcers, or damaged skin in the injection area
- Chronic skin diseases in the injection area (eczema, psoriasis, dermatitis)
- Blood clotting disorders or current anticoagulant therapy

WARNING

- Do not use after the expiry date shown on the pack
- Do not use if the package is open or damaged
- Do not mix with other products
- Do not inject into inflamed areas
- Do not reuse to avoid any risk of contamination
- Store at 1°~30°C away from heat sources
- Once opened, the product must be used immediately and discarded after use