



PLURYAL **DENSIFIERS** A COMPLETE REGENERATION FOR YOUR WHOLE BODY

YOUR MOST BEAUTIFUL AGE IS NOW!

YOUR MOST BEAUTIFUL AGE IS NOW!

Pluryal Densifiers $\,3$



2nd Generation Family Business

PLURYAL INJECTABLES

Reviving self-confidence

2 years



70 countries











OUR MISSION: A PRO-AGING LIFE COACH

At Pluryal we believe that "YOUR MOST BEAUTIFUL AGE IS NOW"

We believe in promoting individual standards of beauty that enhance physical appearance while preserving the natural features and identity.

To help your patients feel confident about themselves at any age, we have developed a 360° approach consisting of a wide range of injectables that will help provide your patients with a full holistic treatment approach, scientifically proven to improve the texture, shape and volume of the skin, hair and body.

QUALITY GUARANTEED

Pluryal products are manufactured in line with strict international standards: ISO 13485 and MDD93/42 (for medical devices) and ISO 22716 (for cosmetics). All of our products are subject to strict quality controls, individually inspected, manually and visually assessed, one by one, before their release to the market.

CONTINUOUS INNOVATION

Pluryal is committed to continuous innovation and dedicates a significant percentage of its yearly revenues to R&D. Pluryal releases an innovative concept of "densifiers", a brand-new generation of injectable devices designed to treat skin (face and body), hair and intimate areas.

STUDIES & CLINICAL TRIALS

To ensure the safety and efficacy of all Pluryal products, clinical trials and tests are continuously conducted. Furthermore, our Pluryal Academy is dedicated to regularly train and educate all Pluryal physicians around the Globe on how to apply the precise protocols in order to guarantee the best results for patients.

OUR SCIENCE IS EXCELLENCE



2 RANGES 2 TECHNOLOGIES 4 PRODUCTS

SKIN & HAIR FACE, HAIR & BODY

	DENSIFIER BIO	Pluryal		
	Pluryal Biosculpture Cross-linked hyaluronic acid 2 x 1.1ml	_		
DENSIFIER PN	DENSIFIER PN	Pluryal	DENSIFIER PN	Pluryal
Pluryal Silk Polynucleotide intradermal gel 2ml	Pluryal Densify Polynucleotide and hyaluronic acid intradermal gel 2ml		Pluryal Hair Density Polynucleotide intradermal gel 2ml	

DENSIFIER BIO Technology: MATRICYAL 3D Product: Pluryal Biosculpture

DENSIFIERS PN Technology: HPN Products:

Pluryal Silk Pluryal Densify Pluryal Hair Density

PLURYAL DENSIFIER

BIO MATRICYAL 3D TECHNOLOGY

PLURYAL DENSIERS BIO

MATRICYAL 3D TECHNOLOGY

THE TECHNOLOGY MATRICYAL 3D: A BIO INNOVATION

MATRICYAL 3D technology consists in using a highly purified hyaluronic acid, combining three different types of molecular weight HA in a layered process: Cross-linked HA, concentrated at 25mg/ml in a blend of two types of HA with different molecular weight (1 million Da and 2 million Da) and a layering with free hyaluronic acid of 500K Da to protect the HA from enzymatic degradation. This innovative technology uses a 3D matrix which allows to have the lowest possible level of residual BDDE (< 0.1ppm) thanks to a long reticulation time at low temperature.

Controlled-release 3D matrix

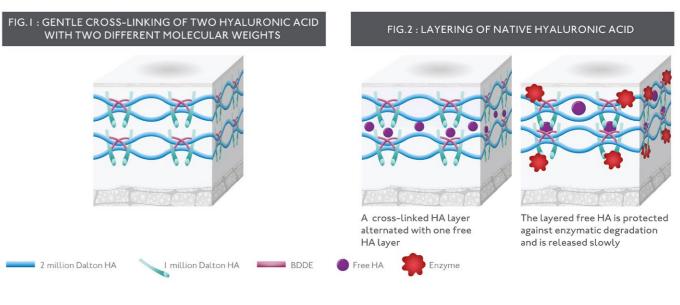


Fig. 1 - Slow crosslinking

Long crosslinking time at low temperature to get a non-calibrated, single-phase gel with optimum viscosity (Fig. 1) 2 types of hyaluronic acid of different molecular weights (one is 1 million Da, the other 2 million Da) are crosslinked with BDDE (Butanediol Diglycidyl Ether) to form a solid 3D matrix.

Fig. 2 – Layering

Only one crosslinked layer alternated with a free hyaluronan layer (of 500,000 Da). When it is layered in the structure, the latter is protected from the hyaluronidase enzymatic degradation. Then hyaluronan is gradually released over time.

TIGHTEN SAGGING SKIN

DENSIFIER BIO

Pluryal Biosculpture Cross-linked hyaluronic acid

2 x 1.1ml

PRODUCTS: PLURYAL BIOSCULPTURE

Pluryal Biosculpture consists of sterile, apyrogenic, physiological and restorable gel implant which acts as a "densifier", improving the quality of the skin of the face and targeting the small losses of volumes and sagging.

Composition Hyaluronic acid 2.5% (25mg/ml) Molecular weight Active matrix (Da) 2 million, 1 million Molecular weight Embedded Free HA (Da) 500,000 Cross-linking ++++ (BDDE \leq 0.1ppm) Endotoxins (EU/ml) < 20 G' factor (mPa) 100,000 Sterilization Steam Extrusion Force (N) 18 \pm 3 N

Indications

Skin destructuration due to age: Bone resorption, burning and modified distribution of fat tissue, structural alteration of the dermal and epidermal configuration, gradual depletion of fluids in junction and extracellular spaces Local hypovolumetries in young patients: 35-40 years old Correction of sagging middle and deep tissue layers, fine lines, wrinkles and scars

Target Areas

Volume loss and flaccidity in the face Face fine line and wrinkles: Nasolabial folds, mouth contour, perizygomatic area Areas requiring tissue filling: cheeks, cheekbones Back of the hands

Target Age Group Starting the age of 35

Injection Technique

Fan pattern, which is similar to the linear retrograde technique. The injection is done at the same angle, but the direction of the needle is modified radially, in several axes, without removing it. This technique is used for large flaws and large volumes (cheeks). Trauma-free, gentle method (5-points injection technique around the malar bone area).

Level of injection Deep dermis

Treatment frequency

Initial Treatment: 2-3 injections at 1-month intervals Maintenance Treatment : 1 injection every 5 to 6 months



1. Nasolabial folds | 2. Mouth Contour | 3. cheeks- cheekbones -Perizygomatic area | 4. Back of the hands

TARGET AREAS WITH PLURYAL DENSIFIER BIO

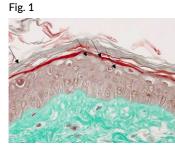
PROVEN EFFICACY

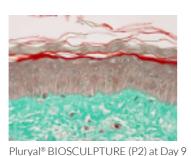
In an ex-vivo study ^[1] conducted by an independent laboratory in France, Pluryal BIOSCULPTURE has proven to:

Improve the epidermal viability without altering dermal viability. It protects and strengthens the epidermis, as well as providing it with higher resistance capacity to offset the slight alterations due to the test (fig.1)

Increase the quantity of hyaluronic acid in the upper papillary and reticular dermis (fig.2)

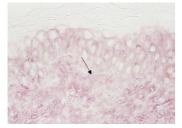
Significantly increase the fibronectin in the upper papillary and reticular dermis (fig.3)



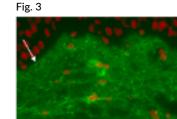


Control on Day 9

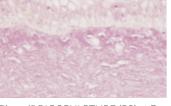
Fig. 2



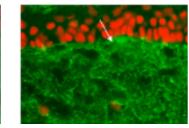
Control on Day 9



Control on Day 9



Pluryal® BIOSCULPTURE (P2) at Day 9



Pluryal® BIOSCULPTURE (P2) at Day 9

Fibronectin is a structural protein found in the extracellular matrix. It is one of the ligands contained in integrins. Fibronectin plays various biological roles in the skin: it represents a growth factor, an adhesion molecule, as well as a chemotactic agent for fibroblasts^[2] and it contributes to collagen fibril deposition and assembly. In addition, it controls the migration of keratinocytes during the healing process^[3].

Fibronectin stimulates fibroblasts and is involved in the collagen network restructuration in the extracellular matrix. Immunolabelling of fibronectin shows that the greener fluorescence there is, the more fibronectin there is.

REVERSE VISIBLE SIGNS OF AGING

Pluryal Biosculpture Cross-linked hyaluronic acid 2 x 1.1ml



PLURYAL DENSIFIERS

PN HPN TECHNOLOGY

PLURYAL DENSIFIERS PN

HPN TECHNOLOGY (HIGHLY PURE POLYNUCLEOTIDES)

HPN TECHNOLOGY: AN EXCLUSIVE PRODUCTION PROCESS OF PHARMACEUTICAL GRADE

Control of every step in the production process, from raw materials to finished product. Pharmaceutical manufacturing standards. PDRN of pharmaceutical grade. High purification of the DNA that guarantees the absence of inflammatory reactions.



POLYNUCLEOTIDES

ABOUT POLYNUCLEOTIDES:

Obtained from the salmon sperm extraction of a fraction of DNA having different chain lengths (molecular weight from 80 to 2,000 K Da) close to the human DNA. Composed of a mixture of deoxyribonucleotide polymers with chain lengths between 50 and 2,000 base pairs. Source of deoxynucleosides, purines and pyrimidines, and deoxyribonucleotides. Purified at high temperature and sterilized.

Non-allergenic and fully absorbable.

No interaction with peptides or pharmacologically active proteins.

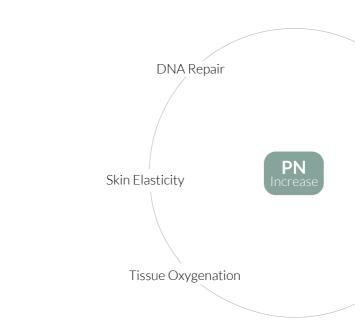
WHAT MAKES THEM UNIQUE?

Compatible, biodegradable and natural polynucleotides are known for their total skin regenerative effect ^[4].



POLYNUCLEOTIDES

A REGENERATIVE ACTION [4,5,6]



EFFECTS



FAST TISSUE REGENERATION [7,8,9,10]

Activating secretion of a number of growth factors such as FGF and EGF to induce differentiation of various blast cells such as fibroblasts, osteoblasts and chondrocytes for fast tissue regeneration.



NEW BLOOD VESSEL GENERATION

Accelerating secretion of Vascular Endothelial Growth Factor (VEGF) for effective generation of new blood vessels. Fibroblasts Growth

Collagen Stimulation

Hydration Levels



ANTI-INFLAMMATORY^[11,12]

Powerful anti-inflammatory effects by reducing various inflammation causing cytokine while increasing anti-inflammatory cytokine.

SCAR REDUCTION [10,13,14,15]

Minimizing scars resulting from the healing process of damaged tissue by keeping extracellular fluid intact through inducing balanced secretion between collagenous and non-collagenous proteins.

Pluryal PN Densifiers (Pluryal Silk, Pluryal Densify and Pluryal Hair Density) are injectable medical devices based on the HPN regenerative technology, which consists in using, as a main component, purified and sterilized polynucleotides extracted from salmon milt.



PRODUCTS: PLURYAL SILK

Composition Polynucleotides 15mg/ syringe (7.5mg/ml) Sterilization Steam Main action Repairs delicate areas

Target patients

Repair of the face and body areas where the skin is thin, delicate and fragile, and which are often overlooked by standard treatments, although they are more exposed and visible Stretch marks Non-homogeneous skin color and malar fat pads Preparation for other aesthetic treatments in order to prolong their effects

Target Areas

Eye contour & upper eyelids Area around the mouth Acne scars Face, neck & décolletage Abdomen (stretch marks) Chest & inner arms

Target Age Group Starting the age of 25

Injection Technique Microdroplet technique or BAP technique (anatomical approach)

Level of injection Deep dermis / mid dermis (around lips and eyes)

Treatment frequency

Young skins Initial treatment: 3 injections with 3-week intervals Maintenance treatment: 1 injection every 2-3 months or 2 treatment cycles per year Aged skins Initial treatment: 4 injections with 2-week intervals Maintenance treatment: 1 injection per month

Treatment protocols by area:

Eye contour, upper eyelids, area around the mouth Initial Treatment: 1 injection per week x 4 sessions Maintenance Treatment: 1 injection per 2-3 months

Face, neck, decolletage, chest and inner arms Initial Treatment: 3 to 5 injections with 2-3 week intervals Maintenance Treatment: 1 injection every 2-3 months

Abdomen (stretch marks) & acne scars

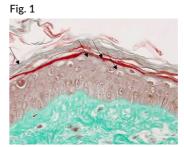
Before EBD** procedure or peeling: 4 injections with 1-week intervals After EBD** procedure or peeling: 3 injections with 1-week intervals *Results can be optimized with one complementary injection of Pluryal[®] Biosculpture. **Energy-Based Devices like laser, RF and "cold plasma".

PROVEN EFFICACY

In an ex-vivo trial conducted by an independent French laboratory, Pluryal SILK has proven to increase the density of the collagen in the dermis^[2].

Cell viability check

(Examination of general cell and tissue morphology after Masson trichrome staining)

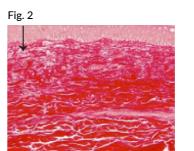


Control on Day 9

Pluryal® SILK improves the viability in the epidermis without changing viability in the dermis. It protects and strengthens the epidermis, giving it increased capacity for resistance, which compensates for small changes due to the test.

Activity in terms of collagen

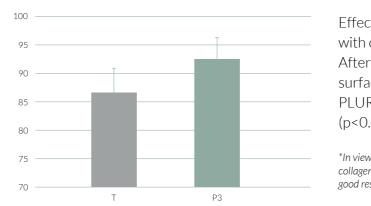
(assessment of total collagen content in the dermis after staining with Sirius red)

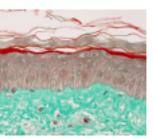


Control on Day 9

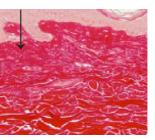
Pluryal[®] Silk Increases the density of the collagen dermis. Pluryal® SILK (P3) induces a significant increase of 7%* of total collagen (p<0.01 or significant at 99%)

PERCENTAGE OF THE SURFACE OCCUPIED BY TOTAL COLLAGENS IN THE DERMIS





Pluryal® SILK (P3) on Day 9



PLURYAL[®] SILK (P3) on day 9 Increase in collagens in the papillary and upper reticular dermis.

- Effect of the product on total collagen content, compared with control batch TJ9:
- After a 9 day survival, in control batch P3J9, 92.7% of the surface of the dermis is occupied by collagens.
- PLURYAL® SILK (P3) induces a significant increase of 7%*. (p<0.01 or significant at 99%)

*In view of the large quantity of collagen in the dermis, the obtained increase in total collagen content usually varies between 5 to 8%. A significant increase of 7% is a very good result for this assessment.

REPAIR DELICATE SKIN AREAS (FACE AND BODY)



DENSIFIER PN

Plurya

Pluryal Silk Polynucleotide intradermal gel 2ml

PRODUCTS: PLURYAL DENSIFY

Composition

Polynucleotides 20mg/ syringe (10mg/ml) Hyaluronic acid 20mg (10mg/ml) of 1 million Da (non-crosslinked): brings an additional hydrating effect. Mannitol 40 mg/ml: prolongs the action of hyaluronic acid by protecting it from degradation. Sterilization Steam Main action Repairs regular areas

Target patients

Whole face rejuvenation (except the under eye area): dull and tired skin, signs of fatigue, lack of radiance and lack of firmness Dehydrated skin Aggressed skin (after an aesthetic procedure) Preparation to other aesthetic treatments: the bio-revitalization phase (one month before the intervention) helps the skin get better prepared for filler injections, laser, peelings, etc.

Target Areas

Whole face (except the under eyes) Back of the hands Neck Décolleté

Target Age Group Starting the age of 30

Injection Technique Microdroplet technique or BAP technique (anatomical approach)

Level of injection Deep dermis

Treatment frequency

Initial treatment: 3 injections at 3-week intervals Maintenance treatment: Young skins: every 3 months Tired skins: 1 injection every other month Recently Aggressed Skins: (post-laser, surgery or fillers), wait 3 weeks before starting the treatment course

PROVEN EFFICACY

Unique composition on the market

PLURYAL DENSIFY

ΡN +

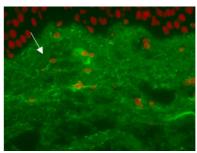
POLYNUCLEOTIDES TROPHIC STIMULUS

FIBROBLAST STIMULATION COLLAGEN INCREASE

> **AESTHETIC IMPROVEMENT** CUSTOMER SATISFACTION

In an ex-vivo study^[1] conducted by an independent laboratory in France, Pluryal DENSIFY has proven to: Significantly increase the suppleness, elasticity and hydration of the skin. Significantly improve the appearance (surface roughness – attenuation of medium wrinkles) of the skin. Increase in fibronectin in the papillary and upper reticular dermis (fig.1)

Fig. 1



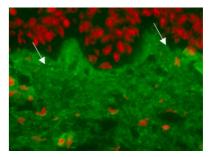
Control on Day 9

ΗA

HYALURONIC ACID ENRICHED WITH MANNITOL SKIN HYDRATION

INCREASED TURGESCENCE ENHANCED FIBROBLAST SYNERGY WITH PNS

RESTORATION OF THE SKIN FUNCTION



Pluryal® DENSIFY (P1) on Day 9 Increase in fibronectin in the papillary and upper reticular dermis.

REGENERATE TIRED SKIN

DENSIFIER PN

Pluryal Densify Polynucleotide and hyaluronic acid intradermal gel 2ml

Pluryal

PROVEN EFFICACY

In a trial comparing 3 formulations, one with pure hyaluronic acid, one with pure polynucleotides and Pluryal Densify^[16], it appears that the stimulating action of the Pluryal Densify on the fibroblasts is significantly higher compared to the other formulations (fig.2)

Synergistic effect of HA + PN association

on human fibroblast cultures

Fig. 2 30 Human fibroblast cultures 25 Plurval® DENSIEY has constantly shown a synergic effect 20 Better result even using a and protein mpared with o percentage of 50% 15 10 % cell growth HA 5 PN Densifier 0 50 110 50 110 Cell growth (fibroblasts) Protein deposition (collagen, elastin..)

PRODUCTS: PLURYAL HAIR DENSITY

Composition Polynucleotides 15mg/ syringe (7.5mg/ml) Sterilization Steam Main action Repairs the hair follicles

Target patients

Weakened hair: fibre thinning Hair loss (baldness): Androgenetic alopecia in women (suspended contraception, pre- or post-partum changes, food deficiency) Androgenetic alopecia in men Pregnancy/birth (local loss) Telogen effluvium (loss following physical or psychic stress) Adjuvant therapy: LED light, PRP (autologous platelet-rich plasma) Adjuvant therapy after hair transplant

Target Areas

Skin of the scalp Eyebrows Beard

Target Age Group Starting the age of 20

Injection Technique Microdroplet technique

Level of injection Deep dermis in the scalp, eyebrows and beard

Treatment frequency

Initial treatment: 1st month: 4 injections at one-week intervals (4 injections) Months 2 and 3: one injection every 2 weeks (4 injections) Next 2 times: one injection every 3 weeks (2 injections) Maintenance treatment: 1 treatment cycle per year is recommended



INCREASE HAIR DENSITY

DENSIFIER PN

Pluryal Hair Density Polynucleotide intradermal gel 2ml







PROVEN EFFICACY

Pluryal HAIR DENSITY Nourishes hair follicles and strengthens the scalp. Increases hair number and diameter.

Polynucleotides stimulate cell growth as well as the metabolism and regeneration of different cell lines. These trophic stimuli in the hair follicles promote hair growth ^[17].

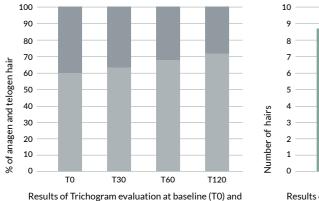
A clinical study conducted by Lotti et al. ^[18,19] confirms that the trophic stimulation performed by polynucleotides in the scalp promoted the growth of hair in cases of female hormonal hair loss. This clinical investigation also confirmed the safety of the medical device and its good tolerability. According to the protocol presented in the study, polynucleotides for scalp injections are an effective, safe, and non-invasive procedure for patients.

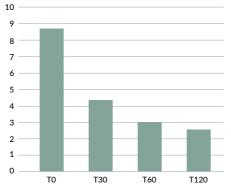
Methods that help highlight the results obtained with PLURYAL® Hair Density:

Trichogramma: normal values restored with a hair increase in the anagen phase (when hair grows) and a decrease in the telogen phase (terminal phase).

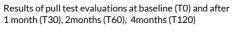
Wash test: reduced hair loss.

Videodermoscopy: (counts the number of hairs on a standard surface): Increased number of hairs. Assessment of the ultrastructure by epiluminescence and size assessment: Increased hair diameter.





after 1 month (T30), 2months (T60), 4months (T120)







1. Eye Contour & upper eyelids | 2. Area around the mouth | 3. Acne Scars | 4. Neck | 5. Décolletage & chest | 6. Inner Arms | 7. Skin of the scalp | 8. Eyebrows | 9. Back of the hands



MAKE THE RIGHT CHOICE

	PLURYAL BIOSCULPTURE	PLURYAL SILK	PLURYAL DENSIFY	PLURYAL HAIR DENSITY	
Composition	25mg/ml cross-linked hyaluronic acid: 2 types of Hyaluronic acid of different molecular weights (one is 1 million Da, the other 2 million Da) are crosslinked with BDDE to form a solid 3D matrix. Only one crosslinked layer alternated with a free hyaluronan layer (of 500,000 Da).	15mg Polynucleotides	20mg Polynucleotides 20mg Hyaluronic Acid 80mg Mannitol	15mg Polynucleotides	
Main action	Restructures & rehydrates	Repairs delicate areas	Repairs regular areas	Redensifies the hair	
Technology	Matricyal 3D	HPN	HPN	HPN	
Syringes	2 x 1.1ml	1 x 2ml	1 x 2ml	1 x 2ml	
CE marking	CE 0373	CE 0373	CE 0373	CE 0373	
Needles / cannulas	2 x 27 G 2 x 30G	2 x 30G ½	2 x 30G ½	2 x 30G ½	
CE marking	CE 0123	CE 0318	CE 0318	CE 0318	

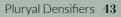
Pluryal Densifiers are class III medical devices which must only be used by doctors who have received specific training on the intradermal injection techniques. Read the instructions before use. Inform the patients about possible side effects.

Sources:

- ¹ Evaluation de l'action de différents produits injectables (Pluryal Densify, Pluryal Biosculpture, Pluryal Silk) à partir d'explants de peau humaine ex vivo», Study 19E4548, conducted by the BIO-EC laboratory. ² Akiyama et al., The journal of Cell Biology. 1989. 109: 863-875; Bitterman et al., 1983. The Journal of Cell Biology. 97: 1925-1932; Postlethwaite et al., 1981 The journal of experimental medicine. 153: 494-499. ^{3.} Larjava et al., 2002. Cell invasion. 3: 42-64.
- ⁴. Polito et al. Polydeoxyribonucleotide restores blood flow in an experimental model of ischemic skin flaps. J Vasc Surg 2012 Feb;55(2):479-88.
- ⁵. Squadrito et al. Pharmacological activity and clinical use of PDRN. Front Pharmacol. 2017 Apr 26:8:224. ⁶. Park et al. Long-chain polynucleotide filler for skin rejuvenation: efficacy and complications in five patients. Dermatologic Ther. Jan-Feb 2016; 29(1):37-40.
- ^{7.} Veronesi et al. Polydeoxyribonucleotides (PDRNs) From Skin to Musculoskeletal Tissue Regeneration via Adenosine A₂₄ Receptor Involvement. J. Cell. Physiol. 232: 2299–2307, 2017.
- ⁸. Thellung et al. Polydeoxyribonucleotides enhance the proliferation of human skin fibroblasts: involvement of a purinergic receptor subtypes. Life Sci. 1999;64(18):1661-64.
- ⁹. Sini et al. Effect of Polydeoxyribonucleotides on Human Fibroblasts in Primary Culture. Cell Biochem. Funct. 17, 107-14 (1999).
- ¹⁰ Muratore, O. et al. A human placental polydeoxyribonucleotide (PDRN) may promote the growth of human corneal fibroblasts and iris pigment epithelial cells in primary culture. New Microbiol 26, 13-26 (2003).
- ¹¹. Bitto et al. Polydeoxyribonucleotide reduces cytokine production and the severity of collagen-induced arthritis by stimulation of adenosine A("A) receptor. Arthritis Rheum. 2011 Nov; 63(11):3364-71.
 - ¹². Bitto et al. Adenosine receptor stimulation by polynucleotides (PDRN) reduces inflammation in experimental periodontitis. J Clin Periodontol 2013; 40: 26-32.
- ¹³ Kim, J. K. & Chung, J. Y. Effectiveness of polydeoxyribonucleotide injection versus normal saline injection for treatment of chronic plantar fasciitis: a prospective randomised clinical trial. Int Orthop 39, 1329-1334, https://doi.org/10.1007/s00264-015-2772-0 (2015).
- ¹⁴ Lazzarotto, M., Tomasello, E. M. & Caporossi, A. Clinical evaluation of corneal epithelialization after photorefractive keratectomy in patients treated with polydeoxyribonucleotide (PDRN) eye drops: a randomized, double-blind, placebo-controlled trial. Eur J Ophthalmol 14, 284-289 (2004).
- ¹⁵ Rubegni, P., De Aloe, G., Mazzatenta, C., Cattarini, L. & Fimiani, M. Clinical evaluation of the trophic effect of polydeoxyribonucleotide (PDRN) in patients undergoing skin explants. A Pilot Study. Curr Med Res Opin 17, 128-131 (2001).
- ^{16.} Kim et al. Comparative evaluation of the effectiveness of novel hyaluronic acid-polynucleotide complex dermal filler. (2020) 10:5127 | https://doi.org/10.1038/s41598-020-61952-w
- ^{17.} Luigi L. Alopecia areata: A combinated subdermal infiltrative therapy. Sci J Clin Res Dermatol. 2015; 1(1):001-003.
- ^{18.} Lee et al. Therapeutic efficacy of autologous platelet-rich plasma and polydeoxyribonucleotide on female pattern hair loss. Original Research-Clinical Science. 18 December 2014.
- ^{19.} Lotti et al. A polynucleotide-based product to treat female hormonal hair loss. Prime Dermatology.

THE 4 R'S OF CONFIDENCE: RESTRUCTURING, REPAIRING, REBUILDING, REDENSIFYING









Pluryal MD Skin Solutions 9AB Boulevard du Prince Henri L-1724 Luxembourg T: +352 26 20 04 06 pluryal.com

Pluryal is aregistered trademark of MD Skin Solutions.