Rose Stem Cell Extracellular Vesicles (RSCE™)

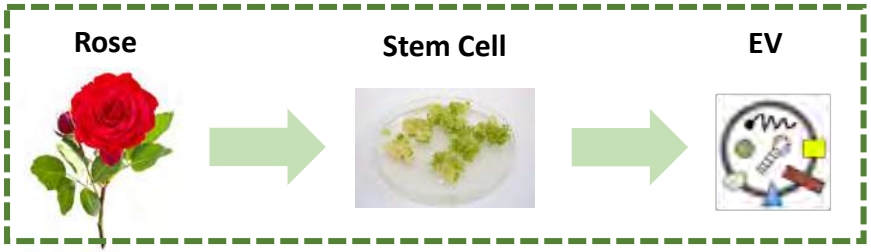
ASCEplus™ SRLV

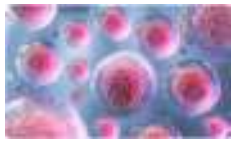
The World's First Exosome-based Regenerative Aesthetics for Skin

Byong Cho, CEO/CTO
ExoCoBio Inc.

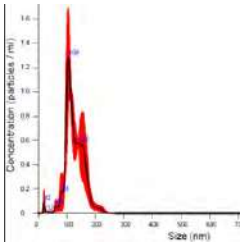
New Exosomes derived from Rose Stem Cells (Callus)

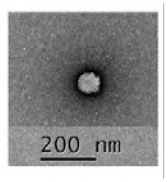
RSCE™ (Rose Stem Cell Exosome)

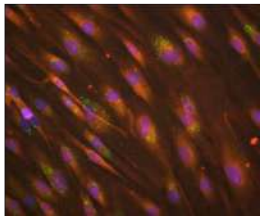


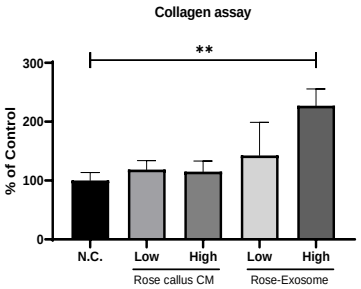


1. Rose stem cells are releasing their EVs or exosomes into conditioned media during callus culture.
2. The size & shape are very similar to human stem cell-derived exosomes.
3. RSCEs are effective in human dermal fibroblasts' proliferation, anti-inflammation, and collagen production (Patented).
4. RSCE can reduce the melanin synthesis of mouse melanoma cell line B16F10 (Patented).
5. Surprisingly, miRNAs of RSCE are mostly de novo sequences. Only 27 miRNAs are matching with human sequences. The top 5 miRNAs are all related to cellular proliferation or housekeeping.
6. Most importantly, RSCE was found to stimulate the EV release of human skin/stem cells (Patent pending).





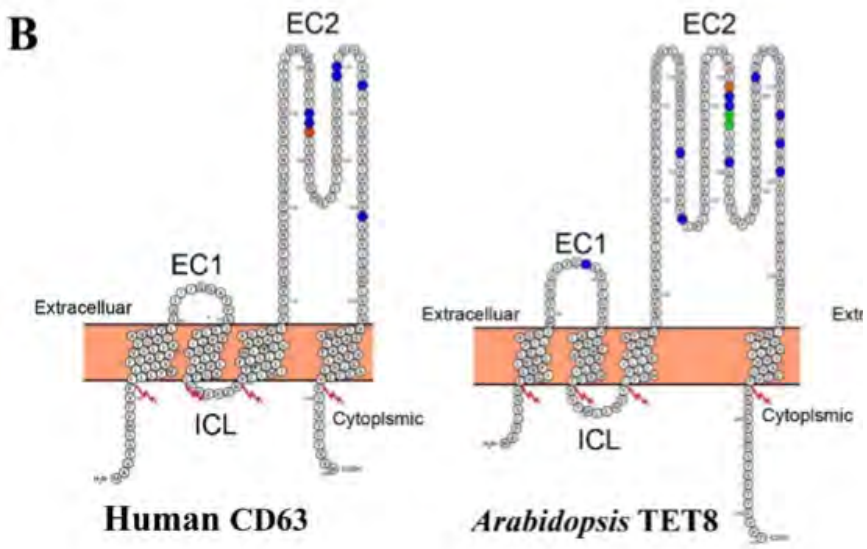




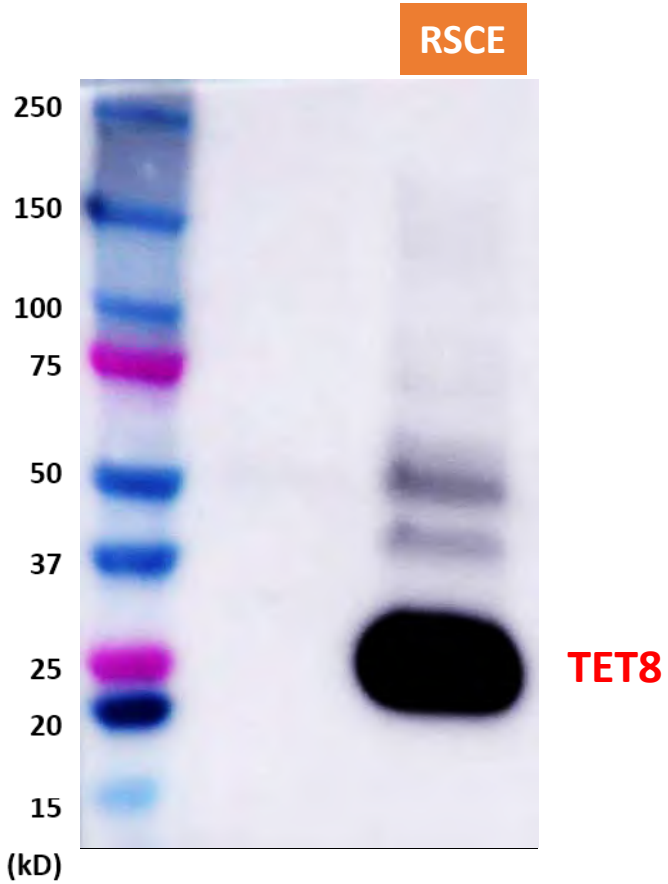
Source: ExoCoBio (To be published)

Plant Exosome Marker

- TET8 is a plant homolog of animal tetraspanin proteins, such as CD9, CD63, and CD81.
- TET8-positive EVs are considered as plant exosomes.



Source: *Plants (Basel). 2023 Dec; 12(24): 4141.*
Front. Plant Sci. 12:757925.



Source: ExoCoBio Inc. (Unpublished data)

The World's First Patent Grant on PSC-Exosome

Europäisches Patentamt
European Patent Office
Office européen des brevets

European Patent Office
80298 MUNICH
GERMANY

European Patent Application No. 19840421.2

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ALLEMAGNE

Title: COSMETIC COMPOSITION COMPRISING ROSE STEM CELL DERIVED- EXOSOME AS EFFECTIVE INGREDIENT
Proprietor: EXOCOBIO INC.

Claims

1. Cosmetic use of a composition comprising exosomes derived from rose stem cells as an active ingredient for skin regeneration, skin elasticity improvement or skin wrinkle reduction.

RSCE™ US Patent (Allowed July 4, 2023)

ExoCoBio
Our Exosomes Your Future

(12) **United States Patent**

(10) **Patent No.: US 11,690,797 B2**

(45) **Date of Patent: Jul. 4, 2023**

(54) **COSMETIC COMPOSITION COMPRISING ROSE STEM CELL-DERIVED EXOSOME AS EFFECTIVE INGREDIENT**

(71) Applicant: **ExoCoBio Inc.**, Seoul (KR)

(72) Inventors: **Yong Weon Yi**, Seoul (KR); **Byong Seung Cho**, Gunpo-si (KR)

(73) Assignee: **ExoCoBio Inc.**, Seoul (KR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 271 days.

(21) Appl. No.: **17/141,693**

(22) Filed: **Jan. 5, 2021**

(65) **Prior Publication Data**

US 2021/0121393 A1 Apr. 29, 2021

A61K 8/14; A61K 8/60; A61K 8/922; A61K 8/99; A61K 36/738; A61K 9/00; A61K 9/0017; A61P 29/00; A61P 17/02

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

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2017/0209365	A1	7/2017	Cho et al.	
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FOREIGN PATENT DOCUMENTS

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(57) **ABSTRACT**

A cosmetic composition containing rose stem cell-derived exosomes as an active ingredient is provided for skin regeneration, skin elasticity improvement or skin wrinkle reduction. The cosmetic composition has excellent effects on skin regeneration, skin elasticity improvement and/or skin wrinkle reduction.

Rose Stem Cell (Callus) – derived Extracellular Vesicles (RSCE)

1. Roses are the most popular plants for human kind and love.
   1) Roses are one of the most beloved cosmetic ingredients.
2. However, so far, there has been little scientific research on plant-derived extracellular vesicles (EV) or exosomes (Exo).
   1) There is one publication on the effect of grape-derived exosomes on inflammatory bowel diseases, which showed the feasibility of clinical applications.
   2) Especially, there is no scientific research on plant stem cell (Callus) – derived EVs or exosomes yet.
3. ExoCoBio has been doing scientific research on RSCE for last 3 years to find out what plant stem cell EVs or exosomes do and how they can be utilized.
   1) Isolation
   2) Characterization
   3) Profiling: Protein/RNA/Lipid
   4) In vitro efficacy & safety studies
   5) Patents
   6) Clinical studies (in the future)

Rose Stem Cell (Callus) – derived Extracellular Vesicles (RSCE)

- RSCEs has the size distribution and shape similar to ASC-exosomes.

Figure 1. Rose-Exosomes NTA results

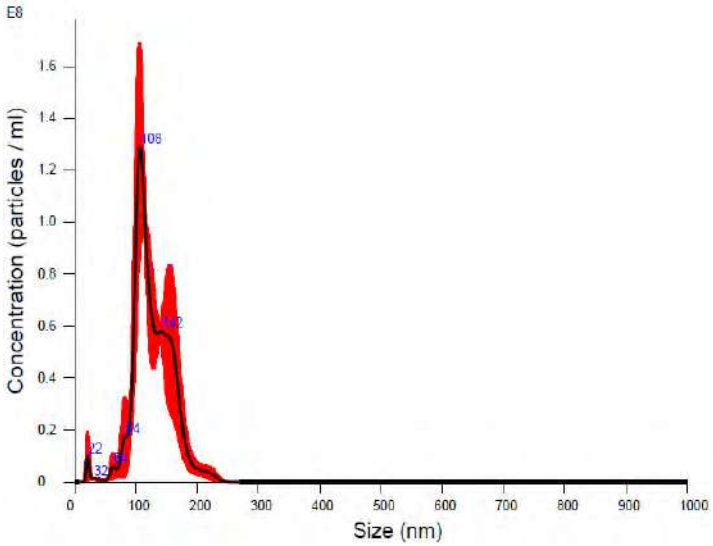
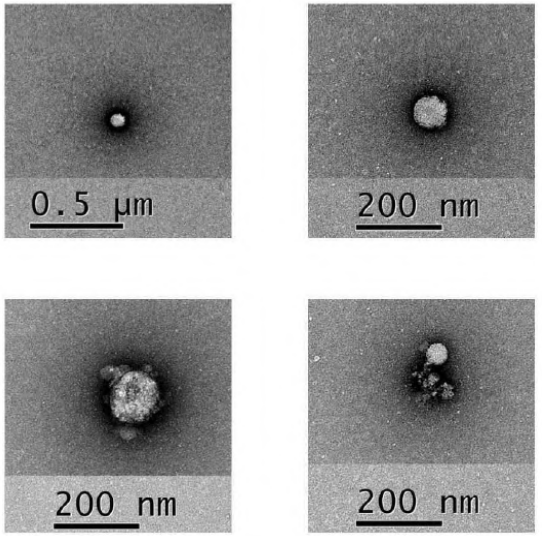


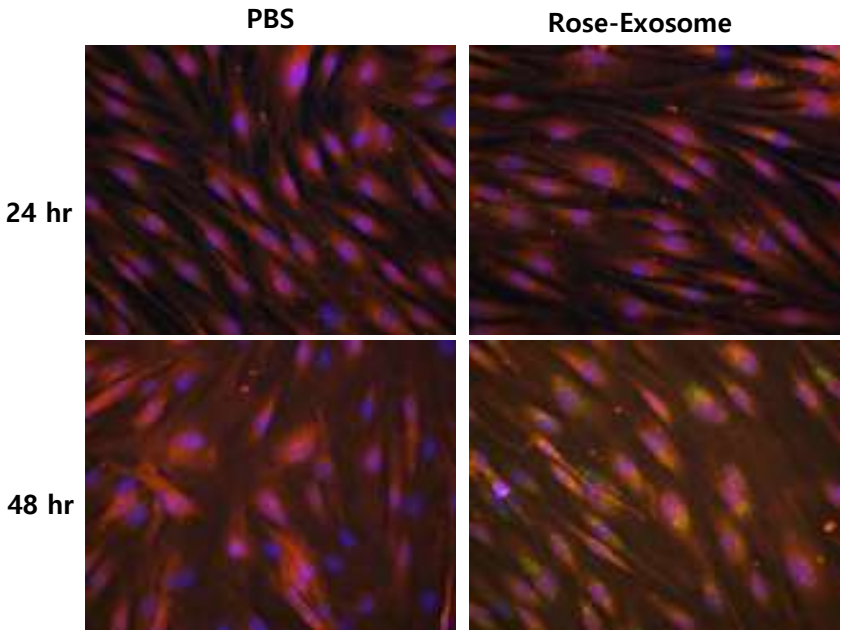
Figure 2. Rose-Exosomes TEM image



Source: ExoCoBio (Unpublished data)

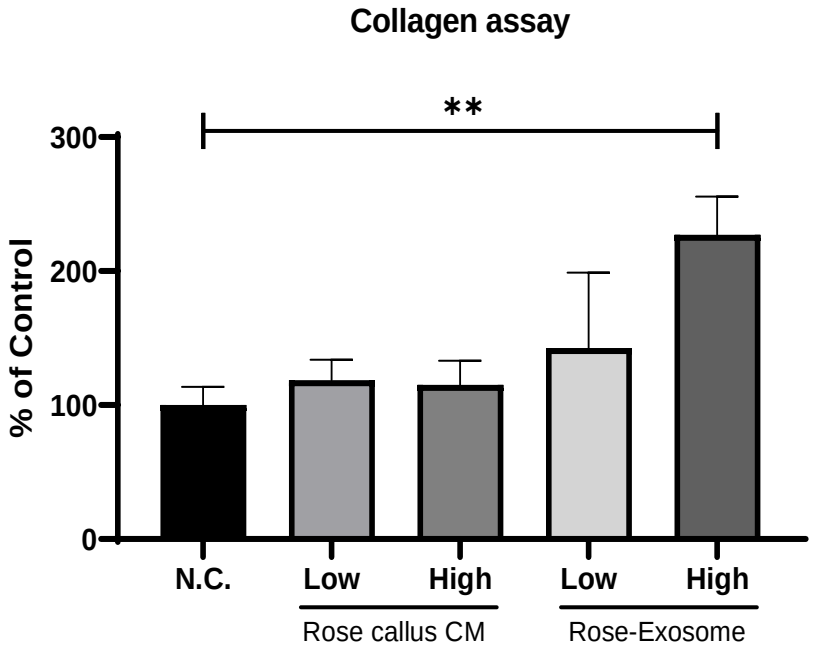
Rose Stem Cell (Callus) – derived Extracellular Vesicles

Figure 3. Cellular uptake of Rose-Exosomes in Human Dermal Fibroblasts (HDF)



Source: ExoCoBio (Unpublished data)

Figure 4. Collagen synthesis of Rose-Exosomes in Human Dermal Fibroblasts (HDF)



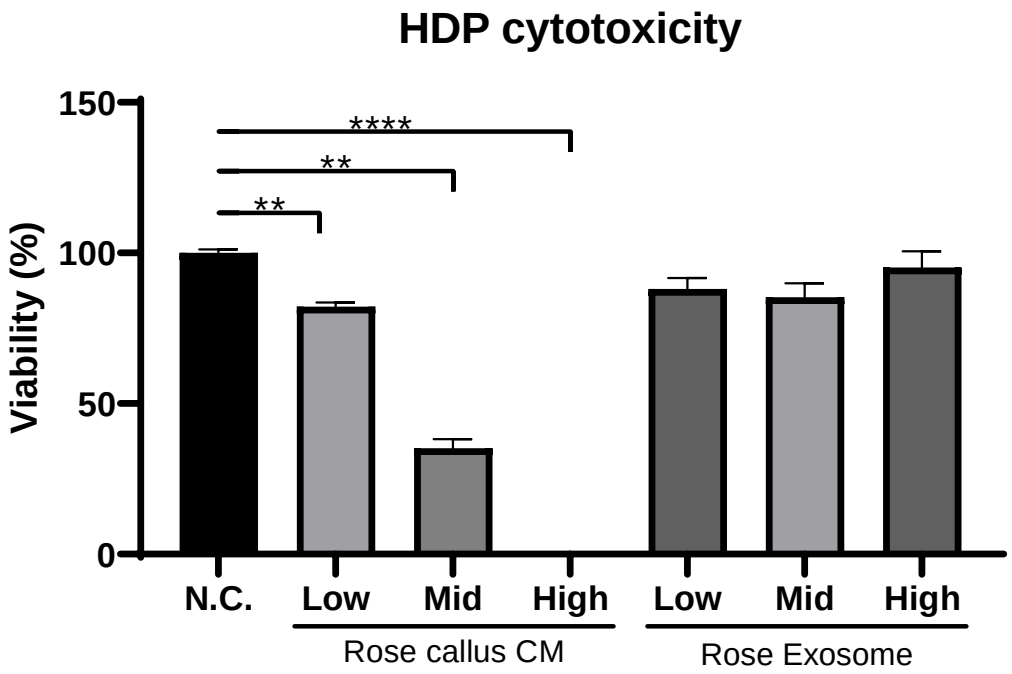
- Low ConC.: 8.0E+08 particles/ml
- High ConC.: 2.5E+09 particles/ml

$p<0.05$ vs N.C
* Procollagen Type I C-peptide

Rose Stem Cell (Callus) – derived Extracellular Vesicles

- RSCEs have lower cytotoxicity than conditioned media.

Figure 5. Cytotoxicity of Rose-Exosomes in Human Dermal Papilla Cells (HDPs)



- Low ConC.: 8.0E+08 particles/ml
- High ConC.: 2.5E+09 particles/ml

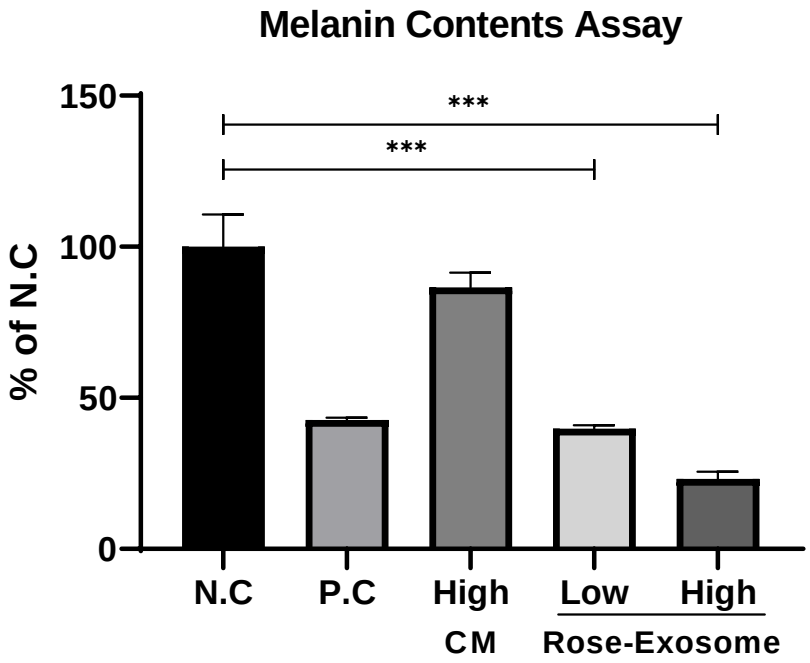
***p<0.01* vs N.C

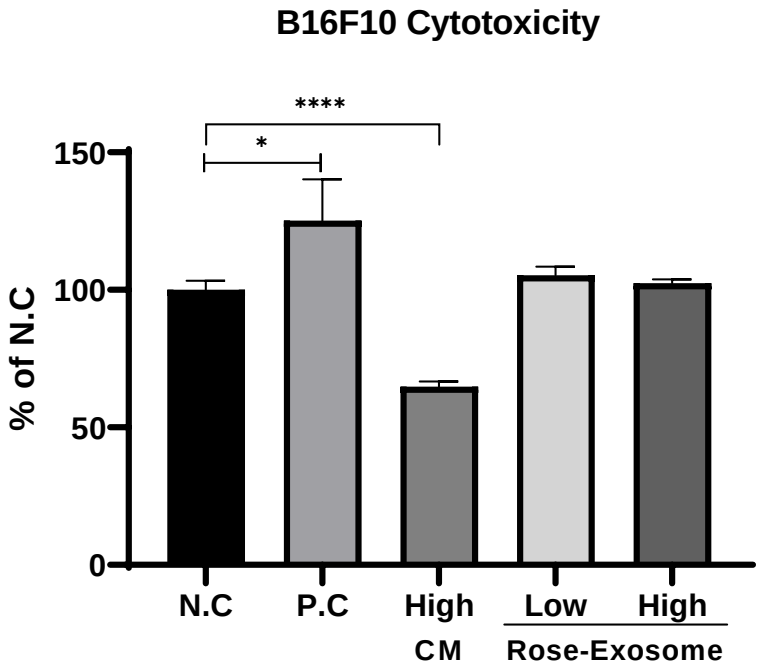
*****p<0.0001* vs N.C

Source: ExoCoBio (Unpublished data)

Rose Stem Cell (Callus) – derived Extracellular Vesicles

Figure 6. Melanin contents and Cytotoxicity of Rose-Exosomes in Mouse melanoma cells(B16F10)





- Low ConC.: 8.0E+08 particles/ml
- High ConC.: 2.5E+09 particles/ml

***;*p<0.001* vs N.C

* Positive Control(P.C): 1mM arbutin

*;*p<0.05* vs N.C

****;*p<0.0001* vs N.C

* Positive Control(P.C): 1mM arbutin

Source: ExoCoBio (Unpublished data)

Rose Stem Cell Extracellular Vesicles (RSCE™)

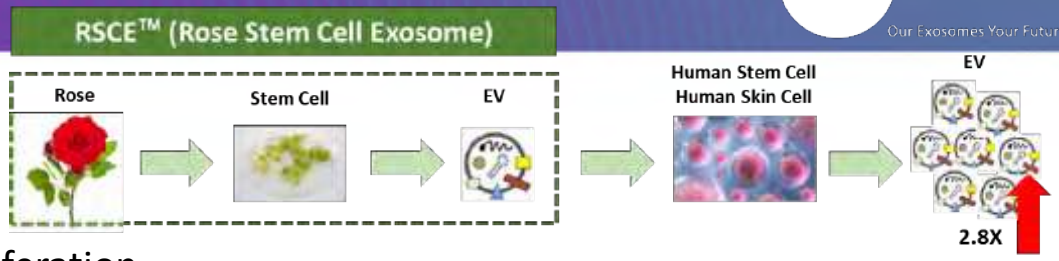
Collagen Synthesis

Byong Cho, CEO/CTO
ExoCoBio Inc.

Executive Summary

- ExoCoBio is the world's first company that developed and commercialized a new patented exosome technology based on rose stem cell-derived exosomes (RSCE™).
- Plant-derived exosomes can increase collagen synthesis, which has been proved by a variety of scientific publications.
- Especially, miR-574 and miR-1246 can promote neo-collagenesis, which are two of the most abundant miRNAs contained in rose stem cell-derived exosomes (RSCE), discovered by ExoCoBio.
- In addition, miR-130 was reported to promote collagen synthesis by another publication.
- There are other miRNAs contained in RSCE as shown below.
  - ✓ miR-let-7: Anti-inflammation and anti-cancer
  - ✓ miR-122: Hair growth
  - ✓ miR-21, 23, 29: Cellular proliferation & anti-scarring
  - ✓ miR-125: Anti-melanogenesis

Rose Stem Cell Exosomes



- Anti-inflammation, Anti-scarring, & cell proliferation

Source: ExoCoBio

[28 types of miRNAs matched with human miRNAs]

No.	Mature ID	No.	Mature ID
1	hsa-let-7a-5p	15	hsa-miR-205-5p
2	**hsa-let-7b-5p**	16	**hsa-miR-21-5p**
3	hsa-let-7c-5p	17	hsa-miR-214-3p
4	hsa-let-7f-5p	18	**hsa-miR-23a-3p**
5	hsa-let-7g-5p	19	hsa-miR-23b-3p
6	hsa-let-7i-5p	20	**hsa-miR-29b-3p**
7	hsa-miR-1-3p	21	hsa-miR-3149
8	hsa-miR-10395-3p	22	hsa-miR-3942-5p
9	**hsa-miR-122-5p**	23	hsa-miR-4488
10	hsa-miR-1246	24	hsa-miR-4508
11	hsa-miR-1290	25	hsa-miR-574-5p
12	**hsa-miR-130a-3p**	26	hsa-miR-7847-3p
13	hsa-miR-184	27	hsa-miR-8485
14	hsa-miR-193b-5p	28	**hsa-miR-125b**

[Top 6 miRNAs & their functions]

No.	Mature ID	Function
1	**hsa-miR-574-5p**	Collagen synthesis, Proliferation, inhibit apoptosis
2	hsa-miR-8485	Wnt/β-catenin signaling Proliferation, migration
[illegible]	**hsa-miR-1246**	Collagen, Anti-photoaging, Proliferation, Modulating T cell balance
4	hsa-miR-1290	Proliferation Metastasis
5	hsa-miR-184	Promote differentiation, Proliferation, Inhibits Apoptosis
6	hsa-let-7c-5p	Anti-tumor function

Cross-kingdom Regulation by Plant-derived miRNAs

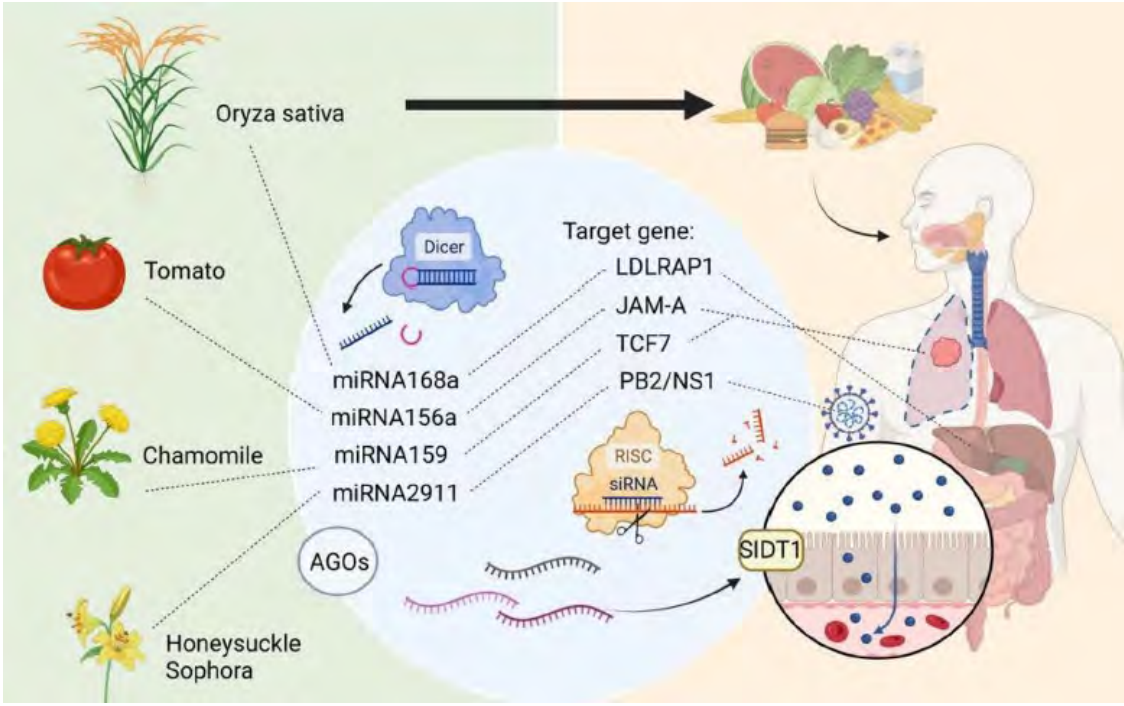
Received: 28 August 2023 | Accepted: 15 October 2023
DOI: 10.1002/ame2.12358

REVIEW

Cross-kingdom regulation by plant-derived miRNAs in mammalian systems

Linpu Yang | Han Feng

- MIR168a is responsible for reducing the levels of LDLRAP1 in both blood and liver, which consequently leads to an elevation in low-density lipoprotein (LDL) levels in the plasma.
- MIR156a targeting JAM-A and MIR159 targeting TCF7 lead to repression of tumor progression.
- MIR2911 targets the influenza viral protein IAV, thereby inhibiting viral replication and preventing infection in human cells.



Serum-derived miR-574-5p-containing exosomes contribute to liver fibrosis by activating hepatic stellate cells

Xia Zhou[1,2] · Ziyu Liang[1] · Shanyu Qin[1] · Xianxian Ruan[1] · Haixing Jiang[1]

Molecular Biology Reports (2022) 49:1945–1954
https://doi.org/10.1007/s11033-021-07008-2

Abstract

Aim To investigate the association of serum exosomes miR-574-5p with liver fibrosis, and explore the effect and mechanism of serum exosomes on HSC activation.

Materials and methods Using serum samples collected from healthy adults and patients with liver cirrhosis, we extracted human serum exosomes via ultra-high-speed centrifugation, and co-cultured them with hepatic stellate cells (HSCs) line LX2. LX-2-mediated intake of human serum exosomes was examined by confocal microscopy. To induce liver fibrosis, we administered 20% CCl_4 to mice intraperitoneally and adopted an exoEasy MIDI kit to extract serum exosomes.Liver fibrosisrelated molecules were determined via qRT-PCR, Western blot, Masson staining, and Immunohistochemical staining.

Results Significantly high miR-574-5p levels were expressed in serum exosomes and were positively correlated with the expression of miR-574-5p, collagen deposition, and α-SMA expression in liver tissues of mice during liver fibrosis. Compared to healthy subjects, serum exosomes from cirrhosis patients were associated with higher expression of miR-574-5p. MiR-574-5p mimic promoted the expression of α-SMA and COL1A1 mRNA and protein in LX-2, whereas miR-574-5p inhibitor exerted no effect.

Conclusion This article demonstrates that miR-574-5p expression in serum exosomes is positively correlated with collagen deposition and HSC activation in liver tissues during liver fibrosis.Serum exosomes potentially activate HSC through the transfer of miR-574-5p to HSC during liver fibrosis.

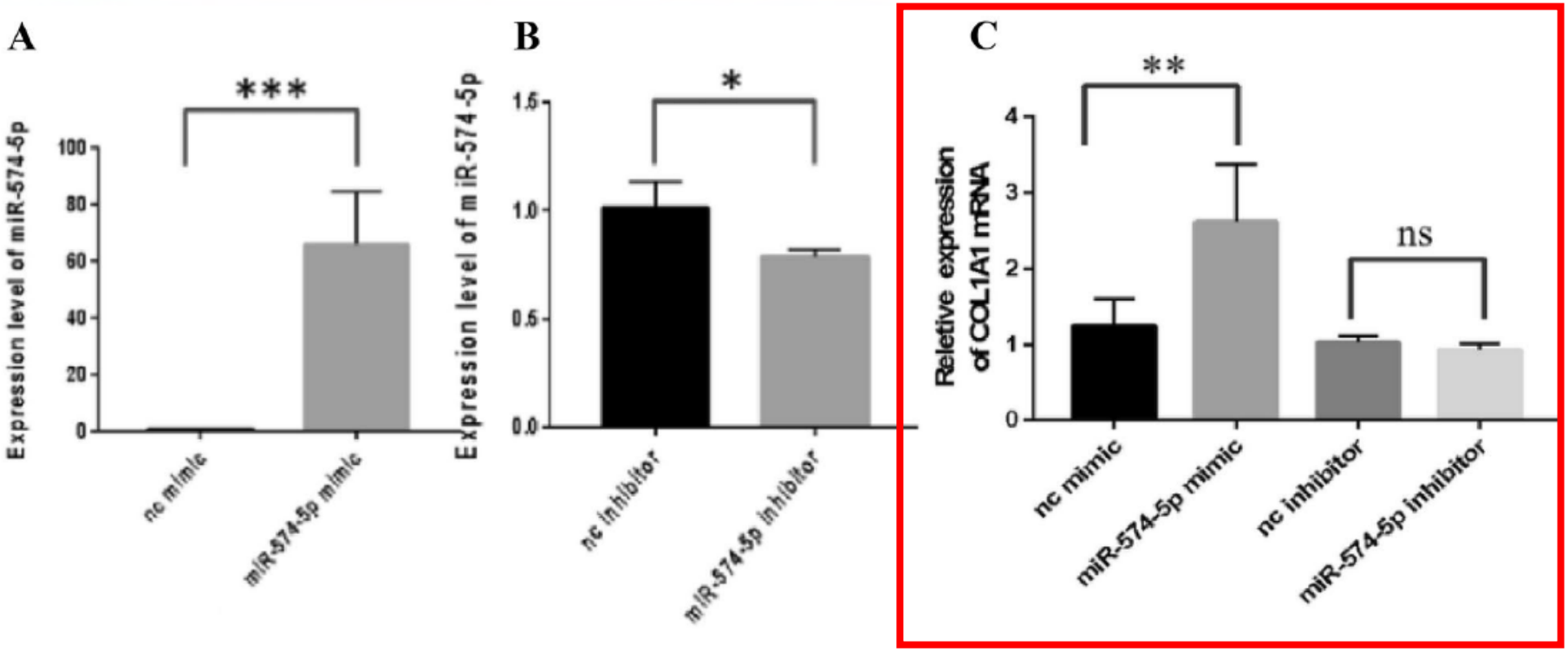


Fig. 4 Effect of miR-574-5p on the expression of COL1A1 and α-SMA in LX-2.Expression of miR-574-5p in LX-2 transfected with **A** miR-574-5p mimic and **B** miR-574-5p inhibitor. **C** Expression of COL1A1 mRNA in LX-2 transfected with miR-574-5p mimic and miR-574-5p inhibitor. **D** Expression of α-SMA mRNA in LX-2 transfected with miR-574-5p mimic and miR-574-5p inhibitor. **E** Expression of COL1A1 and α-SMA protein in LX-2 transfected with miR-574-5p mimic and miR-574-5p inhibitor. **P* < 0.05, ***P* < 0.01, ****P* < 0.001 vs nc group. ns:no signifacance. Data represent means ± SD. (*n* ≥ 3)

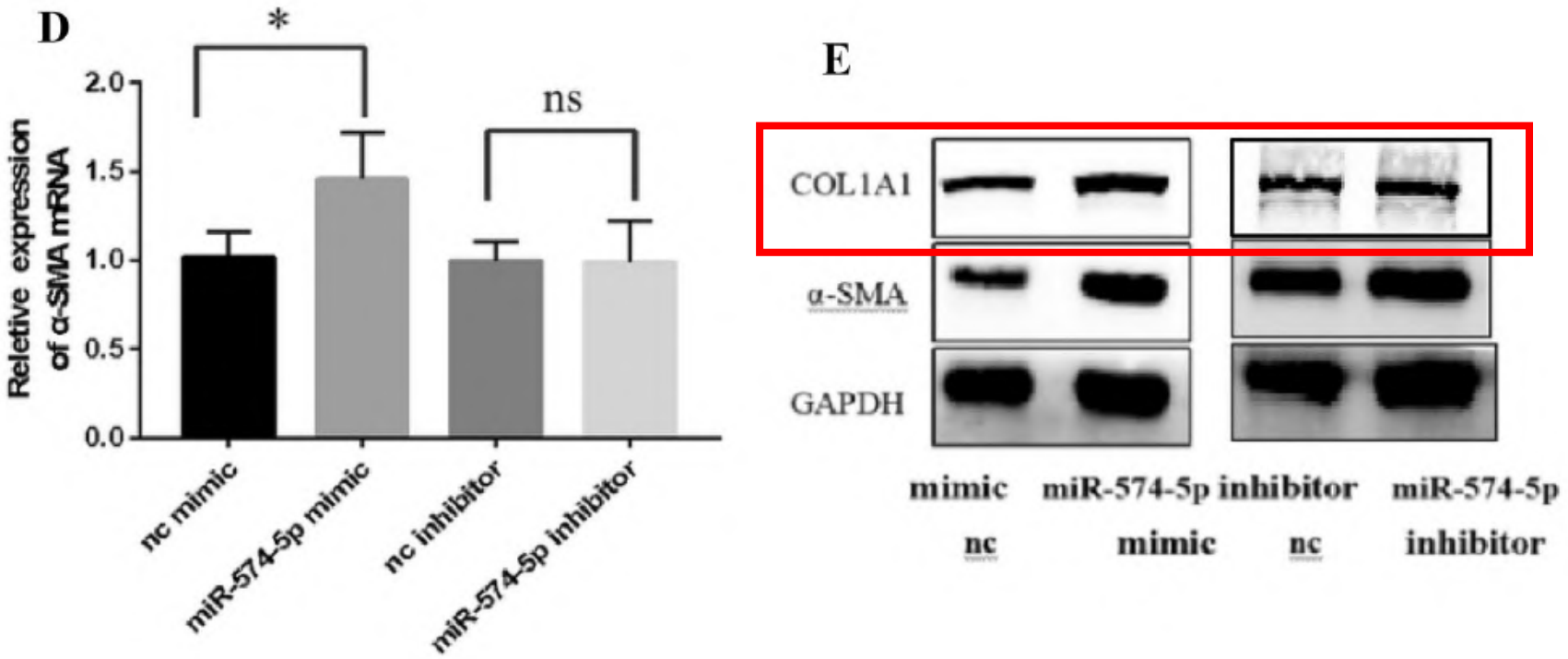


Fig. 4 Effect of miR-574-5p on the expression of COL1A1 and α-SMA in LX-2.Expression of miR-574-5p in LX-2 transfected with **A** miR-574-5p mimic and **B** miR-574-5p inhibitor. **C** Expression of COL1A1 mRNA in LX-2 transfected with miR-574-5p mimic and miR-574-5p inhibitor. **D** Expression of α-SMA mRNA in LX-2 transfected with miR-574-5p mimic and miR-574-5p inhibitor. **E** Expression of COL1A1 and α-SMA protein in LX-2 transfected with miR-574-5p mimic and miR-574-5p inhibitor. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$ vs nc group. ns:no signifacance. Data represent means ± SD. ($n \geq 3$)

Collagen Synthesis Induced by Plant-derived Exosom

Tissue and Cell 76 (2022) 101800

Contents lists available at ScienceDirect

Tissue and Cell

journal homepage: www.elsevier.com/locate/tice

Beta vulgaris juice contains biologically active exosome-like nanoparticles

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Plant-derived exosome-like nanoparticles are an emerging trend in plant biology. For the first time, we have isolated and characterized exosomes from *Beta vulgaris* extract (BEX). The antioxidant capacity, the nitrite, and total phenolic contents of BEX were determined. *In vitro* angiogenesis assay was used to measure the proangiogenic effects of BEX on endothelial cells. Furthermore, we examined the effects of BEX on migration and gene expression profiles of skin-derived fibroblasts. The anti-cancer effects of BEX were also investigated. The results indicated that BEX had antioxidative and scavenging properties. An increase in angiogenic potential was observed in endothelial cells treated with BEX. Furthermore, BEX treatment modulated the potential of fibroblasts to produce collagen 1/3 and hyaluronan synthase enzyme type 2. In addition, BEX treatment inhibited the migration abilities of fibroblasts. Nevertheless, BEX was not found to negatively affect the viability of cancerous cells at the dosage selected. In conclusion, this study identified novel properties of *Beta vulgaris* and its exosomes in the promotion of angiogenesis as well as antiaging and anti-scar capacities of fibroblasts. The findings suggest new cosmetic and therapeutic applications for *Beta vulgaris*.

Collagen Synthesis Induced by Plant-derived Exosom

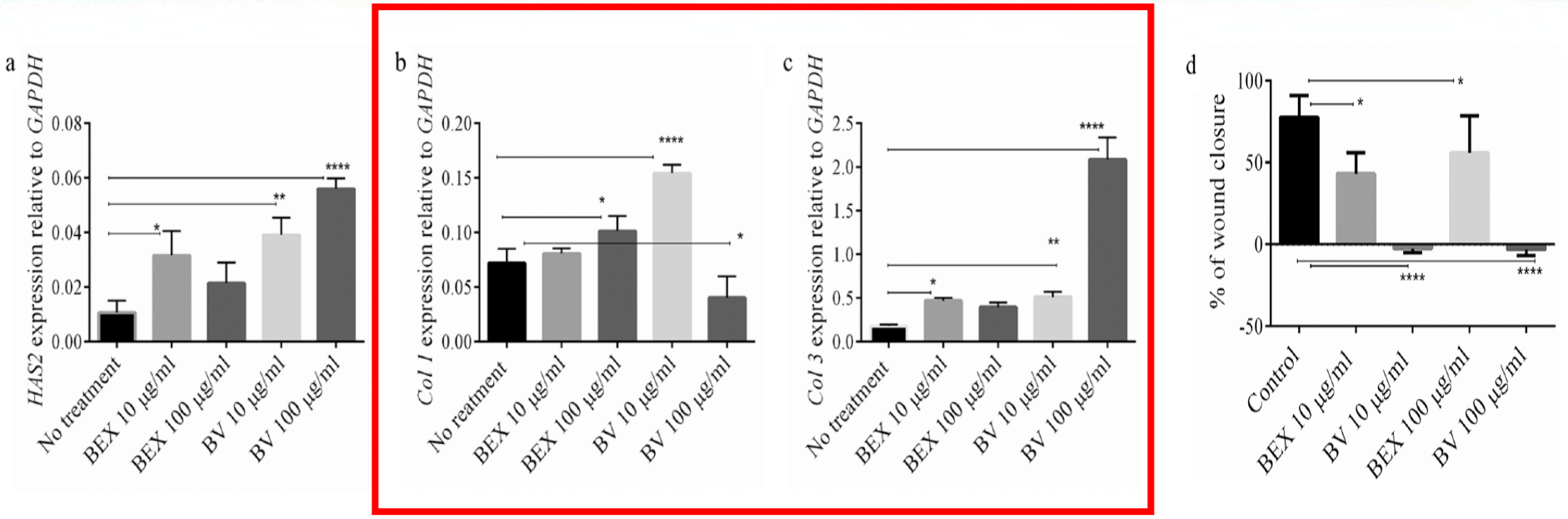


Fig. 6. Gene expression and wound healing assay. Effects of BV or BEX treatments on fibroblasts expression of HAS2 (a) collagen 1 (b) and collagen 3 (c) genes were analyzed using Real-Time PCR. d) the effects of BV or BEX treatments on fibroblasts migration were analyzed using a scratch wound healing assay. Anova one-way and post-hoc Tukey's test using GraphPad Prism 6 software were used for statistical analysis. * $p \leq 0.05$, ** $p \leq 0.01$, **** $p \leq 0.0001$. BEX: *Beta vulgaris*-derived exosome-like nanoparticles, BV: *Beta vulgaris*.

In Vitro Wound Healing Activity of Wheat-Derived Nanovesicles

Fikrettin Şahin[1] · Polen Koçak[1] · Merve Yıldırım Güneş[1] · İrem Özkan[1] · Ezgi Yıldırım[1] · Ezgi Yağmur Kala[1]

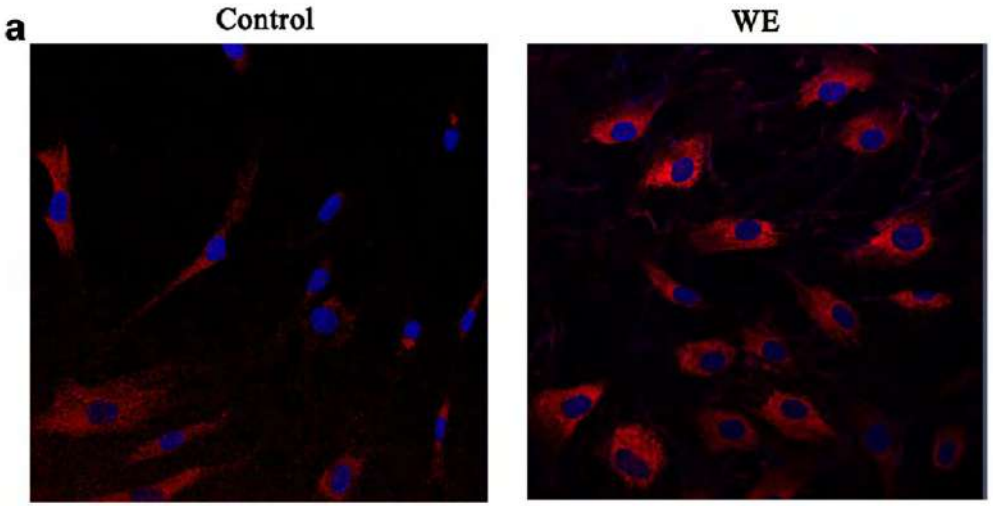
Received: 20 July 2018 / Accepted: 5 November 2018 /
Published online: 26 November 2018

Abstract

Triticum aestivum plant extracts are often used as a natural healer in traditional medicine but which particles mainly have role in these processes are not scientifically proven. In other words, no attempts have been made to investigate the effects of wheat exosomes in regenerative medicine applications or drug development up to now. The current study was first time performed to demonstrate the activity of wheat exosomes in wound healing process using in vitro approaches. Although its fundamental wound healing process remains a mystery, in the current study, the efficiency of wheat grass juice–derived exosomes on cell viability and migration was examined. Increasing concentrations up to 200 µg/mL of the wheat exosome have yielded astonishing proliferative and migratory effects on endothelial, epithelial, and dermal fibroblast cells. RT-PCR analysis also showed collagen type I; mRNA levels were approximately twofold higher in expression after treating with 200 µg/mL wheat exosome.

Additionally, Annexin V staining of apoptotic cells accompanied with the cell cycle analysis resulted with the reduction of the apoptotic cell number with no dispersion to the cell cycle analysis while plant exosomes have also increased tube-like structure formation of the endothelial cells. All in all, this research suggests a brand-new opening for skin wound healing therapy strategy by using wheat-derived exosomes due to its proliferative and migratory characteristics. Plant exosomes require a further research both clinically and in in vivo for wound healing drug development. Moreover, plant exosome therapy strategies would be safer and economical alternative for clinical wound healing.

Collagen Synthesis Induced by Plant-derived Exosom



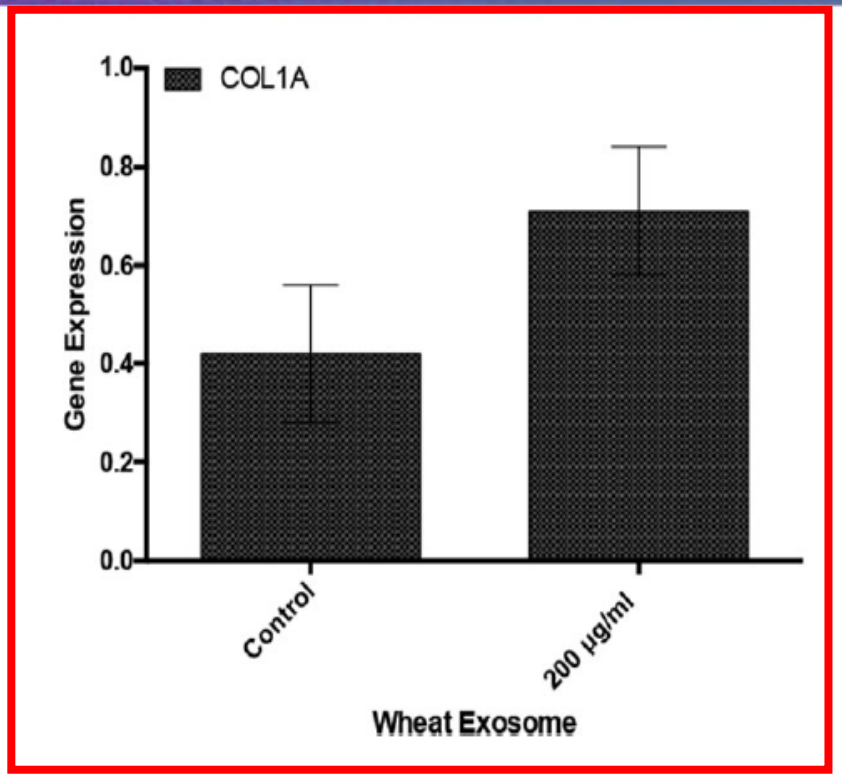


Fig. 5 Confocal scanning microscope (scale bar 100 μm, magnification × 200) image of the immunocytochemistry analysis of human dermal fibroblast (HDF) cells to evaluate collagen type I expression. a Untreated control cells stains relatively weaker than wheat exosome (WE)–treated cells when dyed with antibodies against collagen type I. DAPI (diamidino-2-phenylindole)-stained nuclei appear blue. b mRNA expression levels of COL1A gene in HDF cells. Two hundred micrograms per milliliter wheat exosome–treated group yields nearly twofold higher gene expression levels than untreated control group. Both control group and 200 μg/mL wheat exosome–treated group were incubated (37 °C, 5% CO_2) in DMEM medium supplemented with 10% FBS.

Grapefruit-derived extracellular vesicles as a promising cell-free therapeutic tool for wound healing

Food & Function

ROYAL SOCIETY OF CHEMISTRY

Yağız Savcı, [a] Oğuz Kaan Kırbaş, [a] Batuhan Turhan Bozkurt, [a] Ezgi Avşar Abdik, [a] Pakize Neslihan Taşlı, [a] Fikrettin Şahin [a] and Hüseyin Abdik *[b]

Due to the prevalence of individuals suffering from chronic wounds, developing safe and effective wound care agents are one of the more prominent fields of research in biology. However, wound healing is a complex, multi-stage biological process, involving multiple sequences of biological responses from different types of cells, secreted mediators, and extracellular matrix elements. Plants have a long history of use in the treatment of wounds. Plant-derived extracellular vesicles, which are secreted nano vesicle messengers responsible for intercellular communications, show promise as a new, biotechnological woundcare agent. In this study, we assessed the wound healing potential of extracellular vesicles isolated from grapefruits – a plant with well-known anti-inflammatory and wound healing properties. Grapefruit extracellular vesicles (GEVs) increased cell viability and cell migration while reducing intracellular ROS production in a dose-dependent manner in HaCaT cells. Expression of proliferation and migration-related genes were raised by GEV treatment in a dose dependent manner. Additionally, GEV treatment increased the tube formation capabilities of treated HUVEC cells. These findings suggest that GEVs can be used as plant-derived wound healing agents, and have shown potential as a biotechnological agent for wound healing. Further development and study of plant-derived extracellular vesicles may lead to the realization of their full potential.

Collagen Synthesis Induced by Plant-derived Exosom

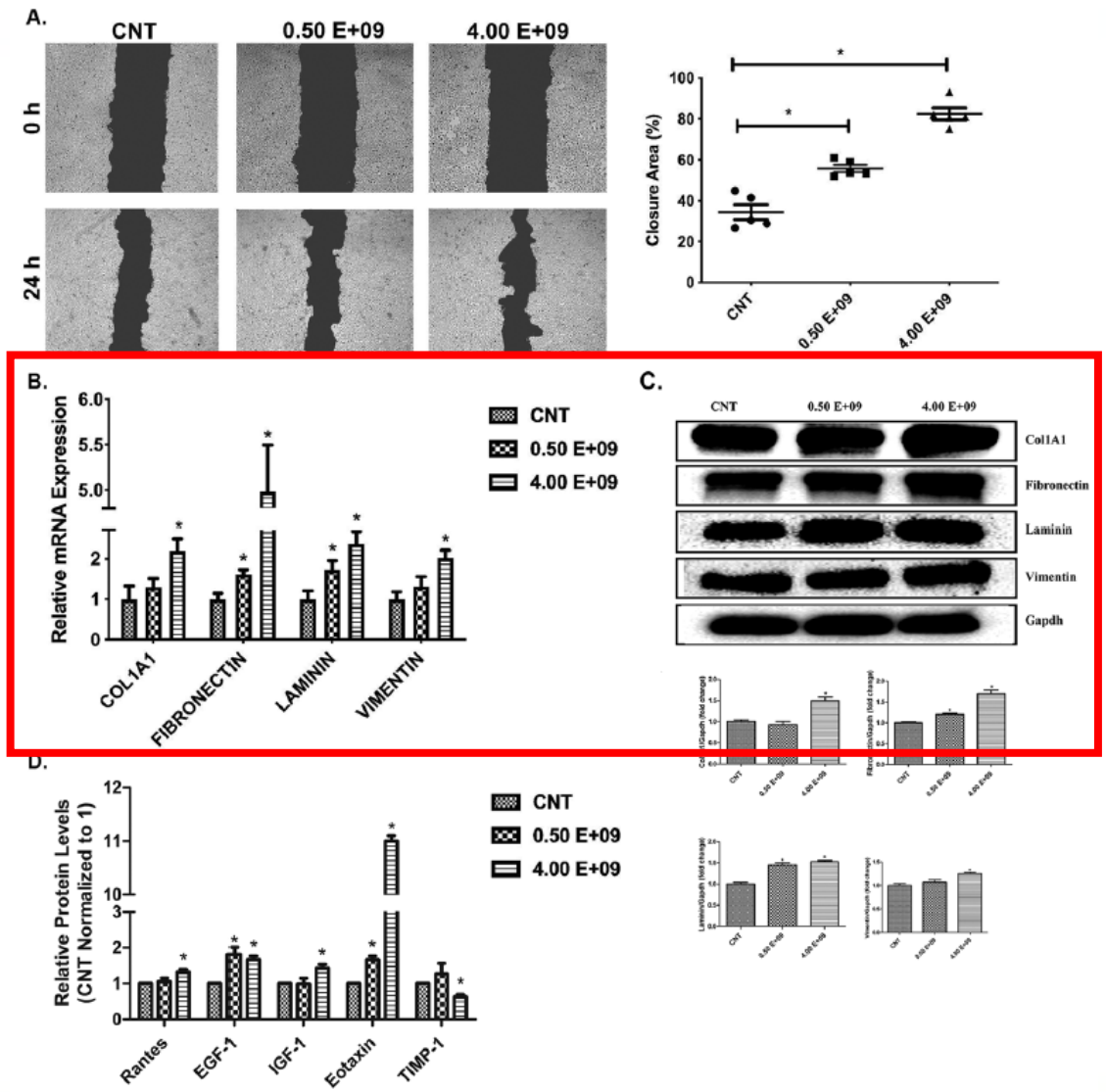


Fig. 3 A. Effect of 4.00 × 109 and 0.50 × 109 particles per mL GEV particle concentrations on the scratch closure of HaCaT cells after 24 hour treatment.

B. The effect of 4.00 × 10^9 and 0.50 × 10^9 particles per mL GEV on the gene expression level of wound healing-related genes (Collagen type I, fibronectin, laminin, and vimentin) in HaCaT cell line after 24 hour treatment.

C. The effect of 4.00 × 10^9 and 0.50 × 10^9 particles per mL GEVs on the expression level of wound healing-related proteins (Collagen type I, fibronectin, laminin, and vimentin) in HaCaT cell line after 24 hour treatment by western blot analysis.

D. The effect of 4.00 × 10^9 and 0.50 × 10^9 particles per mL GEVs on the levels of the cytokines related to migration in the HaCaT cell line after 24 hour treatment. The data were mean ± SD values of three independent experiments conducted in triplicate, n = 3. (CNT: non-treated control group, *p < 0.05).

Collagen Synthesis Induced by Plant-derived Exoson

marine drugs

Mar. Drugs **2024**, 22, 223. https://doi.org/10.3390/md22050223

MDPI

Article

Extracellular Vesicles from *Ecklonia cava* and Phlorotannin Promote Rejuvenation in Aged Skin

Sosorburam Batsukh [1,2], Seyeon Oh [2], Ji Min Lee [3], Judy Hong Jin Joo [4], Kuk Hui Son [5,*] and Kyunghee Byun [1,2,6,*]

Abstract: Plant-derived extracellular vesicles (EVs) elicit diverse biological effects, including promoting skin health. EVs isolated from Ecklonia cava (EV-EC) carry heat shock protein 70 (HSP70), which inhibits key regulators such as TNF-α, MAPKs, and NF-κB, consequently downregulating matrix metalloproteinases (MMPs). Aging exacerbates oxidative stress, upregulating MAPK and NF-κB signaling and worsening extracellular matrix degradation in the skin. E. cava-derived phlorotannin (PT) mitigates MAPK and NF-κB signaling. We evaluated the impact of EV-EC and PT on skin rejuvenation using an in vitro keratinocyte senescence model and an in vivo aged-mouse model. Western blotting confirmed the presence of HSP70 in EV-EC. Treatment with EV-EC and PT in senescent keratinocytes increased HSP70 expression and decreased the expression of TNF-α, MAPK, NF-κB, activator protein-1 (AP-1), and MMPs. Oxidative stress was also reduced. Sequential treatment with PT and EV-EC (PT/EV-EC) yielded more significant results compared to individual treatments. The administration of PT/EV-EC to the back skin of aged mice mirrored the in vitro findings, resulting in increased collagen fiber accumulation and improved elasticity in the aged skin. Therefore, PT/EVEC holds promise in promoting skin rejuvenation by increasing HSP70 expression, decreasing the expression of MMPs, and reducing oxidative stress in aged skin.

Collagen Synthesis Induced by Plant-derived Exosom

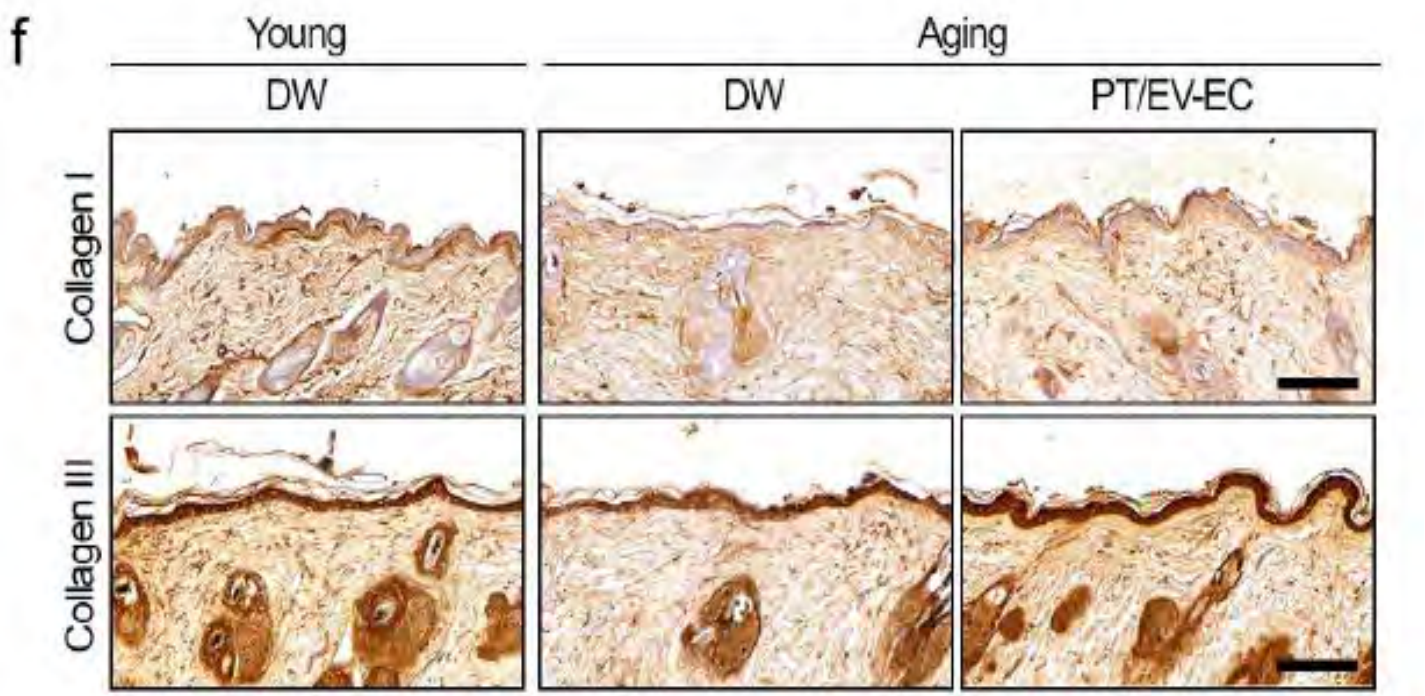


Figure 5. PT/EV-EC treatment reduced ROS levels and increased TGF-β1, TGF-β2, TGF-β3, and collagen I and III expression in the skin of aged mice. (**a**) Western blot analysis of NOX1, NOX2, NOX4, and β-actin in the skin of young and aged mice. (**b**–**e**) ELISA assessment of 8-OHdG, TGF-β1, TGF-β2, and TGF-β3 in the skin of young and aged mice. (**f**) IHC staining of collagen I (upper) and III (lower) in the dermis of young and aged mice (IHC signal: brown, nuclei: blue; scale bar = 100 μm). Quantitative data from (**a**,**f**) are presented in Figure S19. Data represent the mean ± SD of three independent experiments. ***, $p < 0.001$, first bar vs. second bar; $$, $p < 0.01$, second bar vs. third bar (Mann–Whitney U test).

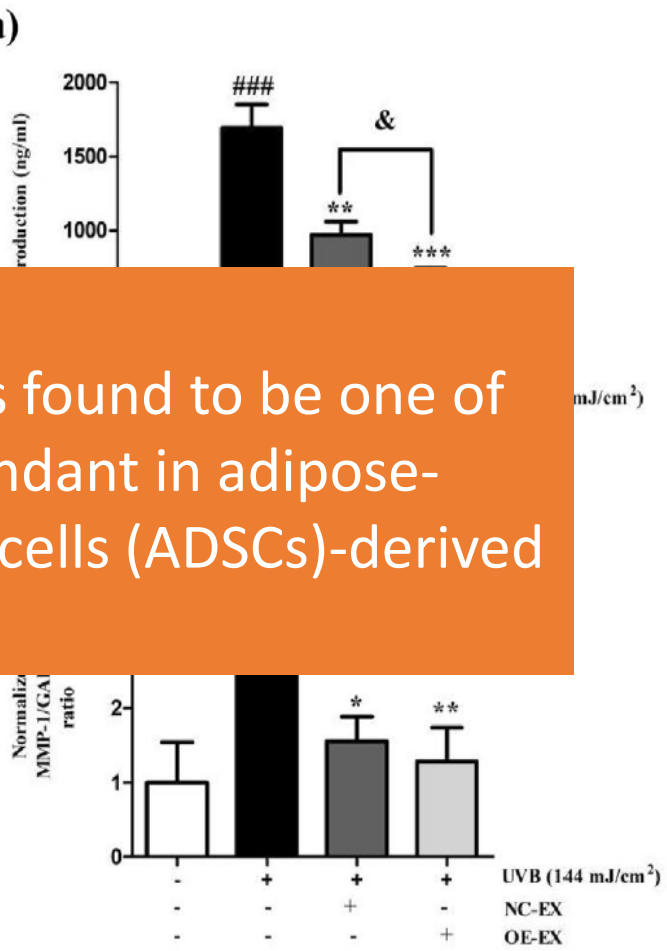
Anti-Photoaging & Collagen Synthesis Induced by miR-1246

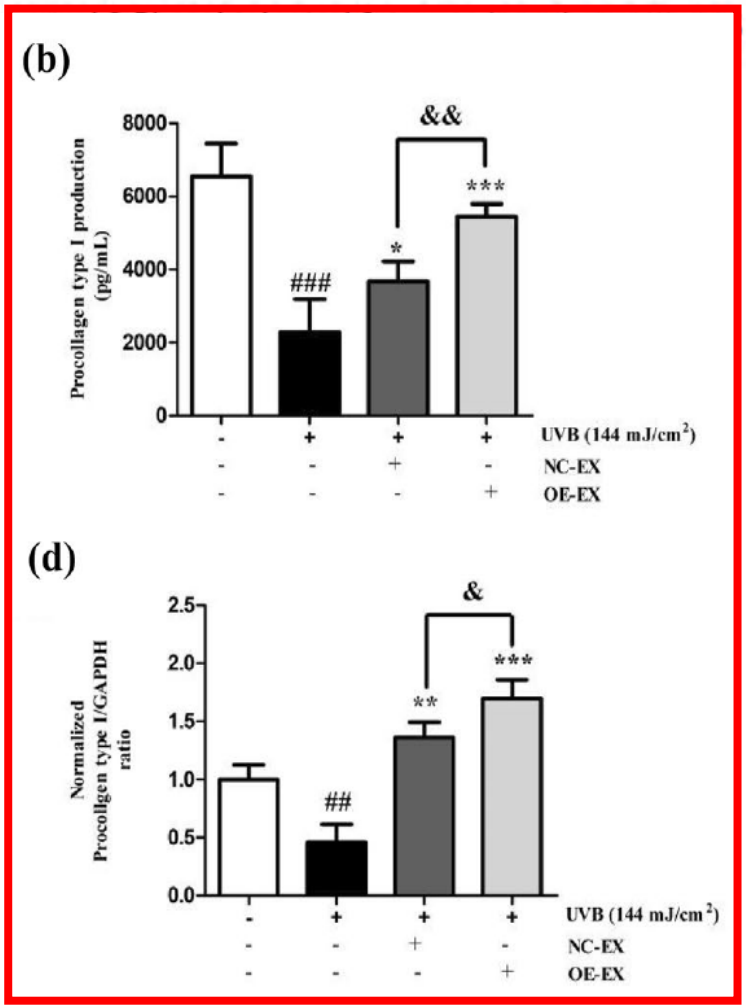
miR-1246-overexpressing exosomes suppress UVB-induced photoaging via regulation of TGF-β/Smad and attenuation of MAPK/AP-1 pathway

Wei Gao[1] · Li-min Yuan[1] · Yue Zhang[1] · F
Yu-shuai Wang[1]

Abstract

miR-1246 was found to be one of the most abundant in adipose-derived stem cells (ADSCs)-derived exosomes.





Anti-Photoaging & Collagen Synthesis Induced by miR-1246

miR-1246-overexpressing exosomes suppress UVB-induced photoaging via regulation of TGF-β/Smad and attenuation of MAPK/AP-1 pathway

Wei Gao[1] · Li-min Yuan[1] · Yue Zhang[1] · Fang-zhou Huang[1] · Fei Gao[1] · Jian Li[1] · Feng Xu[1] · Hui Wang[1] · Yu-shuai Wang[1]

Photochemical & Photobiological Sciences (2023) 22:135–146
https://doi.org/10.1007/s43630-022-00304-1

Abstract

Stem cell therapy is widely employed for the treatment of skin diseases, especially in skin rejuvenation. Exosomes derived from stem cells have been demonstrated to possess anti-photoaging effects; however, the precise components within exosomes that are responsible for this effect remain unknown. Previously, miR-1246 was found to be one of the most abundant nucleic acids in adipose-derived stem cells (ADSCs)-derived exosomes. This study examined whether miR-1246 was the major therapeutic agent employed by ADSCs to protect against UVB-induced photoaging. Lentivirus infection was used to obtain miR-1246-overexpressing ADSCs and exosomes. We then determined the anti-photoaging effects of miR-1246-overexpressing exosomes (OE-EX) on both UVB-irradiated human skin fibroblasts (HSFs) and Kunming mice. The results showed that OE-EX could significantly decrease MMP-1 by inhibiting the MAPK/AP-1 signaling pathway. Meanwhile, OE-EX markedly increased procollagen type I secretion by activating the TGF-β/Smad pathway. OE-EX also exhibited an anti-inflammatory effect by preventing the UVB-induced degradation of IκB-α and NF-κB overexpression. Animal experiments demonstrated that OE-EX could reduce UVB-induced wrinkle formation, epidermis thickening, and the loss of collagen fibers reduction in Kunming mice. The combined results suggested that miR-1246 is the key component within ADSCs-derived exosomes that protects against UVB-induced skin photoaging.

Anti-Photoaging & Collagen Synthesis Induced by miR-1246

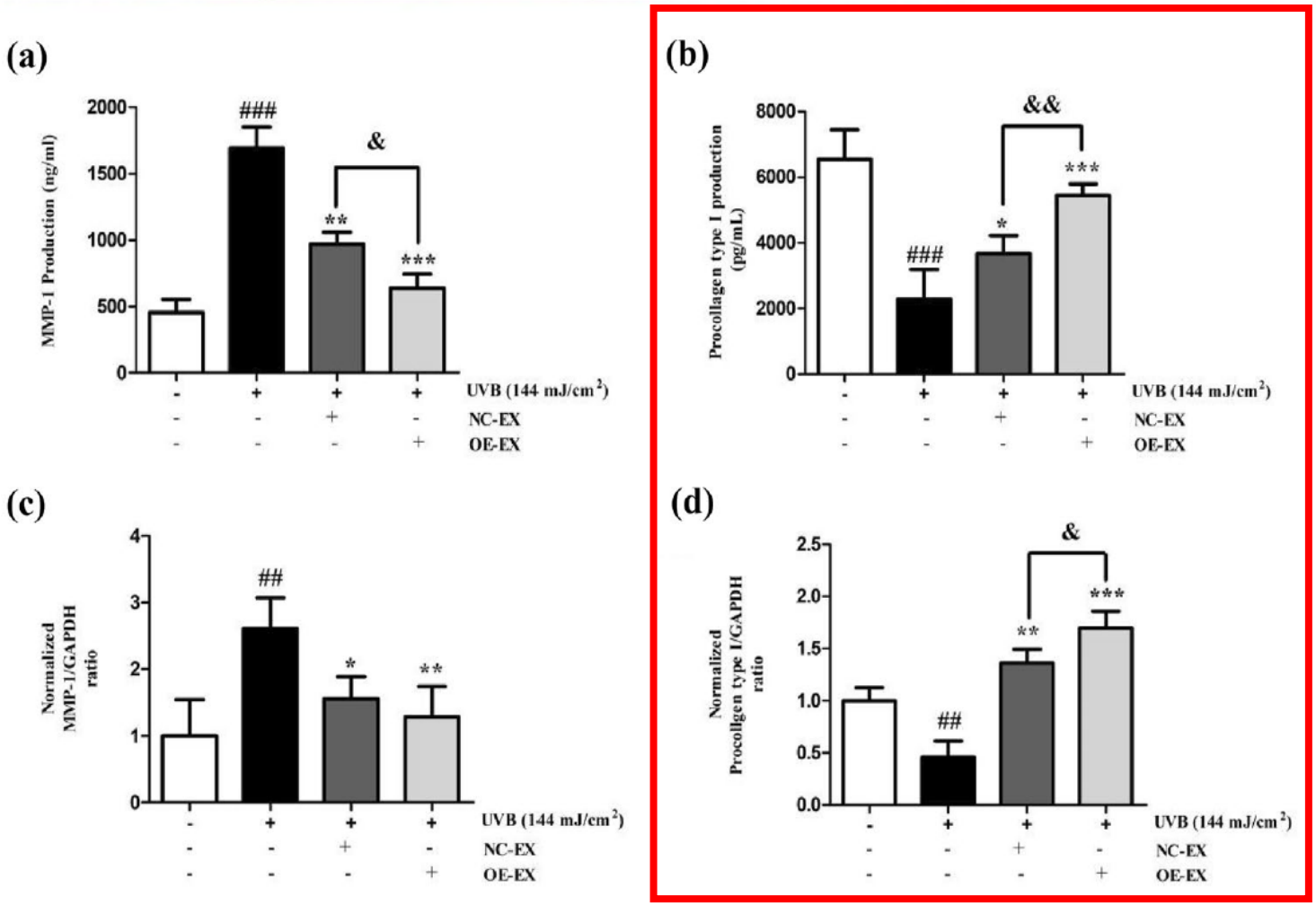


Fig. 5 Effects of NC-EX and OE-EX on MMP-1 and procollagen type I expression. The HSFs cells were treated by 144 mJ/cm2 UVB radiation and then incubated with NC-EX and OE-EX. **a** MMP-1 production, **b** procollagen type I production, **c** MMP-1 mRNA, **d** procollagen type I mRNA.

miRNA-122-5p (ASC-Exo) mitigated the inhibitory effect of DHT on DPCs.

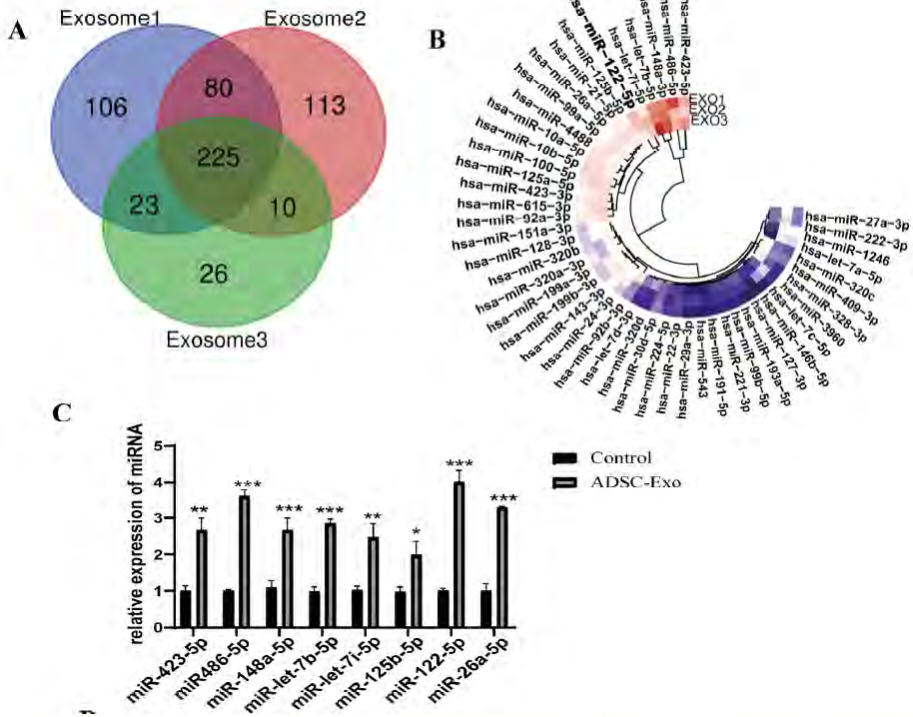
International Journal of *Molecular Sciences*

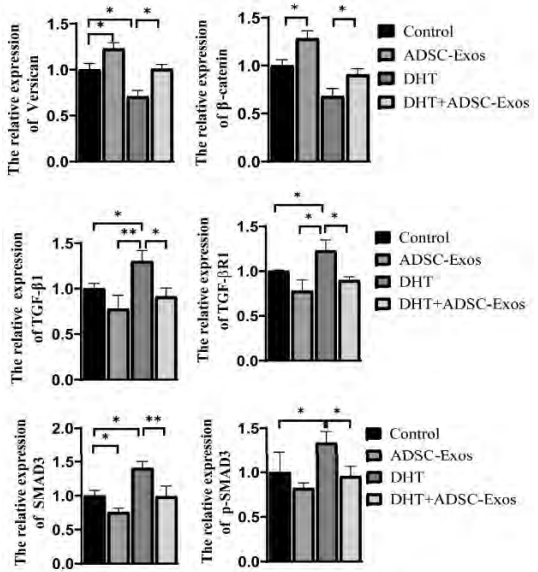
MDPI

Article

Adipose Mesenchymal Stromal Cell-Derived Exosomes Carrying MiR-122-5p Antagonize the Inhibitory Effect of Dihydrotestosterone on Hair Follicles by Targeting the TGF-β1/SMAD3 Signaling Pathway

Yunxiao Liang [1,†], Xin Tang [1,†], Xue Zhang [2], Cuixiang Cao [1], Miao Yu [1] and Miaojian Wan [1,*]





miRNA-let-7b for Hair

MOLECULAR MEDICINE REPORTS 17: 4688-4694, 2018

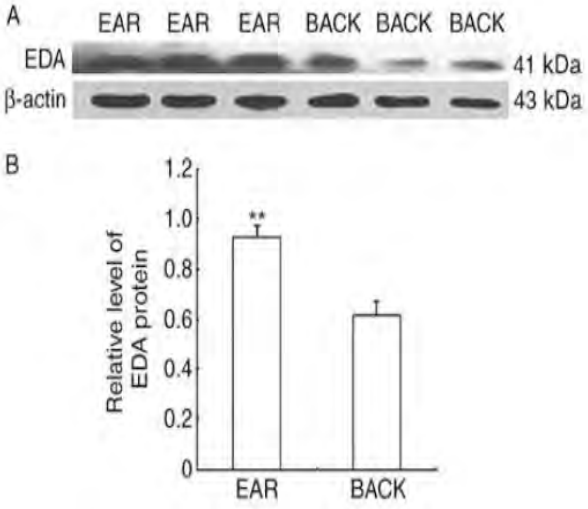
Let-7b regulates alpaca hair growth by downregulating ectodysplasin A

NING LIU, SHU NIU, XIAO-RUI CAO, JIA-QI CHENG, SHU-YUAN GAO, XIU-JU YU, HAI-DONG WANG, CHANG-SHENG DONG and XIAO-YAN HE

Alpaca Bioengineering Laboratory, College of Animal Science and Veterinary Medicine, Shanxi Agricultural University, Taigu, Shanxi 030801, P.R. China

Received September 11, 2016; Accepted August 24, 2017

miR-let-7b → Long hairs



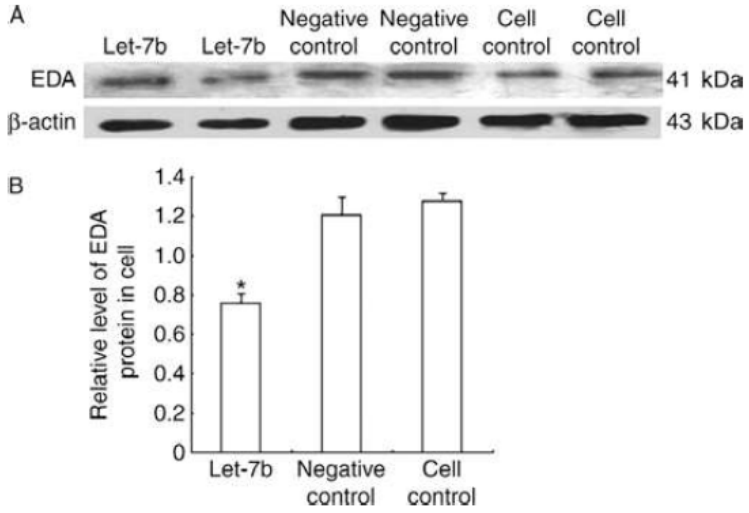
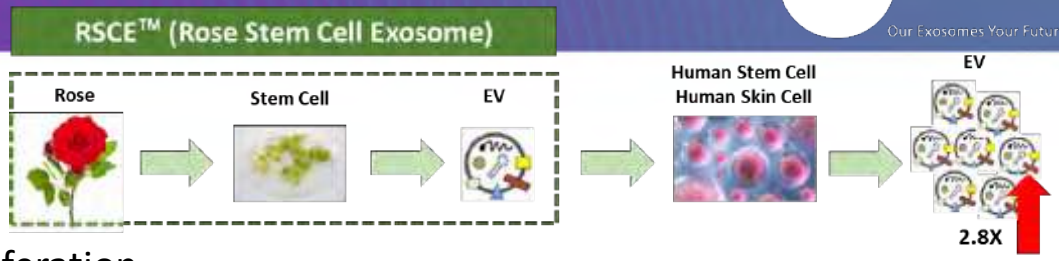


Figure 6. Western blot analysis of the relative protein expression levels of EDA in different groups. (A) Representative western blot analysis demonstrating the different band intensities of EDA protein expression from the two tissues. (B) Data analysis of EDA levels normalized to β-actin; data are presented as the mean ± standard deviation; *P<0.05. EDA, ectodysplasin A.

Rose Stem Cell Exosomes



- Anti-inflammation, Anti-scarring, & cell proliferation

Source: ExoCoBio

[28 types of miRNAs matched with human miRNAs]

No.	Mature ID	No.	Mature ID
1	hsa-let-7a-5p	15	hsa-miR-205-5p
2	**hsa-let-7b-5p**	16	**hsa-miR-21-5p**
3	hsa-let-7c-5p	17	hsa-miR-214-3p
4	hsa-let-7f-5p	18	**hsa-miR-23a-3p**
5	hsa-let-7g-5p	19	hsa-miR-23b-3p
6	hsa-let-7i-5p	20	**hsa-miR-29b-3p**
7	hsa-miR-1-3p	21	hsa-miR-3149
8	hsa-miR-10395-3p	22	hsa-miR-3942-5p
9	**hsa-miR-122-5p**	23	hsa-miR-4488
10	hsa-miR-1246	24	hsa-miR-4508
11	hsa-miR-1290	25	hsa-miR-574-5p
12	**hsa-miR-130a-3p**	26	hsa-miR-7847-3p
13	hsa-miR-184	27	hsa-miR-8485
14	hsa-miR-193b-5p	28	**hsa-miR-125b**

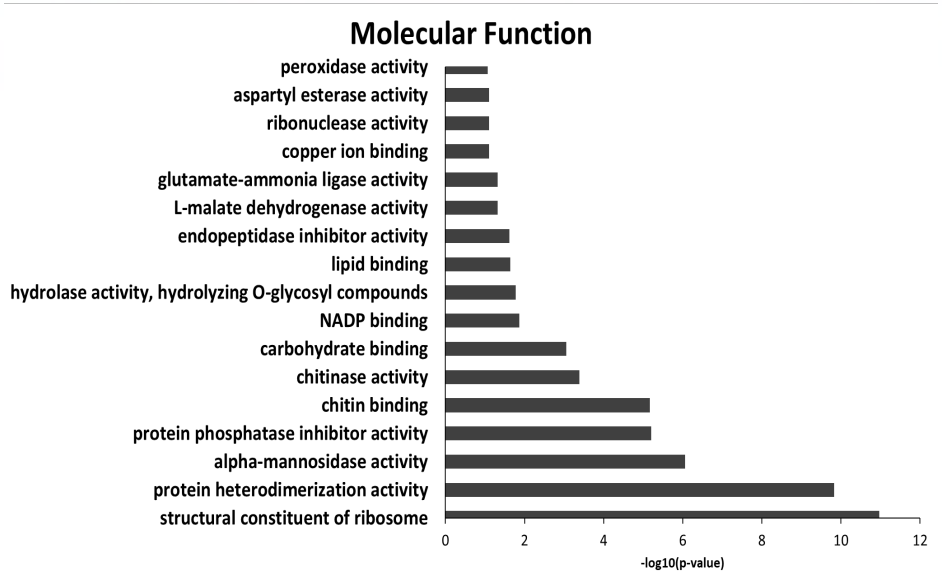
[Top 6 miRNAs & their functions]

No.	Mature ID	Function
1	**hsa-miR-574-5p**	Collagen synthesis, Proliferation, inhibit apoptosis
2	hsa-miR-8485	Wnt/β-catenin signaling Proliferation, migration
[illegible]	**hsa-miR-1246**	Collagen, Anti-photoaging, Proliferation, Modulating T cell balance
4	hsa-miR-1290	Proliferation Metastasis
5	hsa-miR-184	Promote differentiation, Proliferation, Inhibits Apoptosis
6	hsa-let-7c-5p	Anti-tumor function

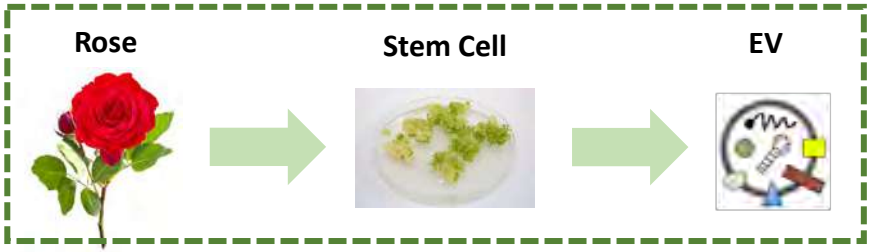
RSCE Conclusions

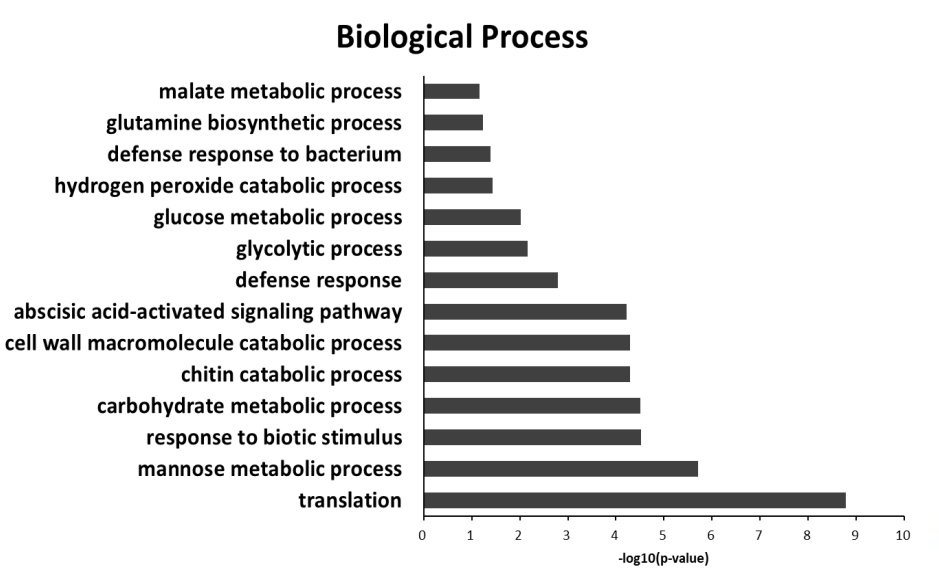
1. Rose stem cells are releasing their EVs or exosomes into conditioned media during culture.
2. The size & shape are very similar to human stem cell-derived exosomes.
3. RSCEs are effective on the proliferation and collagen production of human dermal fibroblasts.
4. RSCE has lower cytotoxicity than rose stem cell conditioned media.
5. RSCE can reduce the melanin synthesis of mouse melanoma cell line B16F10.
6. Surprisingly, miRNAs of RSCE are mostly de novo sequences. However, 27 miRNAs are matching with human sequences. Top 5 miRNAs are all related to cellular proliferation.

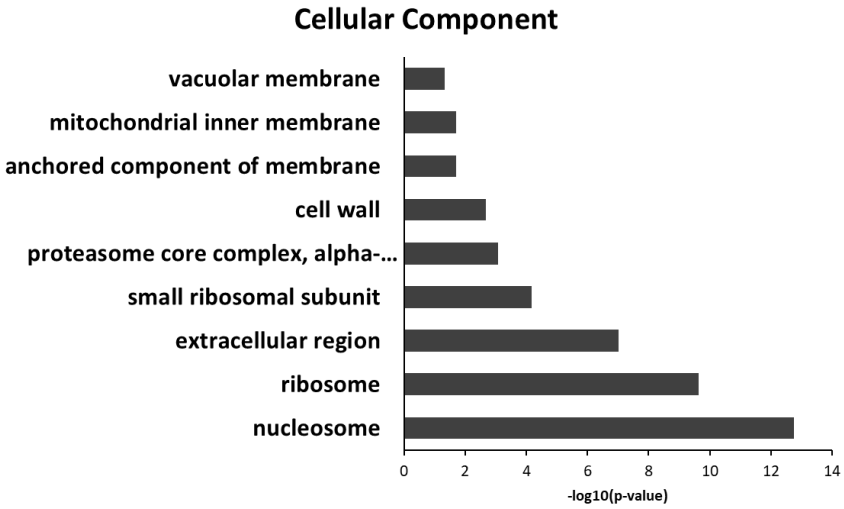
RSCE Protein Analysis



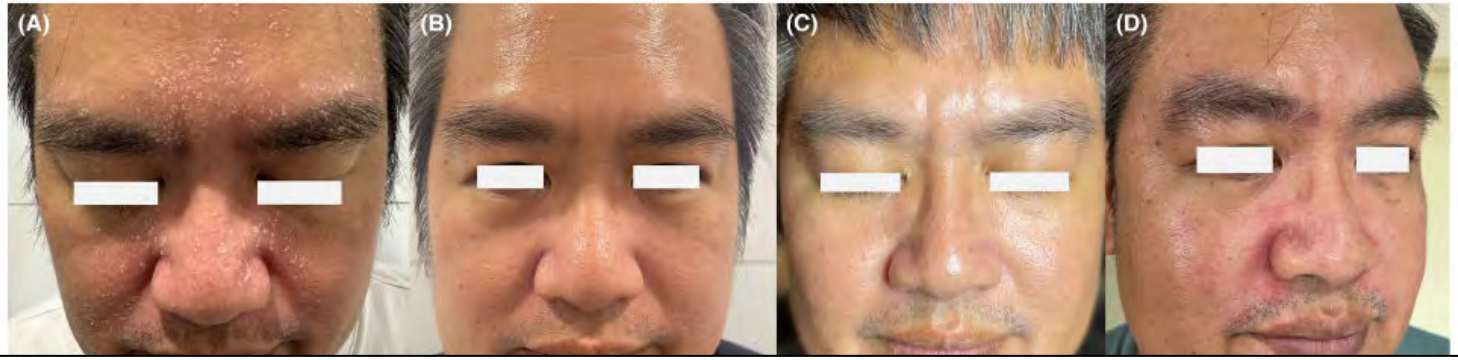
RSCE™ (Rose Stem Cell Exosome)







RSCE™ Case Report: Seborrheic Dermatitis



Received: 11 January 2024 | Revised: 11 April 2024 | Accepted: 6 May 2024

DOI: 10.1111/jocd.16389

CLINICAL COMMENTARY

JCD Journal of Cosmetic Dermatology

WILEY

Topical moisturizer with rose stem cell-derived exosomes (RSCEs) for recalcitrant seborrheic dermatitis: A case report with 6 months of follow-up

Suparuj Lueangarun M.D., MSc.[1,2] | Byong Seung Cho B.S.C.[3] | Therdpong Tempark M.D.[4]

- The clinical manifestations, e.g. redness, scaling, and itching, were improved on the first day after treatment.
- During his 3 months of follow-up, the patient had no disease flare-up and received no additional treatment.

Comparative Study: Human vs Plant

A Comparative Study of Human-Based and Plant-Based Exosomes

ExoCoBio X BENEV

PATIENT TESTIMONIAL

"I loved how cooling it was after my Halo®! I didn't notice a difference between the two sides, but I know I couldn't do a Halo® without the exosomes!"

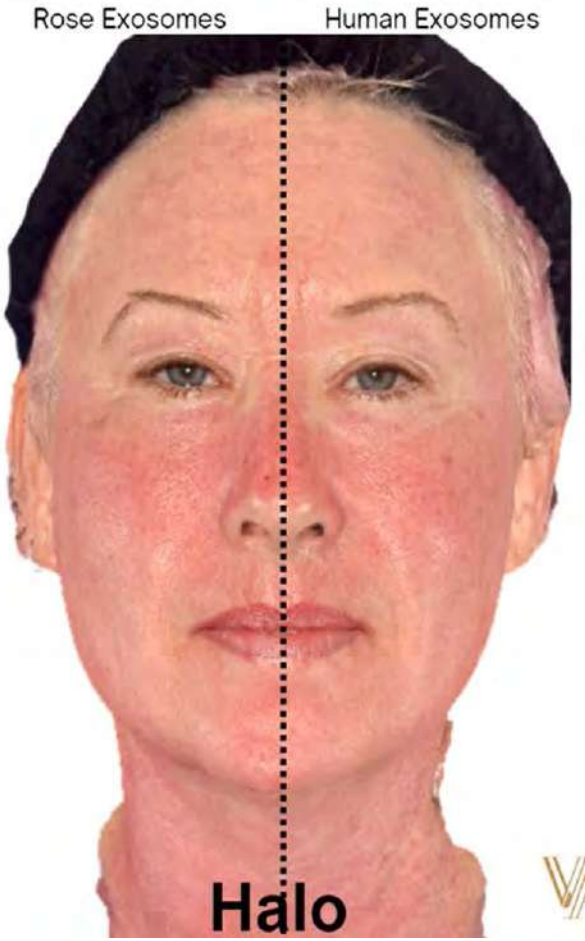
Gender: Female

Skin Type: FST 1

Heat Scale On Left Side: 3/10

Heat Scale On Right Side: 4/10

Source: Dr. Mark Brown (Canada)



Products and Key ingredients " Rose Stem Cell Exosomes"

- Brand Name: ASCEplus
- Product Name : 1) ASCEplus Derma Signal Kit SRLV 2) ASCEplus Scalp Care HRLV
- Our key ingredients for ASCEplus is " Rosa Damascena Callus Extracellular Vesicles", which is the cosmetic ingredient name of 'Rose stem cell' exosomes'

ASCEplus SRLV_Ingredient list

ASCE plus™ Derma Signal Kit | SRLV

Vial 1 : Lyophilized Powder + Vial 2 : Diluent

Lyophilized Powder for Skin Rejuvenation

How To Use | Mix Vial 1(Lyophilized Powder) and Vial 2(Diluent) thoroughly. Apply a proper amount of mixture around the facial area. * One time use ONLY.

Ingredients - Vial 1 : Lyophilized Powder | Rosa Damascena Callus Extracellular Vesicles, Methionine, Trehalose, Mannitol, Glutamine, Potassium Chloride, Ascorbic Acid, Retinol, Magnesium Sulfate, Glutathione, Nicotinamide Adenine Dinucleotide, Disodium Flavine Adenine Dinucleotide, Thiamine Diphosphate, Coenzyme A, sh-Oligopeptide-2, Acetyl Hexapeptide-8, Nonapeptide-1, Palmitoyl Tetrapeptide-7, Palmitoyl Tripeptide-1, sh-Oligopeptide-1, sh-Polypeptide-1, sh-Polypeptide-3, sh-Polypeptide-76, Copper Tripeptide-1, Palmitoyl Pentapeptide-4, Alanine, Arginine, Aspartic Acid, Glutamic Acid, Glycine, Histidine, Isoleucine, Leucine, Lysine HCL, Ornithine HCL, Phenylalanine, Proline, Serine, Threonine, Tryptophan, Tyrosine, Valine

Ingredients - Vial 2 : Diluent | Water, Sodium Hyaluronate, Sodium Chloride, Sodium Bicarbonate, Disodium Phosphate, Sodium Phosphate, Potassium Chloride, Alanine, Arginine, Histidine, Isoleucine, Leucine, Lysine HCL, Phenylalanine, Proline, Serine, Threonine, Valine, sh-Decapeptide-7, sh-Octapeptide-4, sh-Oligopeptide-9, sh-Pentapeptide-5

ExoCoBio Inc. 306, 19, Gasan digital 1-ro, Geumcheon-gu, Seoul / sales@exocobio.com
www.exocobio.com / www.asceplus.com MADE IN KOREA

ASCEplus HRLV_ Ingredient list

ASCE plus™ Scalp Care | HRLV

Lyophilized Powder for Hair Rejuvenation

The special powder containing active components for nourishment & healthy environment of the scalp

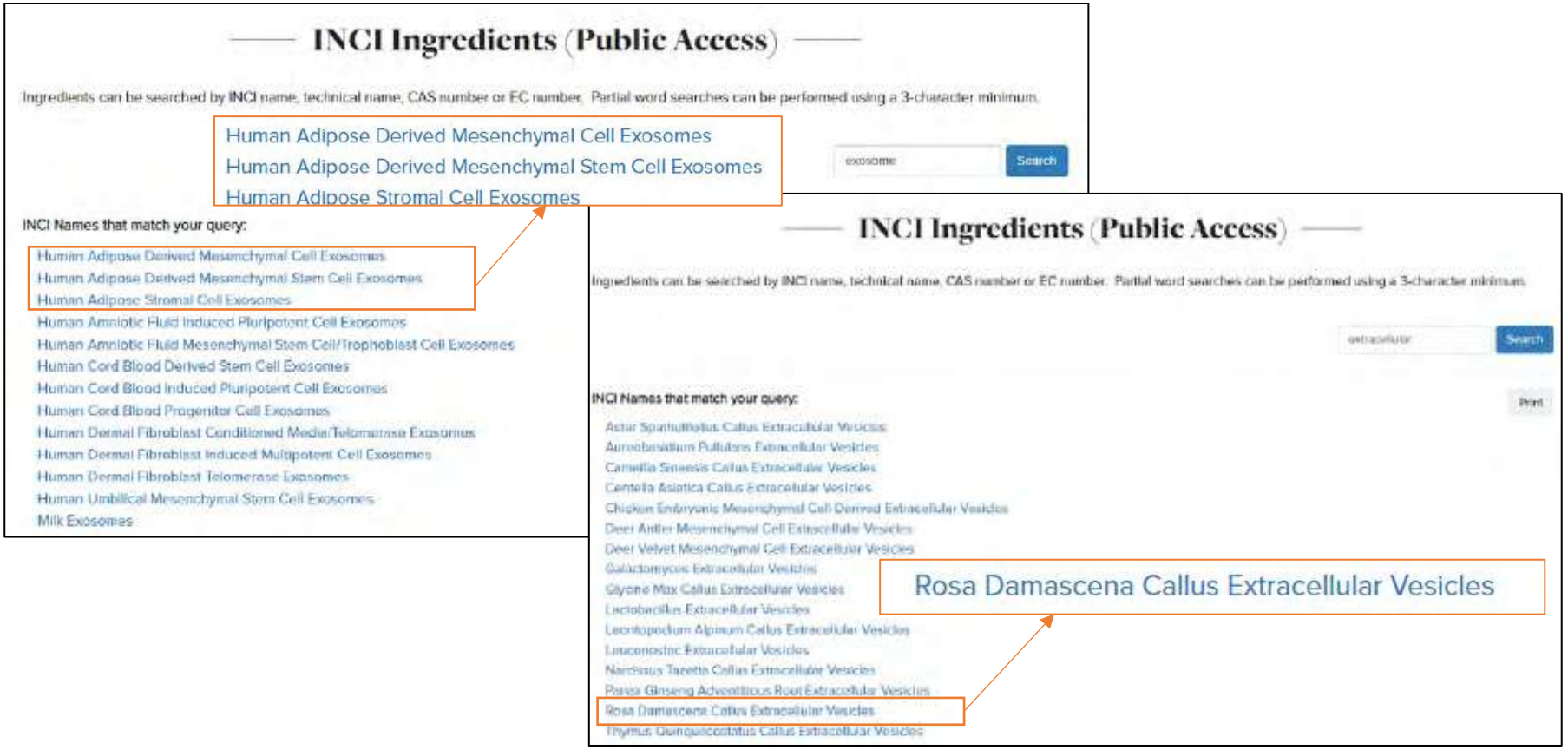
How To Use | 1. Mix the lyophilized powder with 3-5ml of saline. 2. Evenly apply the mixture over the area and rub until it is all absorbed into the dried scalp after shampooing.
* For more intensive care, please apply the mixture after rolling the area with MTS roller.
* One time use ONLY.

Ingredients | Rosa Damascena Callus Extracellular Vesicles, Trehalose, Mannitol, Methionine, Glutamine, Sodium Bicarbonate, Potassium Chloride, Alanine, Arginine, Lysine HCL, Tryptophan, Tyrosine, Valine, Histidine, Aspartic Acid, Glutamic Acid, Biotin, Nicotinamide Adenine Dinucleotide, Disodium Flavine Adenine Dinucleotide, Thiamine Diphosphate, Coenzyme A, sh-Oligopeptide-1, sh-Oligopeptide-4, sh-Polypeptide-4, sh-Polypeptide-9, sh-Polypeptide-13, sh-Polypeptide-8, sh-Polypeptide-1, sh-Polypeptide-3, sh-Oligopeptide-2, sh-Polypeptide-11, Copper Tripeptide-1, Leucine, Isoleucine, Phenylalanine, Glycine, Serine, Ornithine HCL, Threonine, Magnesium Sulfate, Proline, Ascorbic Acid

ExoCoBio Inc. 306, 19, Gasan digital 1-ro, Geumcheon-gu, Seoul / sales@exocobio.com
www.exocobio.com / www.asceplus.com MADE IN KOREA

ASCE™ & RSCE™ Registration (US PCPC/INCI)

- ✓ ExoCoBio registered “exosomes/extracellular vesicles” ingredient in PCPC, that is so call ‘INCI Ingredinets’ for cosmetic use.



* PCPC: Personal Care Products Council
* INCI: International Nomenclature Cosmetic Ingredient [INCI - Personal Care Products Council (personalcarecouncil.org)]
* INCIpedia: [INCI - Personal Care Products Council (personalcarecouncil.org)]

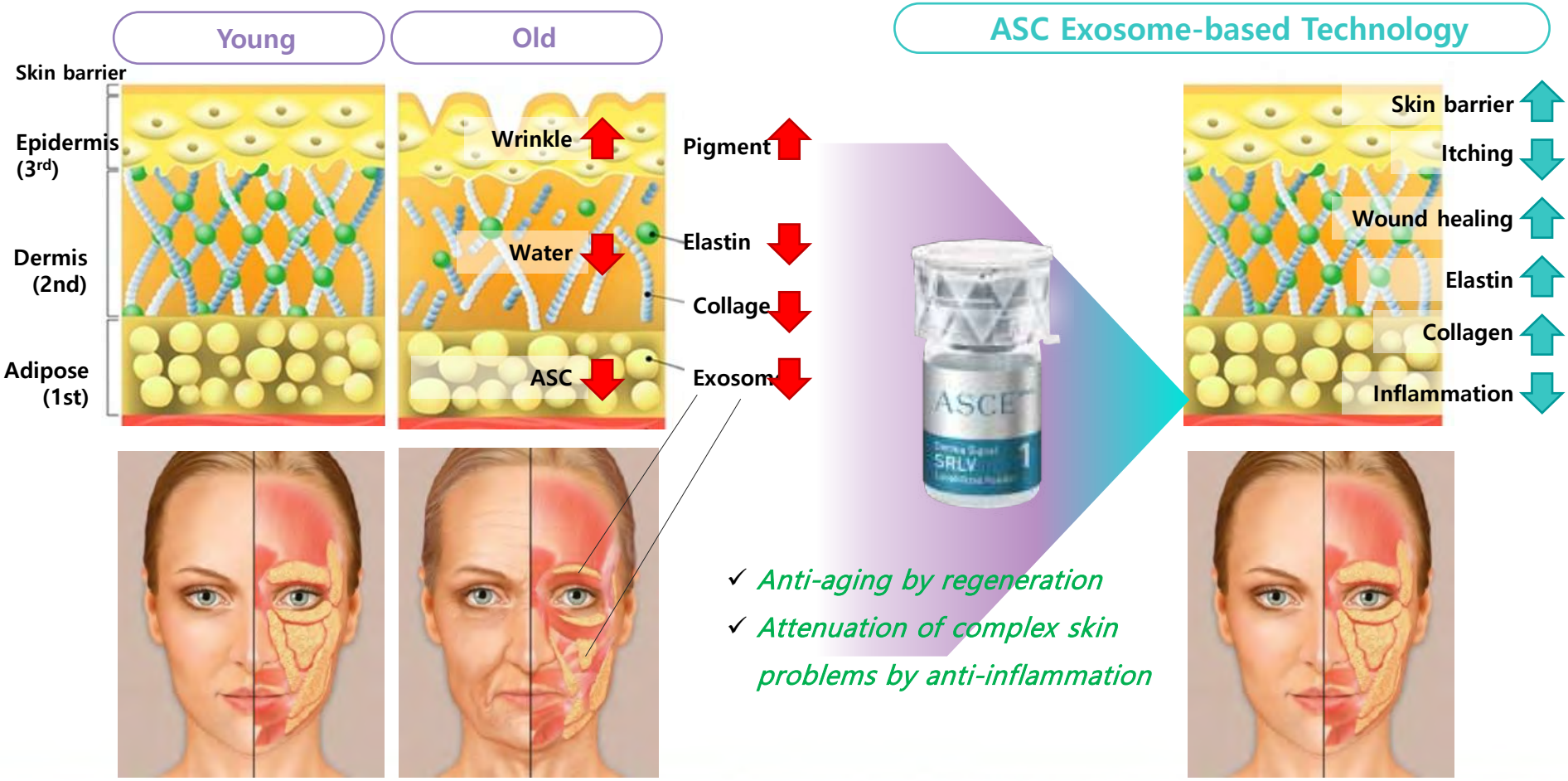
ASCEplus™ SRLV

The World's First Exosome-based Regenerative Aesthetics for Skin

Byong Cho, CEO/CTO
ExoCoBio Inc.
Instagram: exosome_regen_med_aesthetics

Aging & Exosome

- Exosomes are the most important for young and normal skin (Regeneration & Anti-inflammation).
- Aging ➔ Loss of ADSC (1st layer) ➔ Loss of exosomes ➔ Slow regeneration of dermis/epidermis (2nd/3rd)

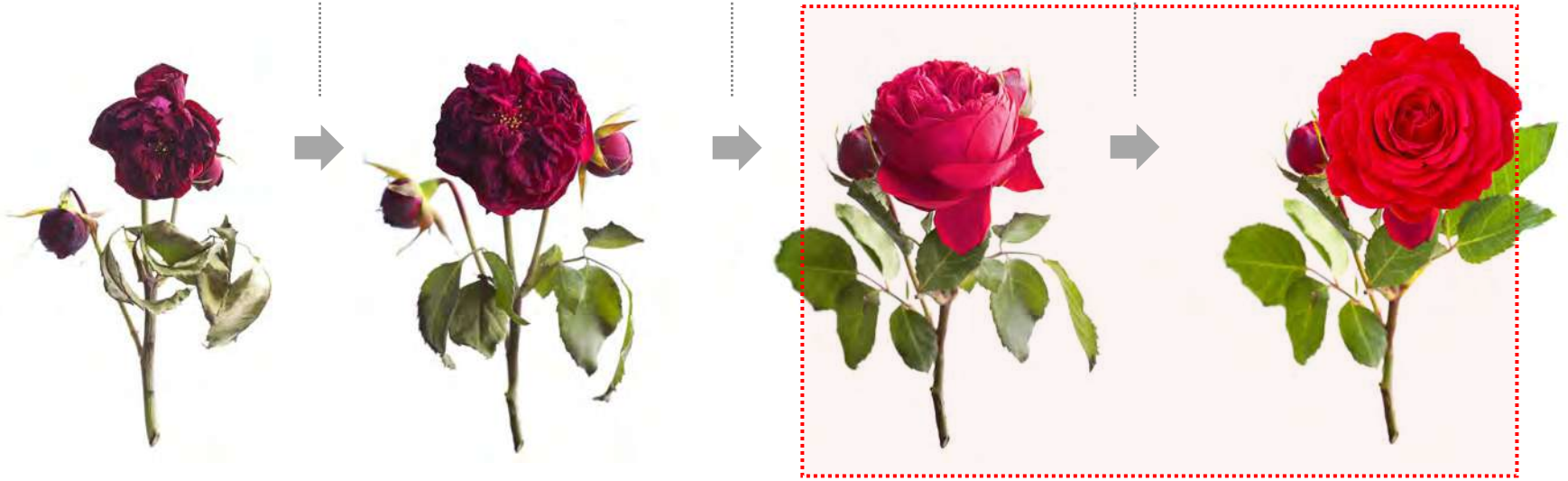


A New Wave OF Medical Aesthetics

VOLUME
REPLACEMENT
REPOSITIONING

SKIN
FIRMING
TIGHTENING

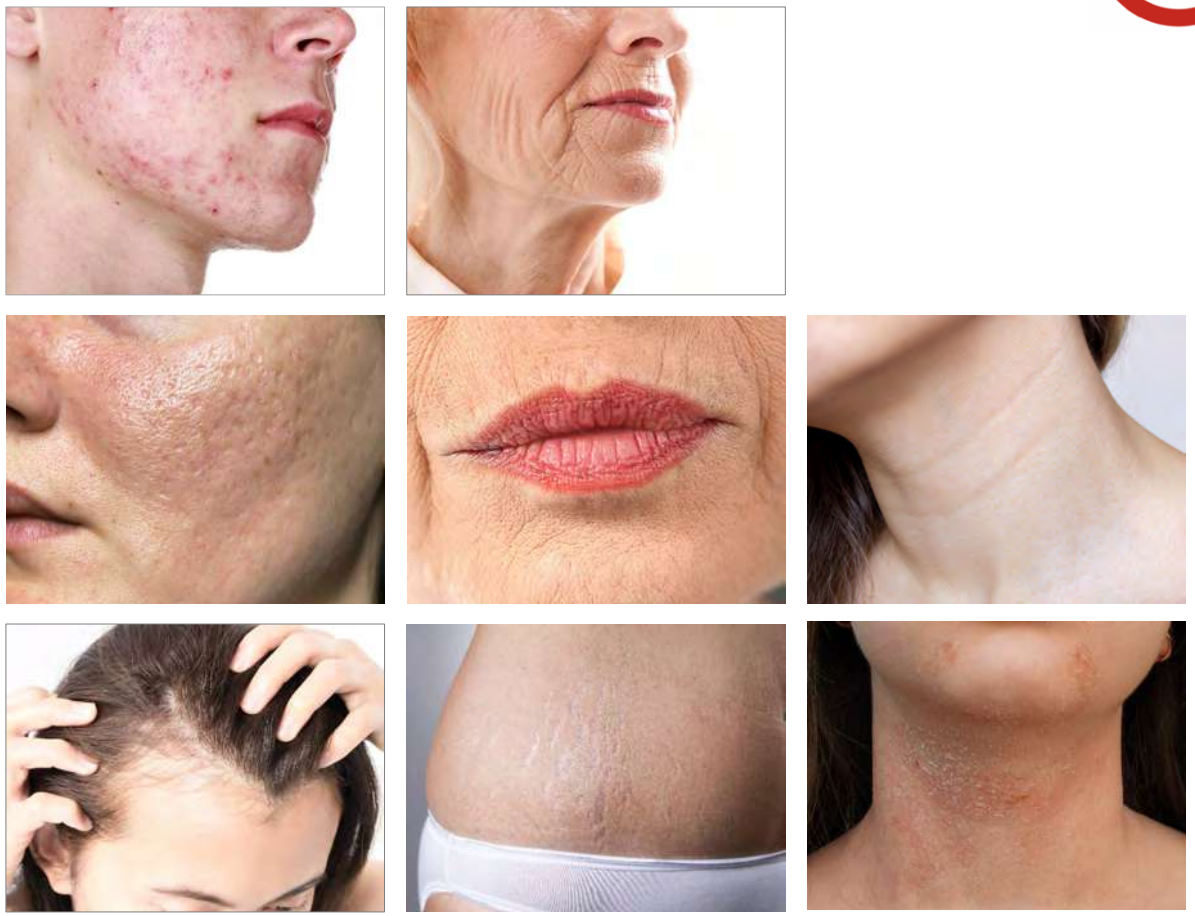
SKIN
Regeneration
Anti-inflammation



Courtesy: Dr. HS Choi, Piena Clinic (Seoul, South Korea)

Clinical Applications

- ✓ Acne (Redness)
- ✓ Wrinkles
- ✓ Pores/Scars
- ✓ Atrophic Lips
- ✓ Neck Lines
- ✓ Hair Loss
- ✓ Stretch Marks
- ✓ Atopic Dermatitis
- ✓ Vaginal rejuvenation



Courtesy: Dr. HS Choi, Piena Clinic (Seoul, South Korea)

Anti-aging Technologies & Exosome


RF Microneedling


LASER


N-toxin


Chemical Peeling


Ultrasound/HIFU


Auto-MTS


Meso-Roller


Multi-needle device


Micro-coring

Collagen booster

Source: Dr. HS Choi, Piena Clinic (Seoul, South Korea) & ExoCoBio

Standard Procedure (Skin)

1-2 weeks

Priming

Laser/RFM

Topical Application

Microneedling

Cooling

Home care

2-3 weeks

Cooling

Home care

2-3 weeks

Combination of Exosome & CO2 Factional Laser for Acne Scar

Efficacy & Safety

Byong Cho, CEO/CTO
ExoCoBio Inc.

Acta Dermato-Venereologica ActaDV

INVESTIGATIVE REPORT

Combination Treatment with Human Adipose Tissue Stem Cell-derived Exosomes and Fractional CO_2 Laser for Acne Scars: A 12-week Prospective, Double-blind, Randomized, Split-face Study

Hyuck Hoon KWON[1], Steven Hoseong YANG[2], Joon LEE[1], Byung Cheol PARK[3], Kui Young PARK[4], Jae Yoon JUNG[1], Youin BAE[5] and Gyeong-Hun PARK[5]

[1]Oaro Dermatology Institute, Seoul, Republic of Korea, [2]Guam Dermatology Institute, Guam, USA, [3]Department of Dermatology, Dankook University, College of Medicine, Cheonan, [4]Department of Dermatology, Chung-Ang University, College of Medicine, Seoul, and [5]Department of Dermatology, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Republic of Korea

A variety of applications of human adipose tissue stem cell-derived exosomes have been suggested as novel cell-free therapeutic strategies in the regenerative and aesthetic medical fields. This study evaluated the clinical efficacy and safety of adipose tissue stem cell-derived
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tissue stem cell-derived exosomes gel and the other side was treated with control gel. Adipose tissue stem cell-derived exosomes-treated sides had achieved a significantly greater improvement than the control sides at the final follow-up visit (percentage reduction in

SIGNIFICANCE

Adipose tissue stem cell-derived exosomes possess the critical properties of mesenchymal stem cells in the repair of organ injuries. Furthermore, adipose tissue stem cell-derived exo-
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effects. The combined use of adipose tissue stem cell-derived exosomes with resurfacing devices could provide synergistic effects on the efficacy and safety of atrophic acne scar treatments.

But still clinical necessity for better efficacy & shortened post-treatment downtime is needed for these procedures !

Regimen Components of ASC-Exosome Solution & Control

■ **Preparation of ASCE gel solution for clinical application**

ASC-exosomes were prepared as gel solutions with two different doses for clinical application. To prepare ASCE gel, ASC-exosomes were subjected as 9.78 X 10^{10} particles/mL (for the day of Fraxel treatment) or 1.63 X 10^{10} particles/mL (for days after Fraxel treatment) in a gel solution containing 30% ASC-exosomes, 2% 1, 2-hexanediol (COSBON, Hwaseong-si, Gyeonggi-do, Republic of Korea), 1% glycerin (Procter and Gamble Chemicals, Cincinnati, OH), 0.6% ammonium acryloyldimethyltaurate/VP Copolymer (Clariant international Ltd., Muttenz, Switzerland), 0.0045% L-Arginine (DAESANG, Seoul, Republic or Korea), and 66.3955% water for injection (DAI HAN PHARM. Co., Ltd., Seoul, Republic of Korea). The percentage means weight per weight. For control group, 30% of 0.03X PBS was subjected into a gel solution.

Exosome solution	Control solution
30% Exosome	30% PBS
2% 1,2-hexanediol	2% 1,2-hexanediol
1% glycerin	1% glycerin
0.6% ammonium acryloyldimethyltaurate/VP Copolymer	0.6% ammonium acryloyldimethyltaurate /VP Copolymer
0.0045% L-arginine	0.0045% L-arginine
66.3955% H2O	66.3955% H2O

ASC-Exosome: Efficacy (1)

- ASC-Exosomes-treated sides had achieved a significantly greater improvement than the control sides at the final follow-up visit.
- Percentage reduction in ECCA scores: 32.5 vs 19.9% ($p < 0.01$)

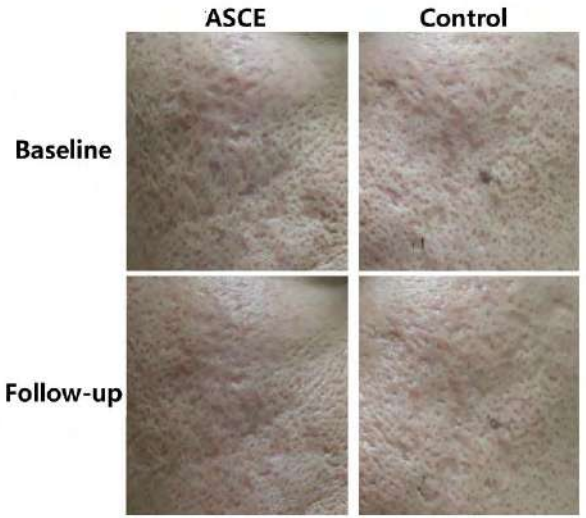


Fig. 3. Clinical photographs of the adipose tissue stem cell-derived exosomes (ASCE) and control sides at baseline and 6 weeks after 3 treatment sessions in a 30-year-old male.

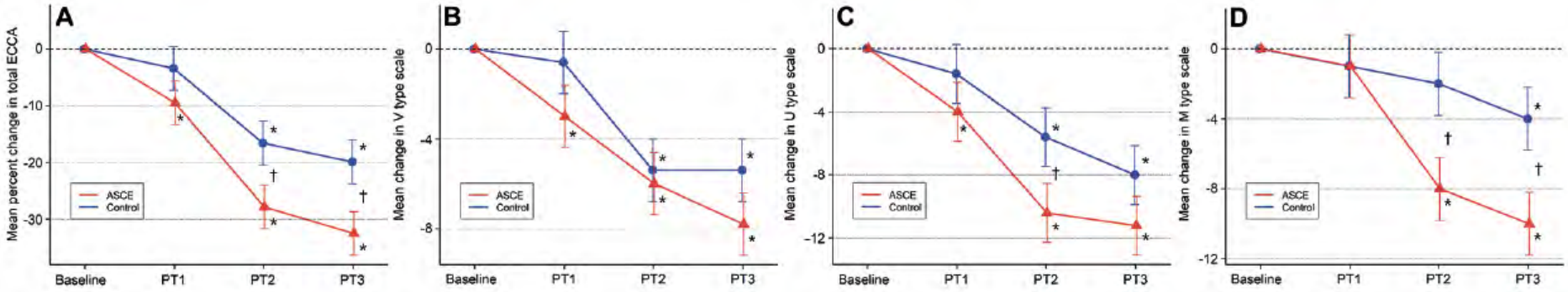


Fig. 2. Evaluation of scar improvement based on échelle d'évaluation clinique des cicatrices d'acné (ECCA) scores. (A) Mean percentage changes in total ECCA scores and mean changes in ECCA scores for (B) V-shaped (icepick), (C) U-shaped (boxcar), and (D) M-shaped (rolling) atrophic scars on the adipose tissue stem cell-derived exosomes (ASCE) and control sides. *$p < 0.05$ compared with baseline; †$p < 0.05$ between the 2 sides. Error bars indicate standard errors. PT: post-treatment.

ASC-Exosome: Efficacy (2) - Investigator's global assessment

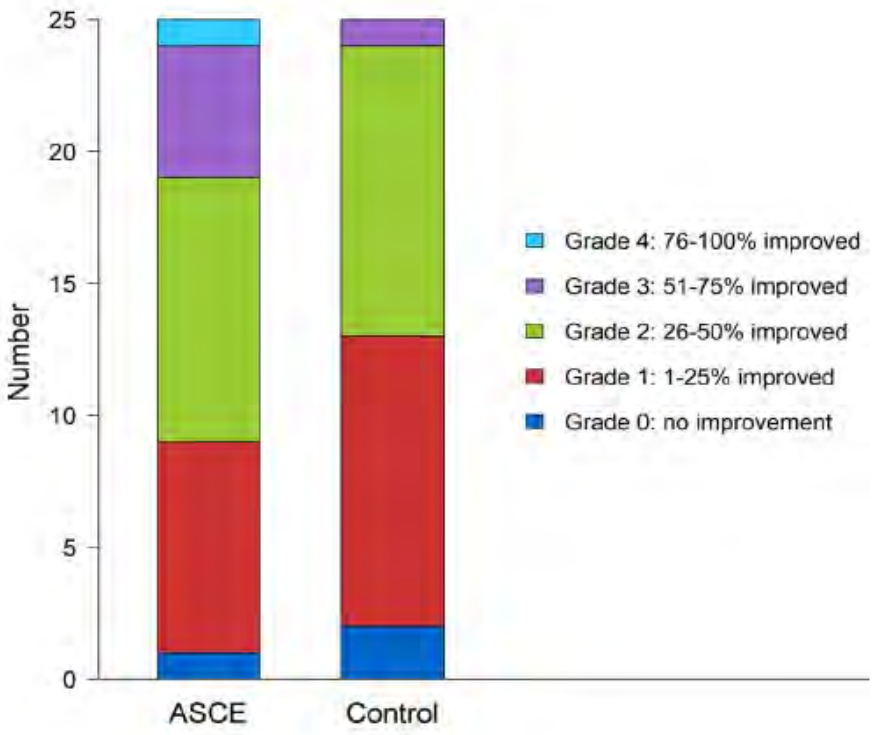


Fig. 3. Investigator's global assessment for scar improvement on the ASCE and control sides at the final follow-up visit. ASCE: adipose tissue stem cell-derived exosomes.

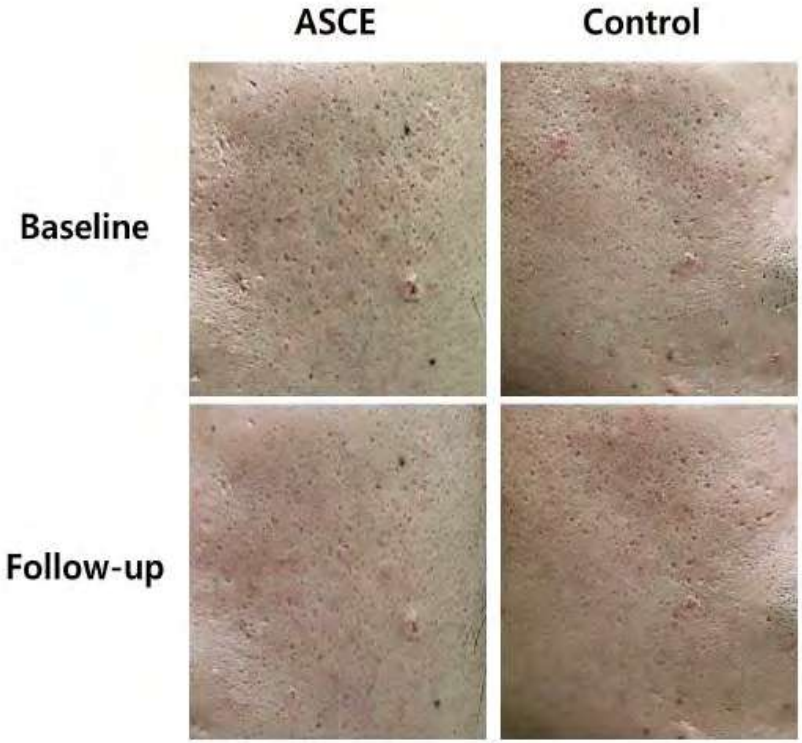


Fig. 4. Clinical photographs of the ASCE and control sides at baseline and 6 weeks after three treatment sessions in a 38-year-old male. ASCE: adipose tissue stem cell-derived exosomes.

- Various treatment-related side-effects, including posttreatment pain, erythema, oedema, and dryness, were experienced on both ASCE and control sides (Figs 5), but they were nearly resolved within 5 days.
- The severity of erythema during the first post-treatment week was significantly lower on the exosome side than on the control side (p = 0.03).
- Post-treatment pain, oedema, and dryness also tended to be milder on the exosome side, although not statistically significant.
- The mean duration of downtime was shorter on the ASCE side compared with the control side (4.1 (95% CI 3.5–4.8) days vs 4.3 (95% CI 3.7–5.1) days, p = 0.03).
- Two patients reported mild hyperpigmentation on the control side; one patient reported mild hyperpigmentation on the ASCE side (p = 0.32).

Safe!!

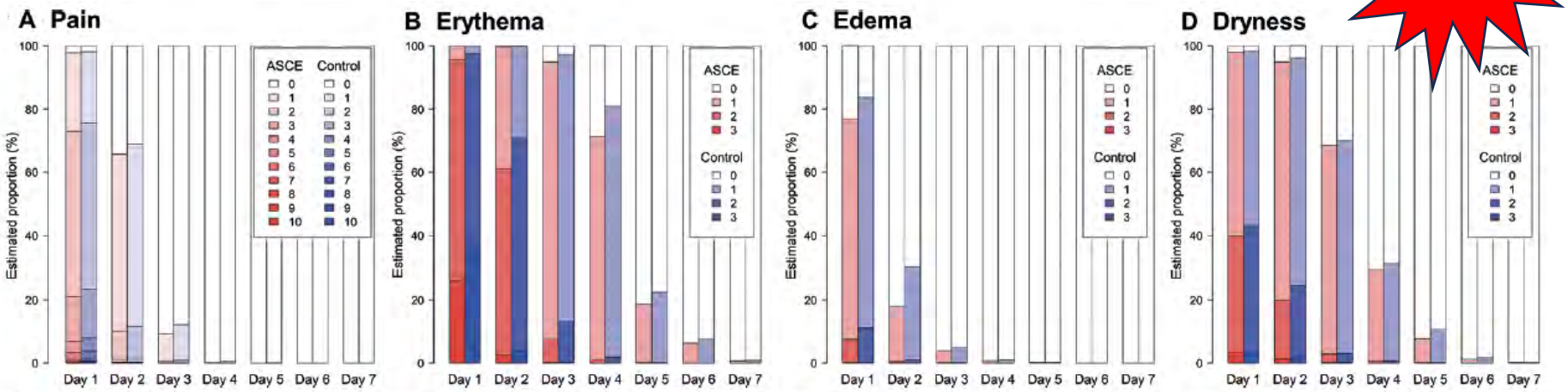


Fig. 5. Evaluation of: (A) pain, (B) erythema, (C) oedema, and (D) dryness on both adipose tissue stem cell-derived exosomes (ASCE) and control sides for post-treatment 7 days.

Received: 12 July 2022 | Revised: 24 May 2023 | Accepted: 2 June 2023

DOI: 10.1111/jocd.15872

JCD Journal of Cosmetic Dermatology

WILEY

ORIGINAL ARTICLE

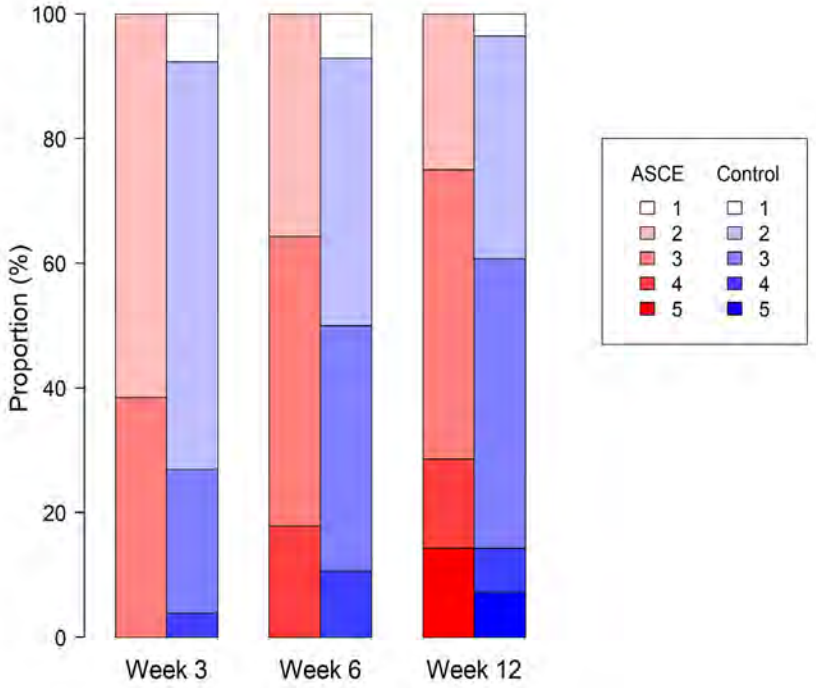
Efficacy of combined treatment with human adipose tissue stem cell-derived exosome-containing solution and microneedling for facial skin aging: A 12-week prospective, randomized, split-face study

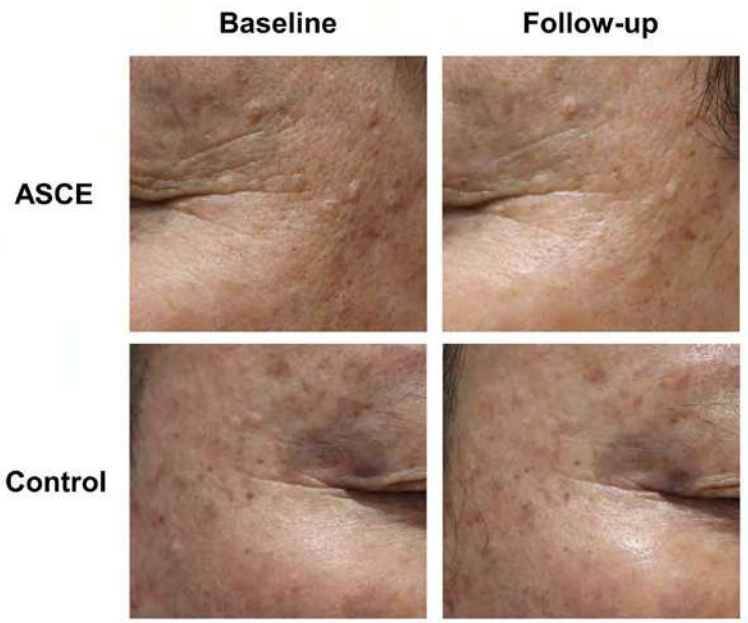
Gyeong-Hun Park MD, PhD[1] | Hyuck Hoon Kwon MD, PhD[2] | Joon Seok MD, PhD[3] | Steven Hoseong Yang MD, PhD[4] | Joon Lee MD, MS[5] | Byung Chul Park MD, PhD[6] | Eun Shin MD, PhD[7] | Kui Young Park MD, PhD[3]

"Taking the Message Further"

Clinical Evaluation of Overall Improvement

- The difference between the two treatments was not significant at week 3 (p = 0.202).
- But, it became statistically significant at week 6 (p = 0.023).
- At the final follow-up visit (week 12), 13 cases (46%) had a GAIS score of 3, *4 cases (14%) scored 4, and 4 cases (14%) scored 5 for the ASCE side*; whereas 13 cases (46%) scored 3, *2 cases (7%) scored 4, and 2 cases (7%) scored 5 for the control side*.
- These results indicate that the ASCE side exhibited *a significantly greater improvement in facial skin aging* than the control side at the final follow-up visit (p = 0.005).

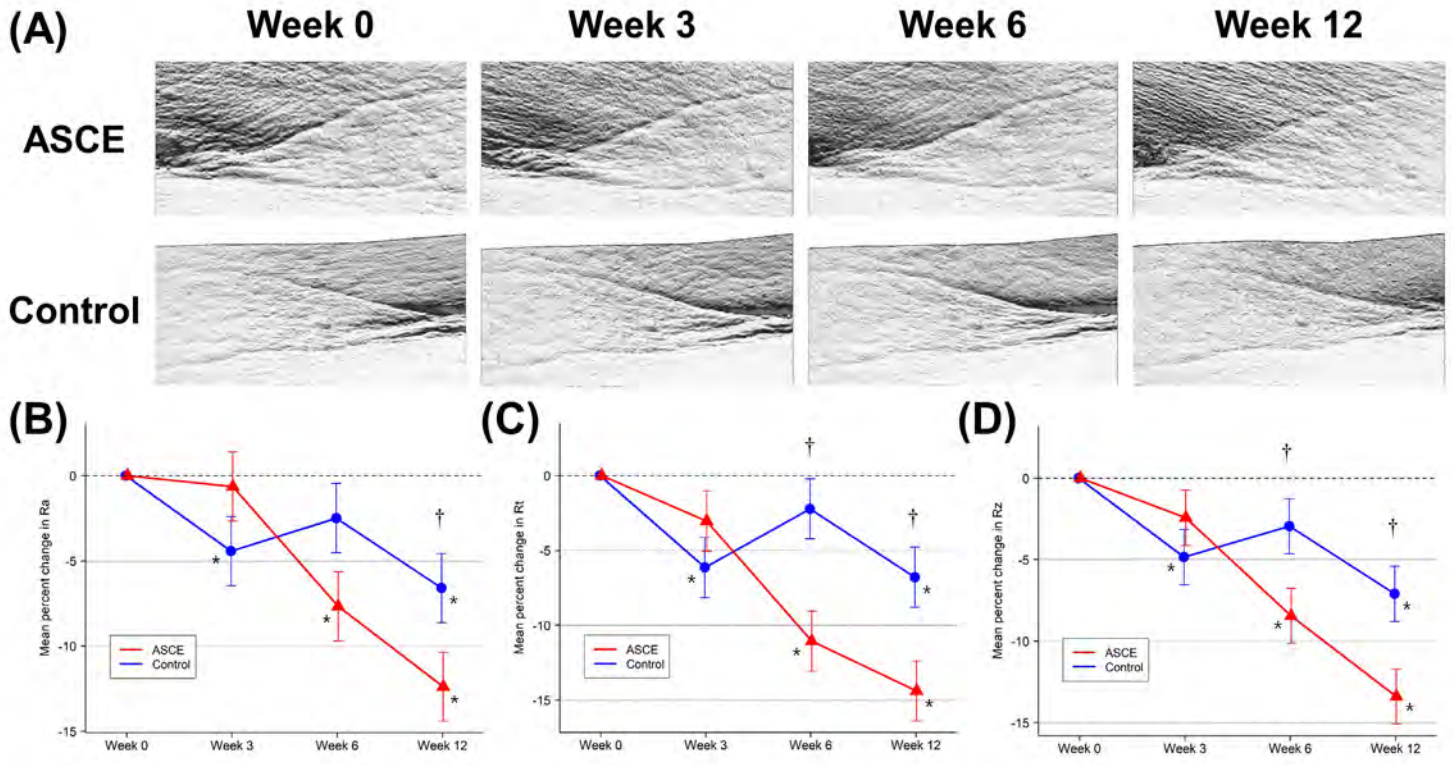




Source: Dr. GH Park et al.

Improvement in Skin Wrinkles

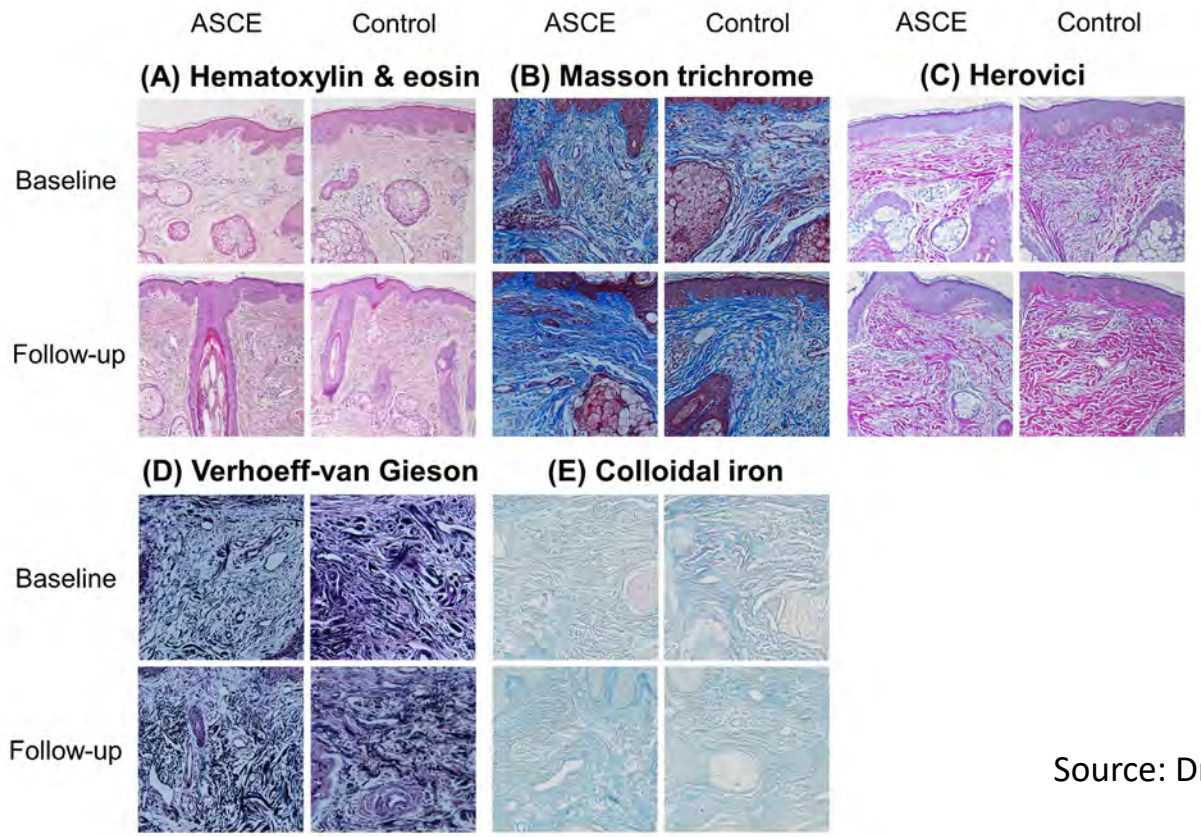
- At the final follow-up visit, the mean percent reductions in Ra, Rt, and Rz were 12.4%, 14.4%, and 13.4%, respectively, on the ASCE side.
- In contrast, these were 6.6%, 6.8%, and 7.1%, respectively, on the control side, showing *statistically significant differences between the two regimens (p = 0.031, 0.008, and 0.007, respectively).*



Source: Dr. GH Park et al.

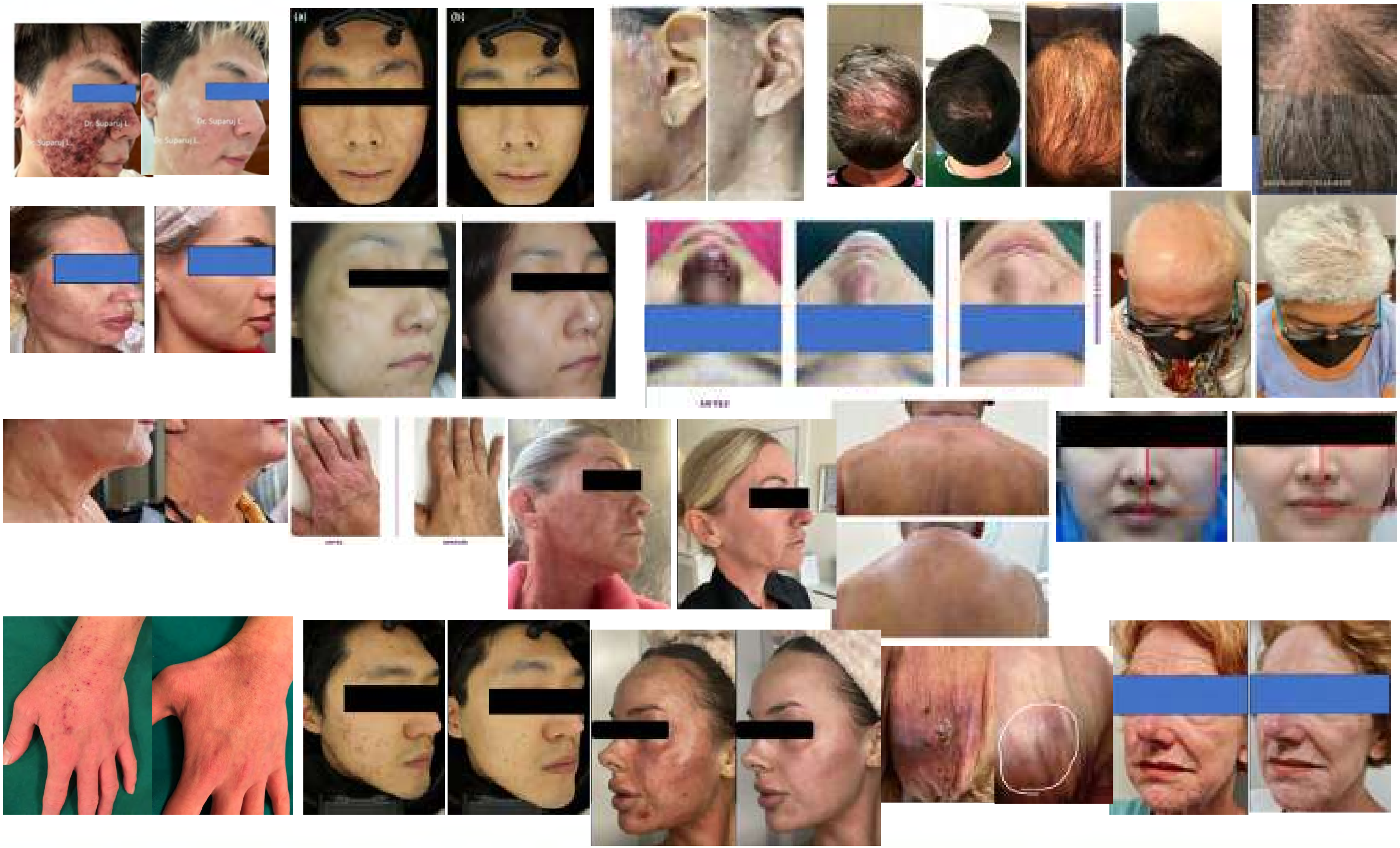
Histopathologic Evaluation

- Histological specimens obtained from the ASCE side showed *a greater density of collagen and elastic fibers, and, increased deposition of mucin and newly synthesized collagen* compared to those at baseline.
- Similar patterns of histological changes were observed on the control side, but these were less pronounced than those on the ASCE side.



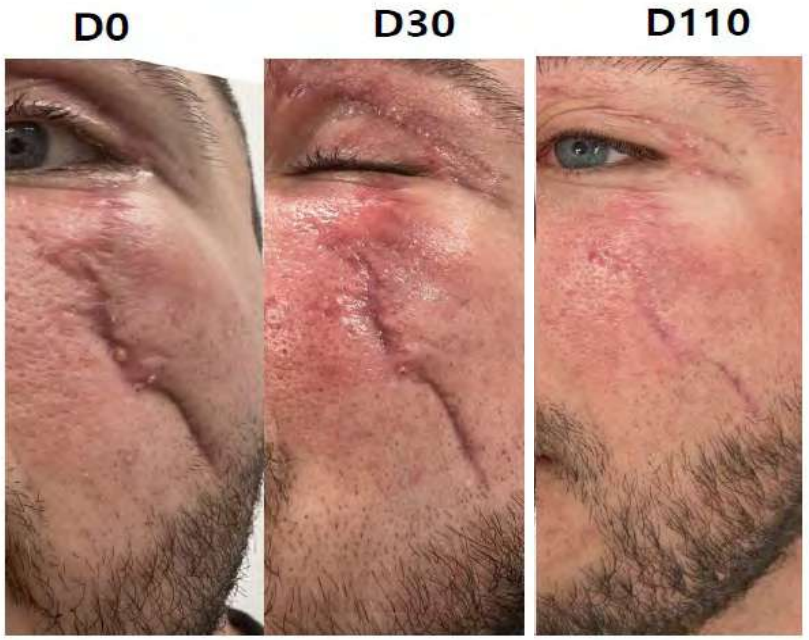
Source: Dr. GH Park et al.

Clinical Cases (2M)



Clinical Cases

Source: Dr. Agnieszka Kondraciuk (Poland)



Sebastian Krak i Agnieszka Kondraciuk w "Pytaniu na Śniadanie". "Wracam do zdrowia po wypadku"

Sebastian Krak omal nie stracił życia po tym, gdy porywisty wiatr przewrócił drzewo na kierowaną przez niego betoniarkę. Lekarze dokonali niemożliwego. Mężczyzna wraca do zdrowia. O zabiegach i leczeniu w studiu "Pytania na śniadanie" mówili Sebastian oraz dr Agnieszka Kondraciuk.

Nieprawdopodobny wypadek

Sebastian Krak and Agnieszka Kondraciuk in "Pytanie na Śniadanie". "I'm recovering after an accident"

Sebastian Krak almost lost his life after gusty winds overturned the drzewo na concrete mixer he was driving. Doctors did the impossible. The man is recovering. Sebastian and Dr. Agnieszka Kondraciuk talked about the treatments in the "Pytania na breakfast" studio

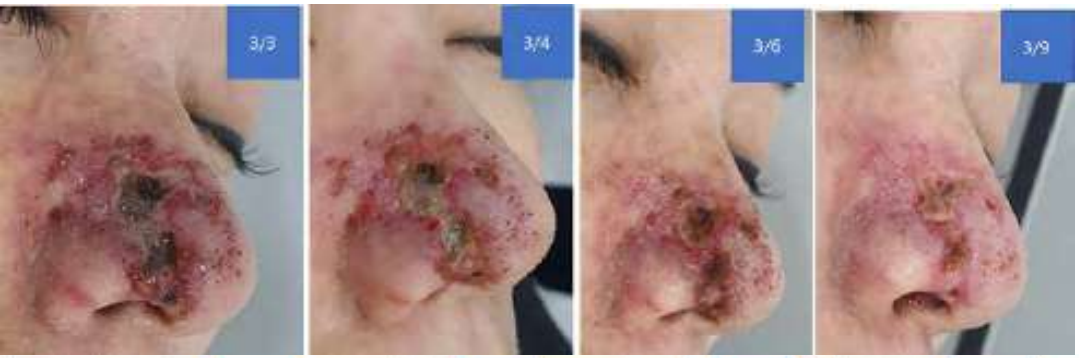
An unlikely accident

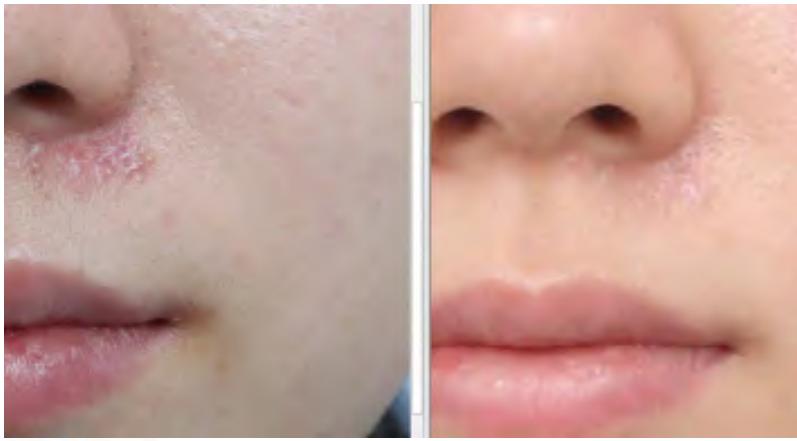
The accident occurred on Thursday evening, December 21, 2023, near Wizna Łomża. Gusty winds knocked down a large tree. Unfortunately, a thick branch crushed the cab of a truck (concrete mixer) driven by 24-year-old Sebastian, a resident of the commune. Lelis.

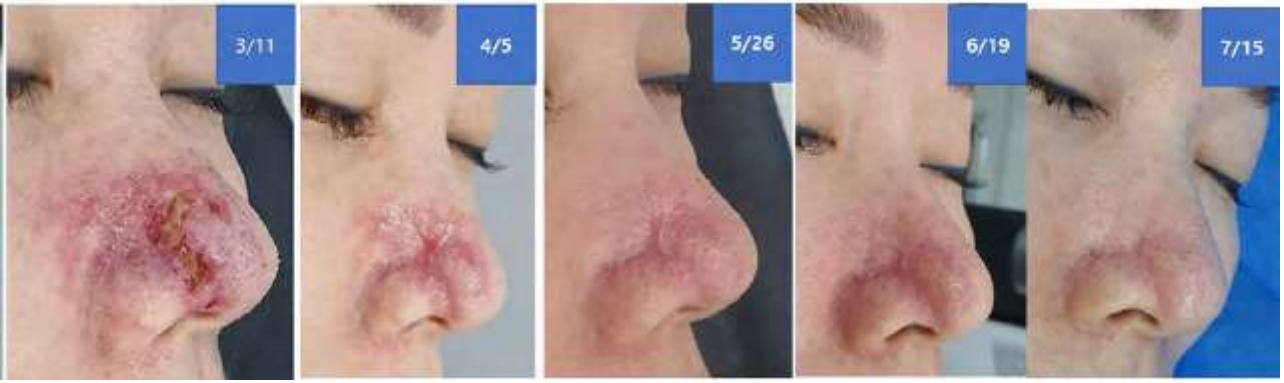
- *Scar-cutting cannula*
- *Topical ASCE™ + microneedling & thulium laser, 4 sessions, every 3-4 weeks*
- *"The patient not only sees incredible aesthetic improvement. The procedure improved motor functions in the facial area, allowed for free speech and facial expressions. The procedure significantly improved the patient's psyche and returned to social functioning."*

Vascular Occlusion

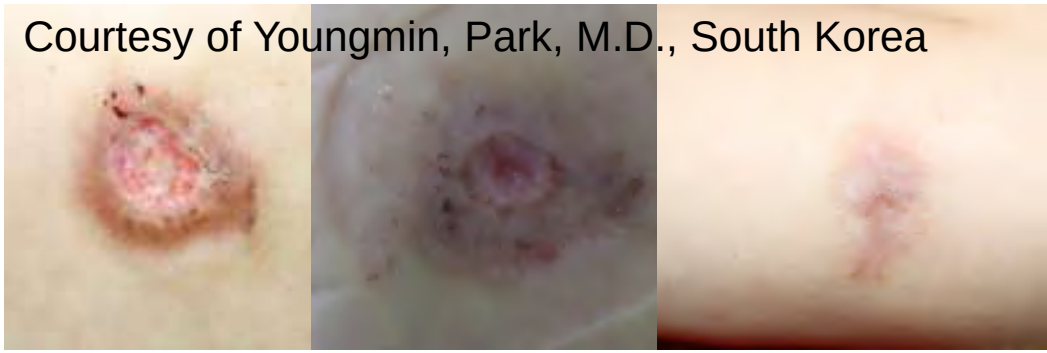
Courtesy of SooYeon, Park, M.D., South Korea



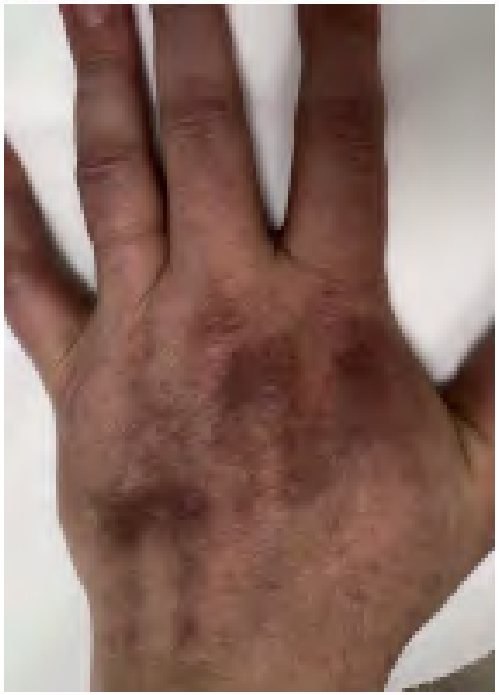




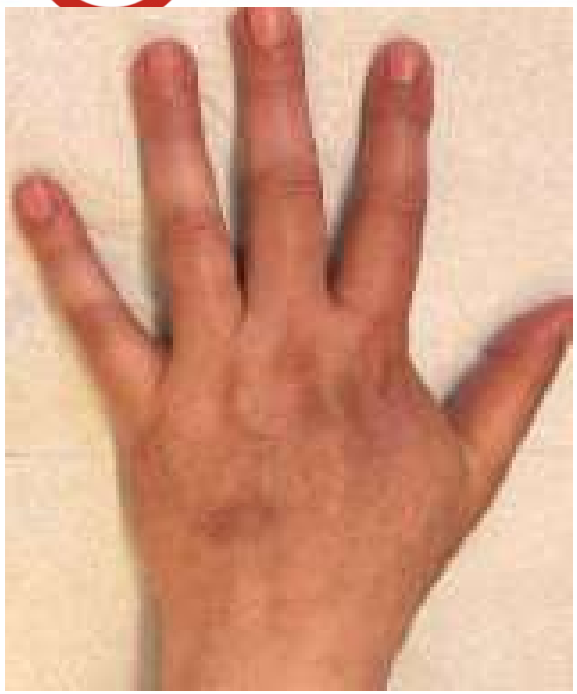
Courtesy of Youngmin, Park, M.D., South Korea



Clinical Cases: Skin Rejuvenation

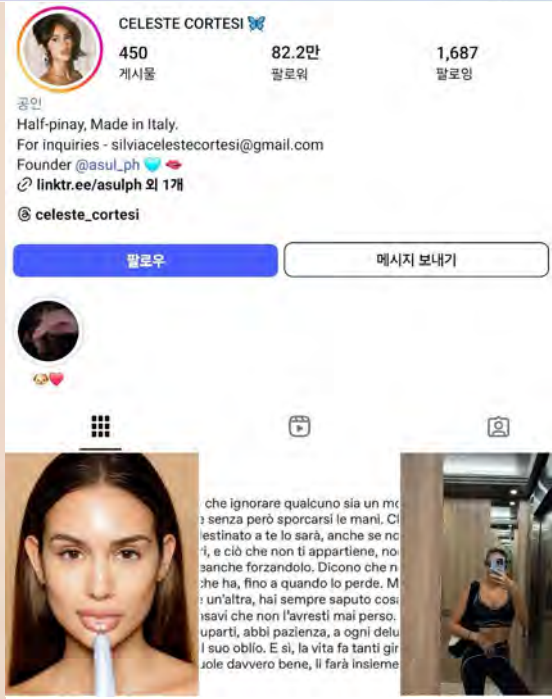


44 days



Indication	Skin Rejuvenation	Device	Sylfirm X SkinPen	Rose or Human	Rose
Interval	2 weeks	Treatments	3	Product	SRLV
Detail	First applied cicabio spf 50 and when noticed discromia and uneveness of the skin, we started the ASCE therapy: First Sylfirm PV2, 0,5mm, energy level 5, and SRLV ASCE, at home Exobalm. The second and 3rd sessions Skin Pen 0,5 and 1mm depth.				
Doctor	Irinel Nedelcu	Country	Romania		

Clinical Cases



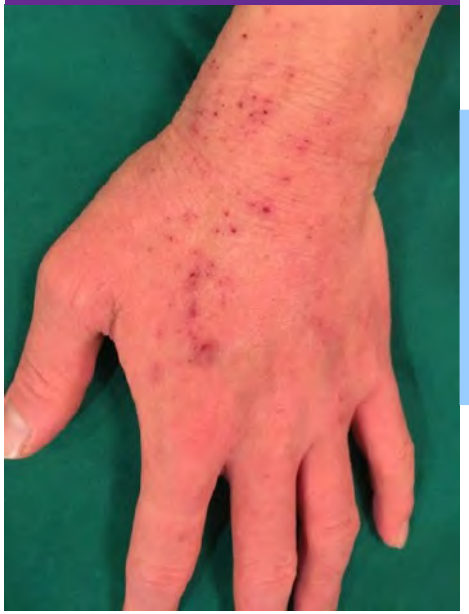
[@belobeauty](#) [@celeste_cortesi](#) knows the power of being real. After Miss Universe 2022, she faced the worst breakout of her life. One that took a toll not just on her skin, but on her mental health too. Instead of hiding, she chose to open up, reminding us that breakouts don't define us. With the right care, healing is possible, inside and out. Now, she's glowing brighter than ever! 🤍

Pure ASC-Exosome: Chronic Hand Eczema (CHE)

- 24-year-old male, 3 years
- Various steroid ointments, oral steroids, oral antihistamines and emollients
- Hyperkeratotic erythematous plaques with some scaling and fissuring

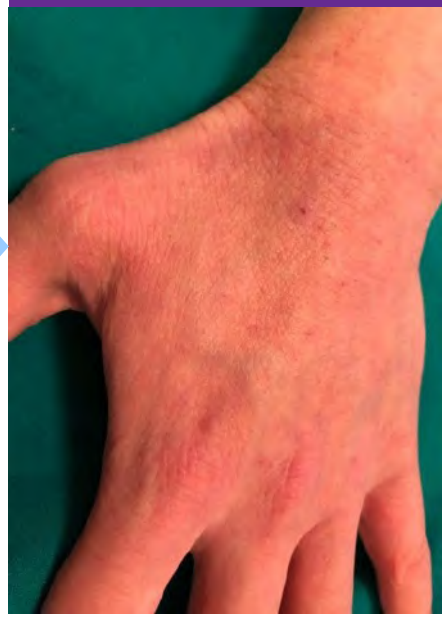
Strong Regenerative & Anti-inflammatory Effects

Before



- Topical application and iontophoresis 50mA
- 2 times/week, 3 day interval (Total 6 treatments)
- No other treatments
- No recurrence for 6 months

After



Source: Dr. Joon Lee (DOD Dermatology Institute, Korea)

ASC-Exosome: Lower Face & Neck Rejuvenation

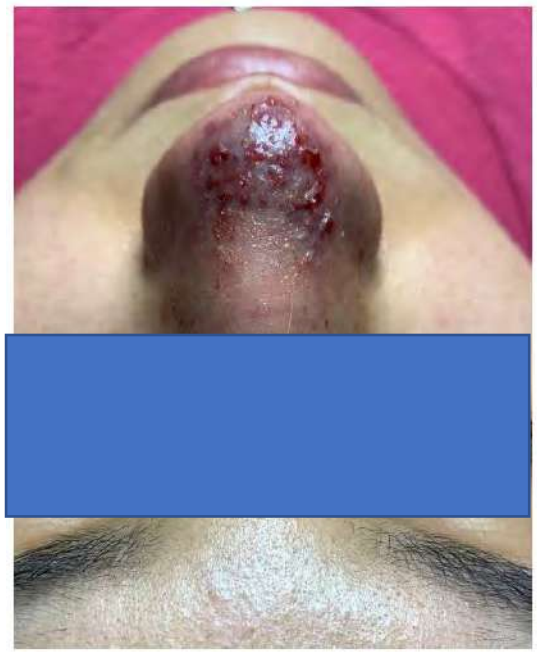
- 62 F
- Combination of RF Microneedling with ASC-exosome
- 2 sessions

Before

After

Courtesy: Dr. Shameema Damree, UK

Courtesy: Dr.José Manuel Pino, Mexico.



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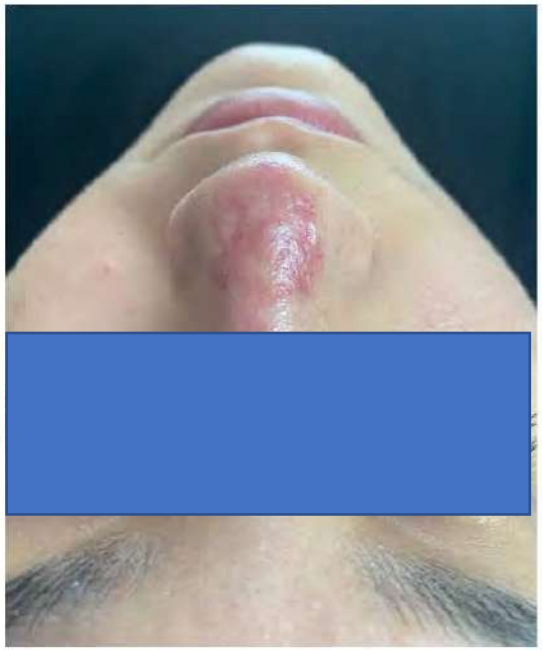

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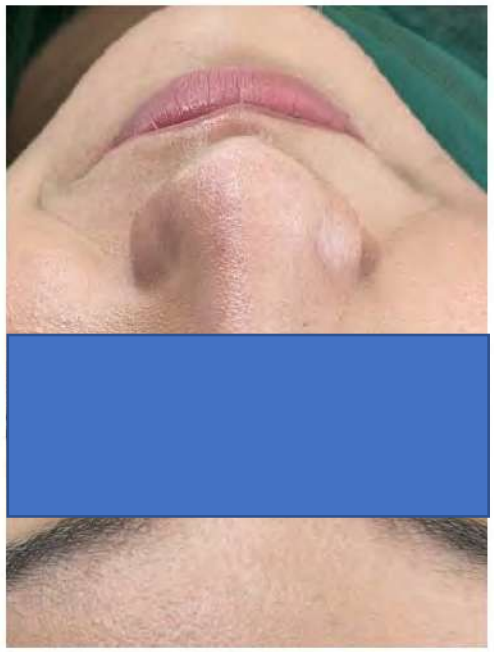
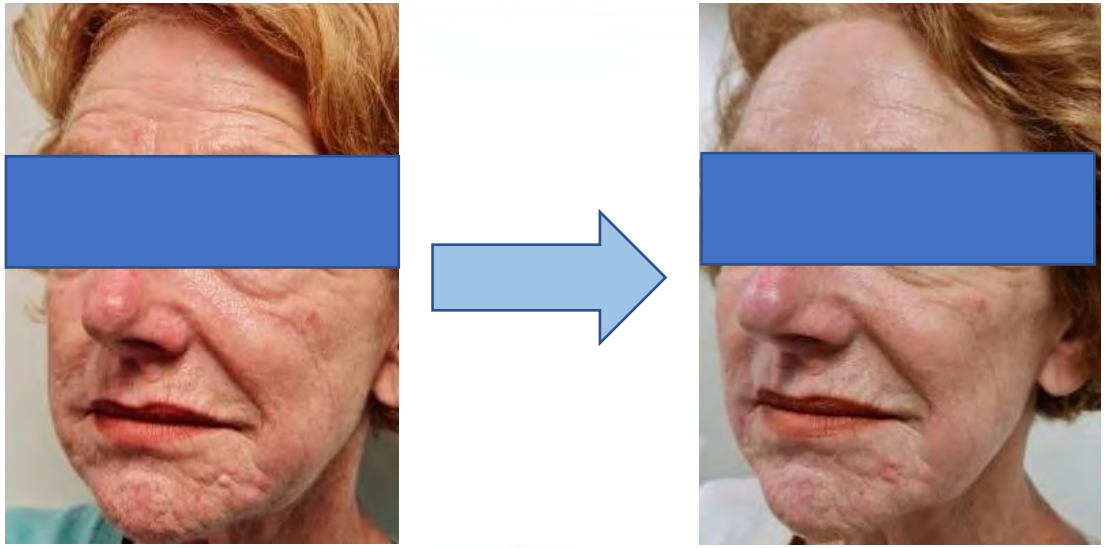


DESPUÉS

EXOSOME COMPLEJO REGENERADOR

Overnia®
Y SU RED DE DISTRIBUIDORES AUTORIZADOS

ASCE SRLV & RF Microneedling: mRNA Vaccine-induced Side Effects



73 yrs old lady presented with exacerbation of facial rosacea and skin sensitivity nine days post booster dose Pfizer mRNA COVID-19 vaccination. Rosacea over the nose and cheeks and chin was significantly worse in comparison to baseline level. The patient reported worsening of skin sensitivity over the entire face and neck. On examination, significant redness over nasal tip, cheeks and chin along with signs of global facial ageing (deep wrinkles and photo ageing hyperpigmented areas, skin laxity) and severe old acne scarring over the chin area.

Significant reduction in redness over tip, cheeks and chin area. Significant Improvement in deep wrinkles over t forehead, periorbital, malar and chin Improvement in acne scar area over Minimised pore size over the nose ar Smoother skin texture. Skin tightenir face and in jowls area.

Source: Dr. Shameema Damree

Products utilized (brand and type)

1. Adipose Derived Stem Cells Exosomes - ASCE+ SRLV manufactured by ExoCoBio 2. Microneedling Radiofrequency device - VIVACE Microneedling RF manufactured by SHENB

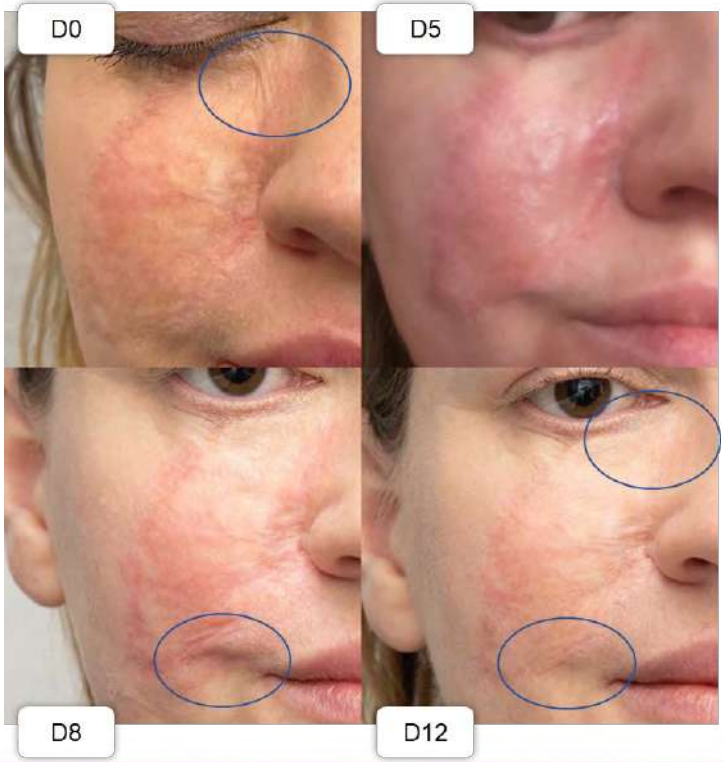
Chemical Peeling

Week 1: Peeling with glycolic acid
Week 2: ASCE SRLV + 1 mm Microneedling
Week 4: ASCE SRLV

Source: Dr. Narcisa Corlan (Romania)

Autologous Skin Graft

- Autologous skin graft in the middle part of the face 30 years ago
- The effect was satisfactory, scar was visible but not overgrown, and skin color was even. However, patient has been seeking for further improvement.
- 18 months ago patient underwent 4 sessions of collagen product injections (name of the product unknown). 2 months after the last injection margins of the graft started to overgrow, and became thick and red, stimulating effect of the collagen injections was progressing. The whole area of the graft became thicker and changed color.
- To stop the process the physician decided to inject glucocorticosteroid in the area of the graft (name and dose of the product unknown). The patient had 2 sessions, with 4 weeks intervals. The effect was atrophy of the skin, discoloration, thinning and wrinkling the whole area of the graft.



- The treatment was performed in a series (2x) of microneedling (0.25-0.5mm using the stamp method) with ASCE+ exosomes applied immediately after procedure in three layers.
- In addition, ASCE+ exosomes were smeared 2x/daily into the scarred tissue for two weeks.

Source: Dr. LIDIA MAJEWSKA (Poland)

Autologous Skin Graft

AMWC 2025 Aesthetic Medicine AWARDS

ExoCoBio Our Exosomes Your Future

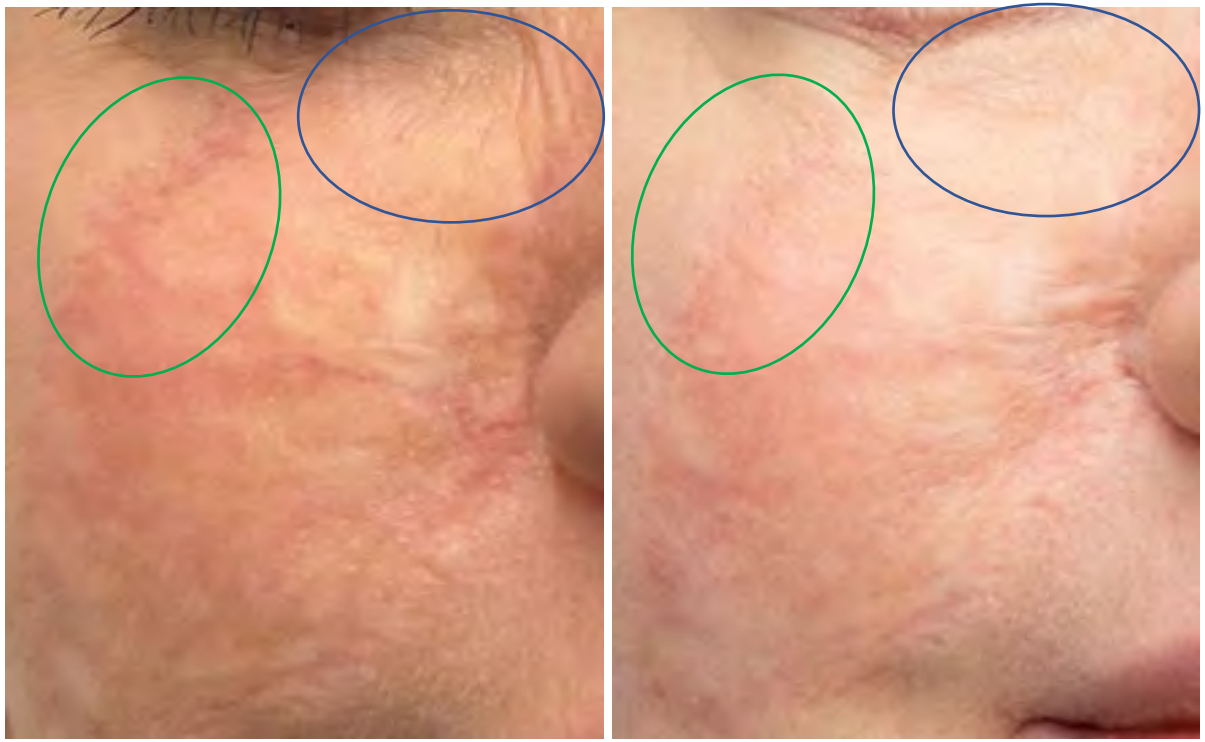
Efficacy of Rose Stem Cell-Derived Exosomes (RSCEs) in Skin Treatment: From Healing to Hyperpigmentation Management: Case Series and Review

Lidia Majewska[1] | Karolina Dorosz[2] | Jacek Kijowski[3]

[1]ESME Clinic, Kraków, Poland | [2]University of Chicago, Chicago, Illinois, USA | [3]Małopolska Centre of Biotechnology, Stem Cell Laboratory, Jagiellonian University, Kraków, Poland

Published, Jan 2025

JCD Journal of Cosmetic Dermatology



- Reduction of hypertrophic scar margins
- Reduction of visibility of the blood vessels
- Reduction of discoloration
- Brightening of the skin
- Wrinkle smoothing (eye area)
- Skin hydration
- Improved patient comfort and satisfaction

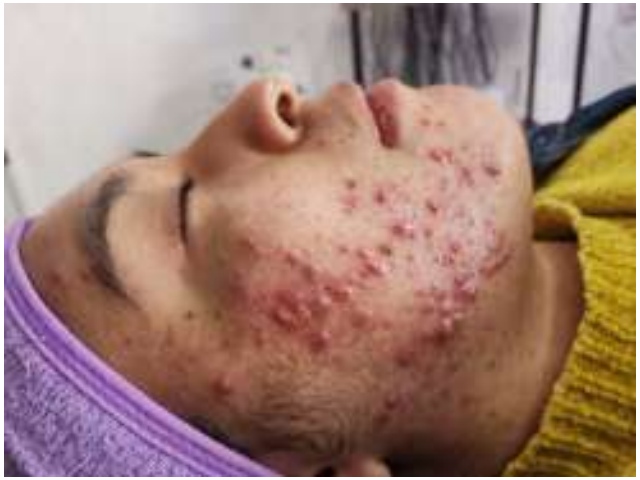
Source: Dr. LIDIA MAJEWSKA (Poland)

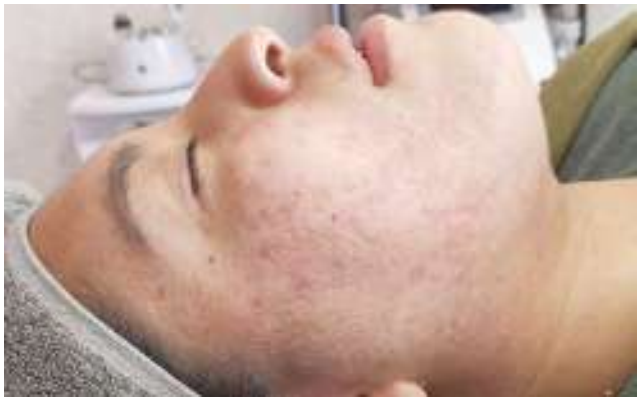
Dark Eye

- 45-year-old women
- Wrinkles and flaccidity of the lower eyelid
- Treatment: 3x, every 3 weeks, microneedling

Source: Dr. Karolina Pazera (Poland)

Acne with IPL/Microneedling



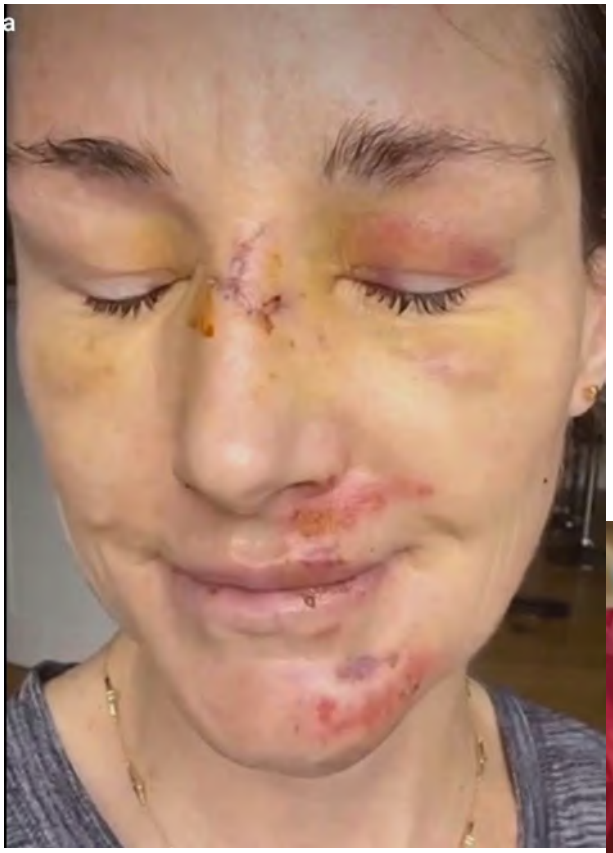


- Interval and Sessions: 6 sessions with an interval of 4 weeks
- Treatment methods: Microneedling
- Procedure: Before starting the protocol, a deep facial cleansing was performed. Skin care was indicated for the patient using SVR Sebiaclear gel mousant every 12 hours, Metrogel every 12 hours, SVR hydra every 12 hours, SVR Pretector Blur every 4 or 6 hours, and Vastionin 20 mg 1 every third day.
- After 15 days, the first exosome session was performed, the first **IPL** was used, followed by pisacain spray along with telica. After 10 minutes the micropuncture began with 0.25 mm and at the end we finished with 20 minutes of chromotherapy (red and blue).
- This protocol was performed every 4 weeks for 5 more occasions.

Source: Dr. Cinthya Susana Rodriguez Solis (Mexico)

Clinical Cases

- Serious bike accident
- Microneedling with ASCE plus



Source: Anna Tsankova, UK

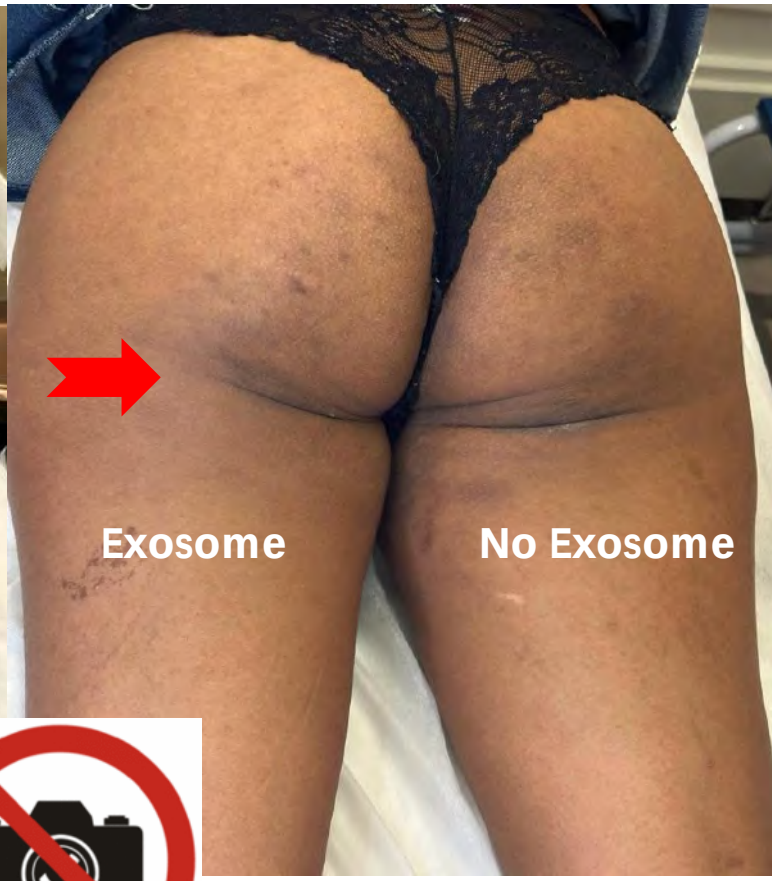
Dermatitis & Thulium Laser Combination (Brazil)

Dr. DANIELA LEMES

LAVIEEN 1927nm
Thulium Fractional Laser

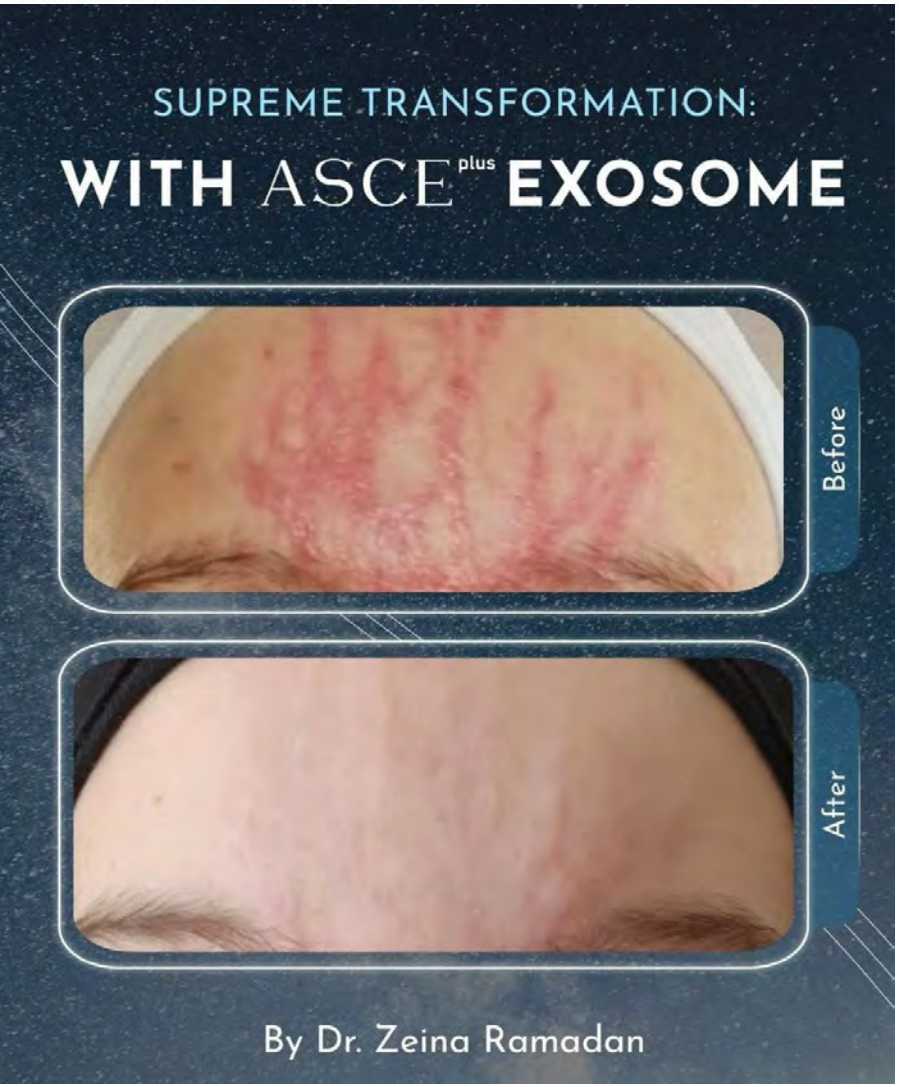
Before

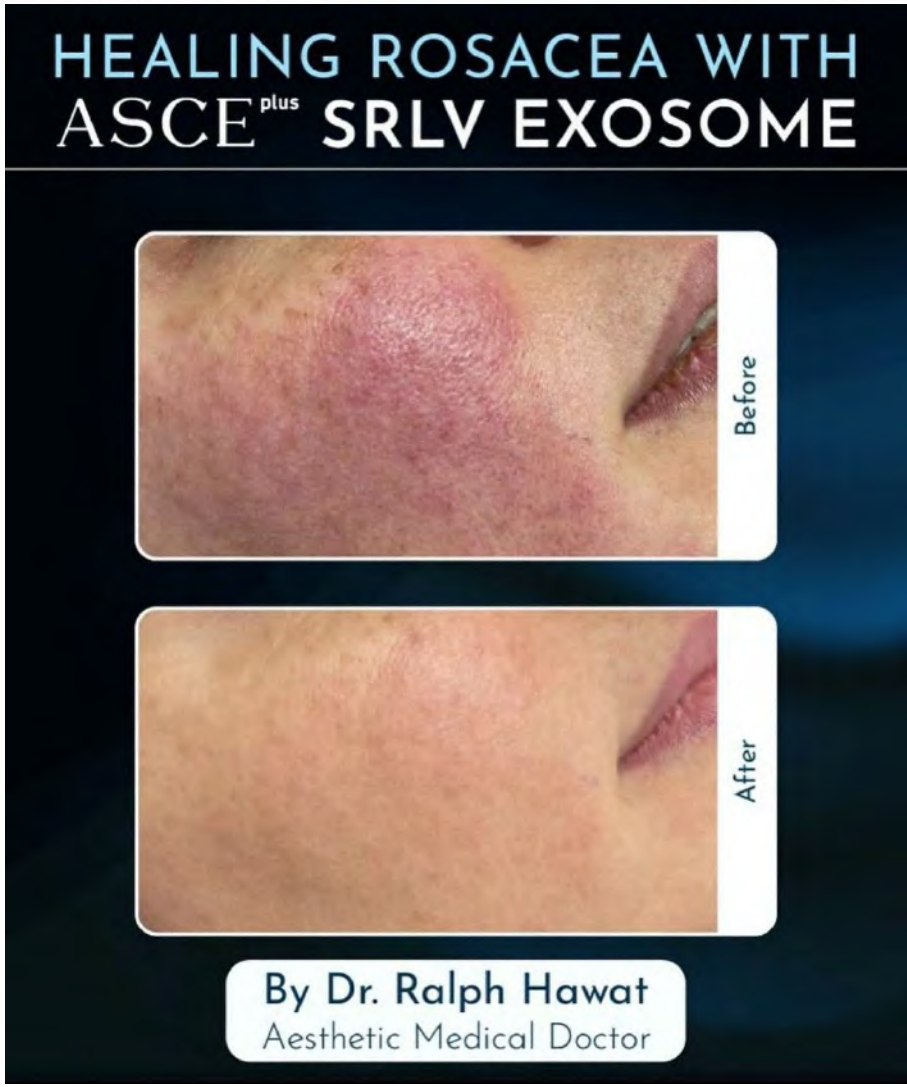
After



Clinical Cases

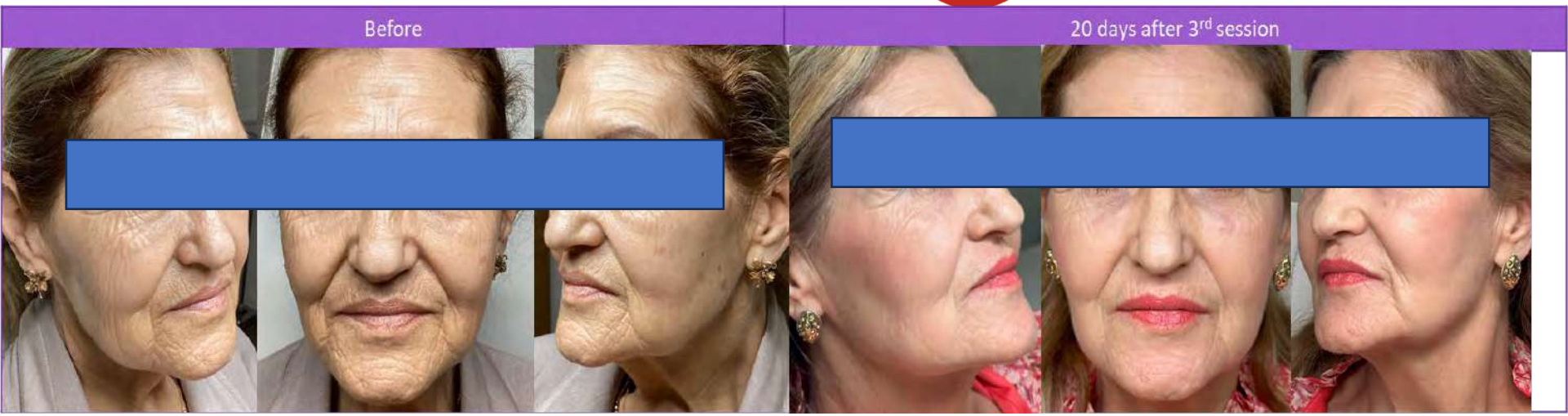
Clinical Cases





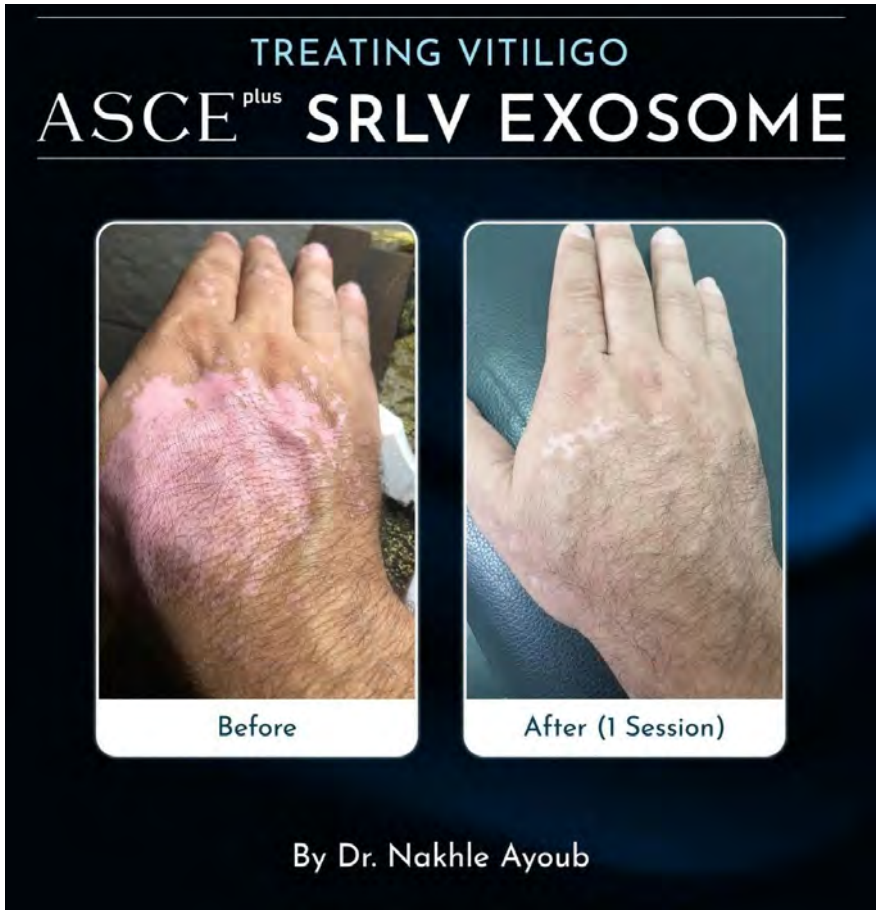
Clinical Cases

Clinical Cases

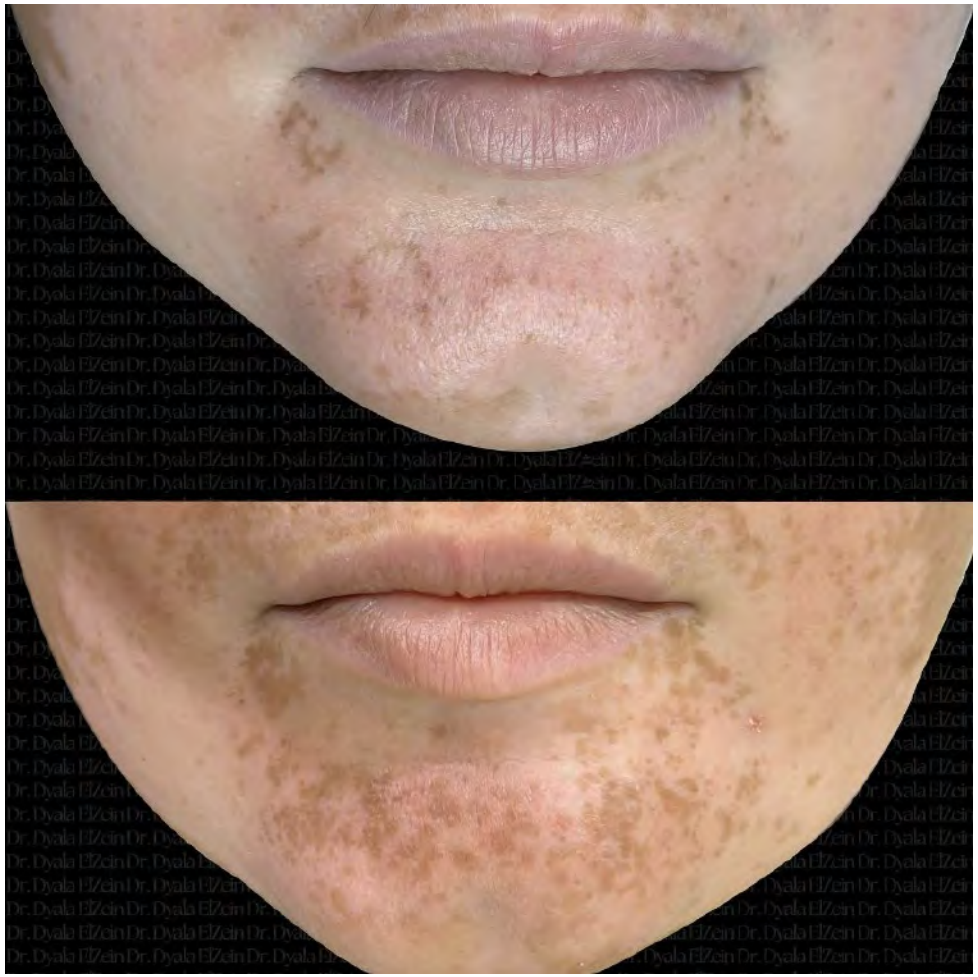


Indication	Facial Rejuvenation	Device	CO2 laser	Rose or Human	Rose
Treatment	1 Month	Treatment	3	Product	SRLV
Detail	• Co2 Laser accompanied by exosomes because the patient has thin and sensitive skin. • Doing Co2 resurfacing and with the help of exosomes to tighten and improve the quality of the skin in all aspects at the same time. • Faster recovery and less symptoms post co2 laser using exosomes vs not using them.				
Doctor	Itzel Durand	Country	Mexico		

Clinical Cases



Clinical Cases: Vitiligo

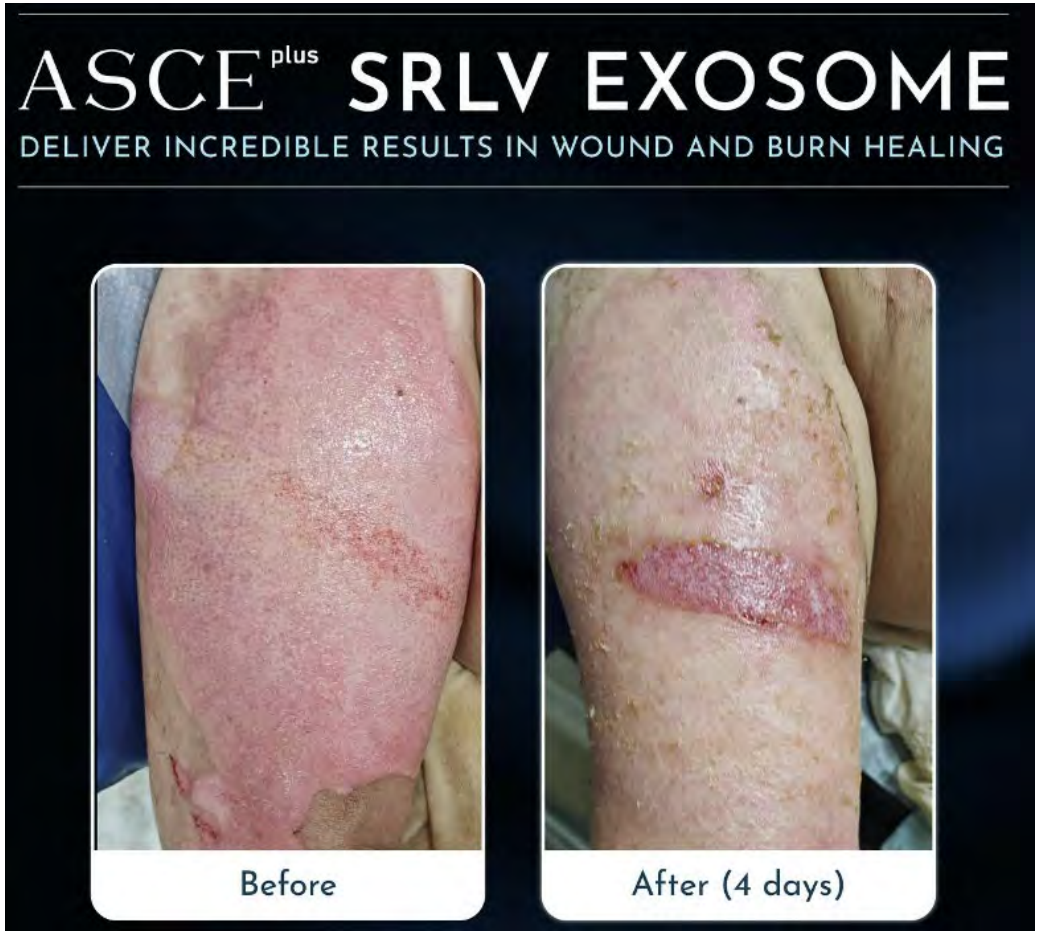


Dr. Dyala Elzein (Beautologyclinic) ft. ExoCoBio ASCE SRLV (Exosomes)

#Vitiligo treatment with ASCE exosomes due to its immunosuppressive and anti-oxidative properties acting on two mechanisms of vitiligo: autoimmune response & excessive oxidative stress leading to epidermal melanocyte destruction.

🏆 Results above are after ONE SESSION ONLY.

Clinical Cases



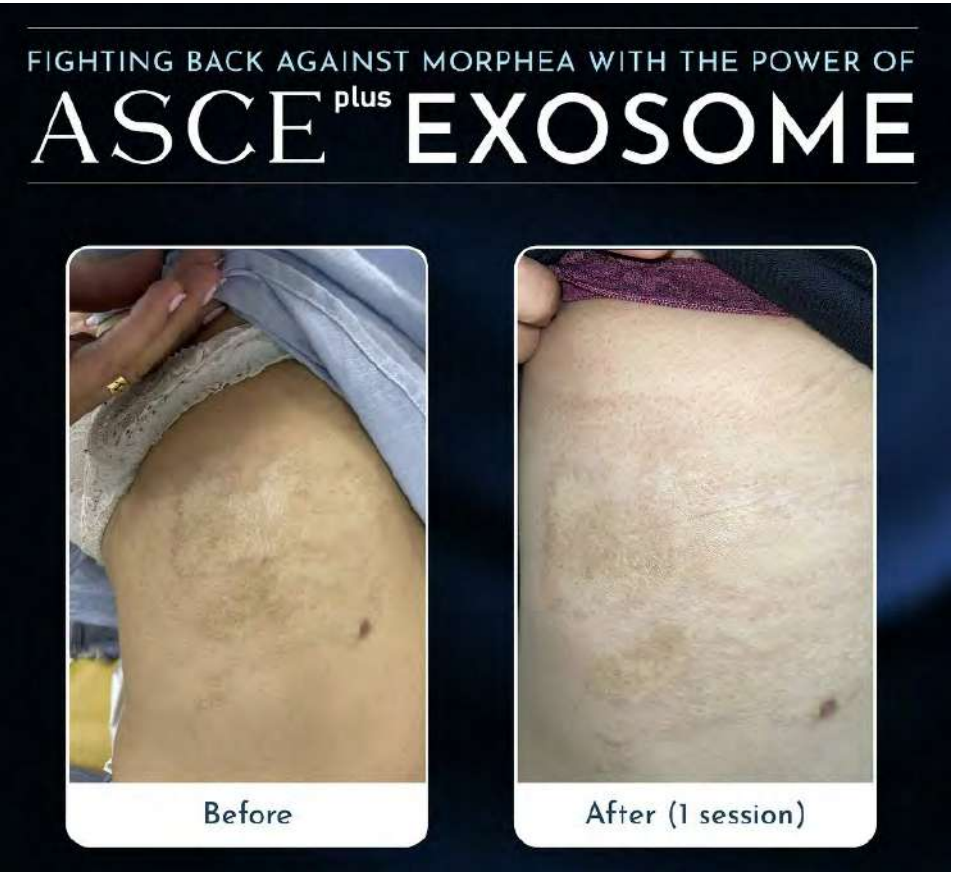
- Dr. @omar.tabbouche , a wounds and burns specialist from the University of Southern Indiana, has been a consultant in Lebanon since 2013. He also specializes in Molecular Diagnostics, Pain Management, and Anticoagulant Therapy.
- Dr Tabbouche was the first in Lebanon to explore the effect of ASCE+ SRLV Exosomes on deep second degree burns.
- For this treatment, the wound was cleansed with normal saline, dried with sterile gauze, ASCE+ SRLV was applied with gentle tapping. A paraffin tulle dressing and fusidic acid ointment were used to enhance absorption, followed by sterile gauze and a bandage.

Clinical Cases

Dr. Zeina Nehme (Lebanon)

Dr. Nakhle Ayoub (Lebanon)

Morphea (Dr. Ghada Kassir, Lebanon)



Melasma

applied sciences

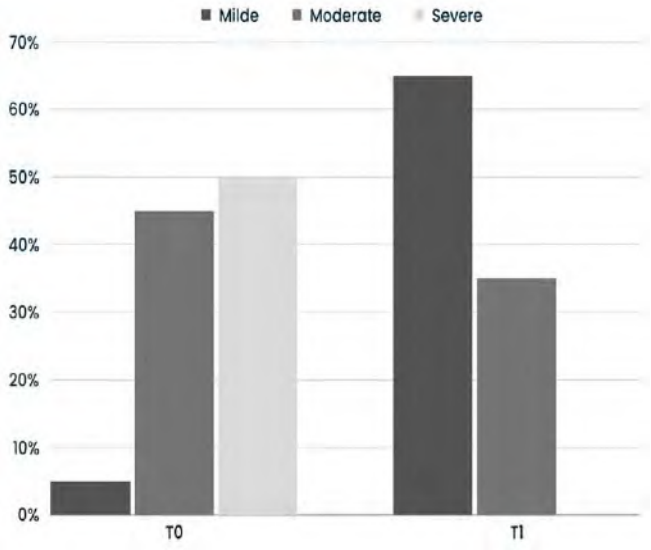
MDPI

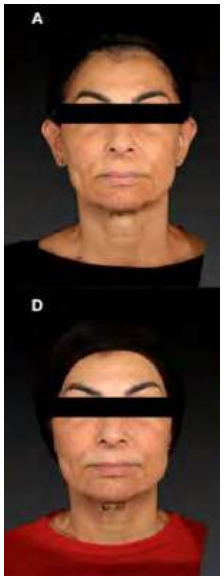
Article

Efficacy and Tolerability of a Microneedling Device Plus Exosomes for Treating Melasma

Ilaria Proietti [1,†], Chiara Battilotti [1,*,†], Francesca Svara [1], Carlotta Innocenzi [1], Alessandra Spagnoli [2] and Concetta Potenza [1]

Abstract: Melasma is a challenging skin condition that involves both structural and functional skin alterations. Despite the availability of various treatment options, the management remains complex. This is the first study to investigate topical application of Rosa damascena stem cell exosomes when used concomitantly with microneedling in women and men with facial melasma. We recruited 20 subjects with Fitzpatrick skin types I-III, exhibiting melasma of varying severity. The modified Melasma Area and Severity Index (mMASI) and Global Aesthetic Improvement Scale (GAIS) were utilized to evaluate treatment response. The treatment protocol involved microneedling followed by exosome application over four or five sessions, at 4-week intervals. Ninety percent of subjects demonstrated a significant improvement in mMASI scores, while only 10% showed no change. GAIS assessment further supports overall improvement, with just 10% categorized as "not changed". Tolerability was favorable, with mild, transient side effects. Our findings suggest promising outcomes with this combined therapy, underscoring its potential as a safe and effective approach for treating melasma, particularly in severe and moderate cases. However, further research with larger sample sizes and control arms is warranted to validate these findings and explore long-term efficacy.





Clinical Cases

Before (frontal)	Before (right lateral 37 °)	Before (left lateral 37 °)	after 5th Session (frontal)	after 5th Session (right lateral 37 °)	after 5th Session (left lateral 37 °)

Indication	Facial Melasma	Device	SkinPen Precision System, USA	Rose or Human	Rose
Treatment Interval	4 week	Number of Treatments	5	Product name	ASCE plus SRLV
Detail	1. Microneedling Treatment with Exosomes: • Device: Microneedling device (SkinPen Precision System, USA) featuring 14 solid needles • Diameter: 0.25mm • Operation Speed: from 6300 to 7700 rpm • Max. extension of the cartridge needles: less than 2.5mm • Intervention: Dermapen equipped with 1.5mm long needles. And followed by topical application of ASCEplus SRLV exosomes • Application: Maximum five sessions with 4-week intervals 2. Application Areas: Only facial area affected by melasma				
Doctor Name	Dr. Ilaria Proietti	Country	Italy		

Pigmentation

AESTHETIC SURGERY JOURNAL
OPEN FORUM

A New Therapeutic Approach With Rose Stem Cell Derived Exosomes and Non- Thermal Microneedling for the Treatment of Facial Pigmentation

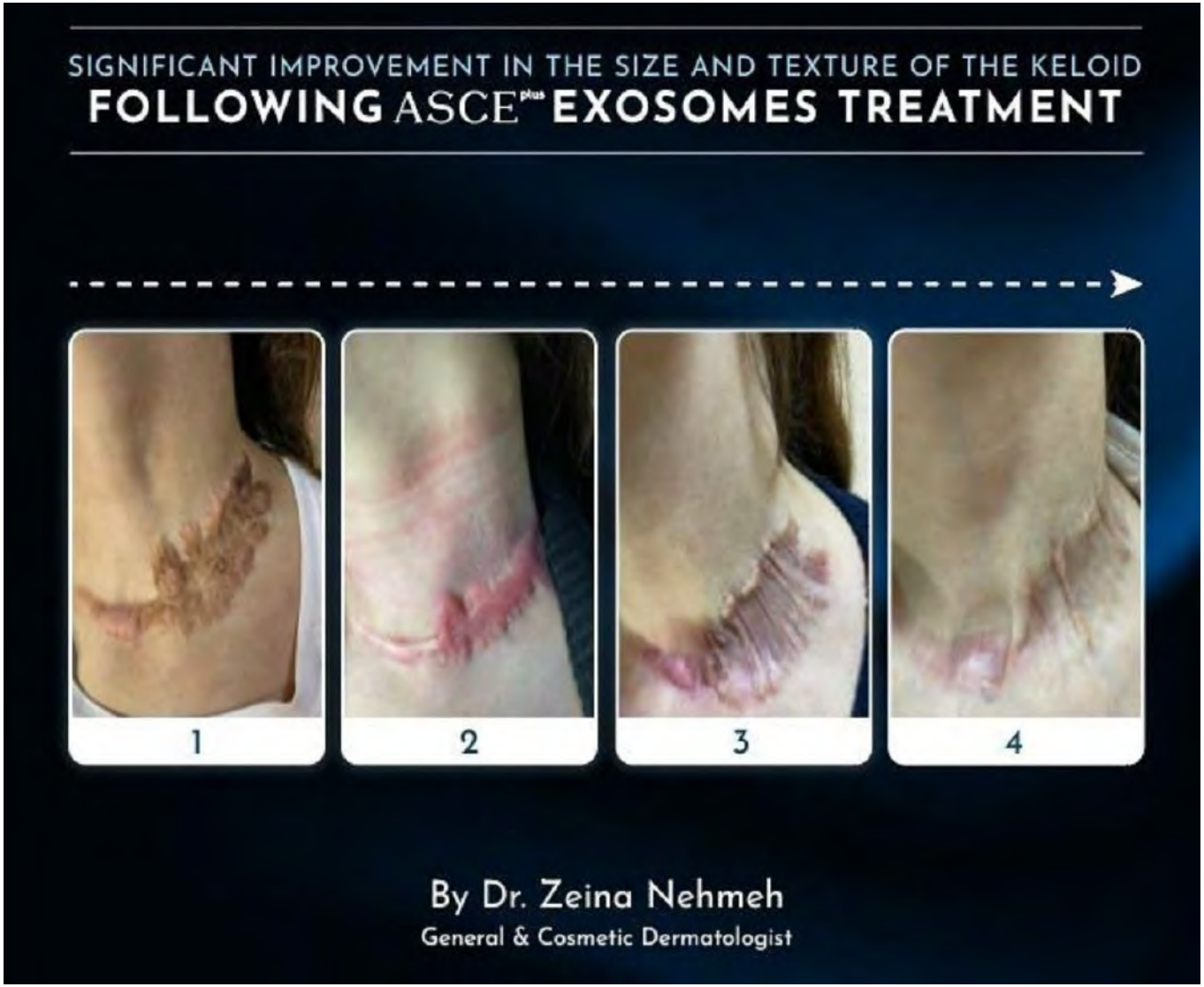
Elina Theodorakopoulou, MD, PhD, Shino Bay Aguilera, DO, FAAD, Diane Irvine Duncan, MD, FACS

Objectives This study using rose stem cell derived extracellular vesicles (RSCE) was performed as a proof-of-concept case series to evaluate the efficacy and safety of microneedling and topical RSCE, for the reduction of pigmentation and photoaging in adult volunteers.

Methods Twelve female volunteers were recruited, with a mean age of 46.64 years and a moderate to severe facial pigmentation, due to solar lentigines, melasma, post inflammatory hyperpigmentation and periorbital hyperpigmentation. Three treatments were performed at three weeks intervals. These consisted of the topical application of RSCE with microneedling and a 20 minute LED-light with an RSCE infused mask. A 3D facial analyzer was used to quantify improvement in superficial, deep pigmentation, skin redness and wrinkles at baseline, weeks 3, 6, and 12. GAIS, DLQI and MELASQoL scores were noted at the same timepoints.

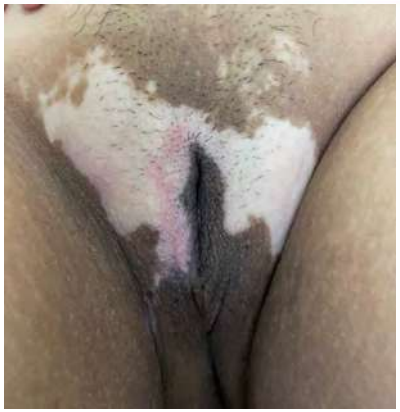
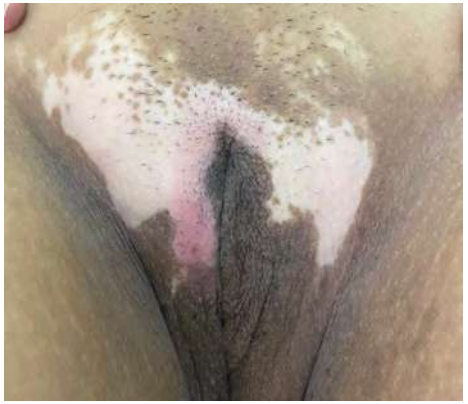
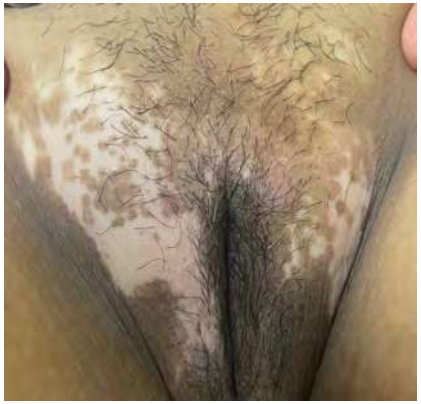
Results Gais scores improved by at least one scale point. **Superficial pigmentation and spots decreased by 12.95% and deep pigmentation improved by 15.9%, by week 12**. Skin redness was reduced by 7.34% at the same timepoint. Measured wrinkle reduction was 6.34%. DLQI scores were reduced by 10 points, and MELASQoL scores had a mean reduction of 30 points at week 12.

Clinical Cases: Keloid



- 30s/F
- 6 sessions, Morpheus
- Dr. Zeina Nehme (Lebanon)

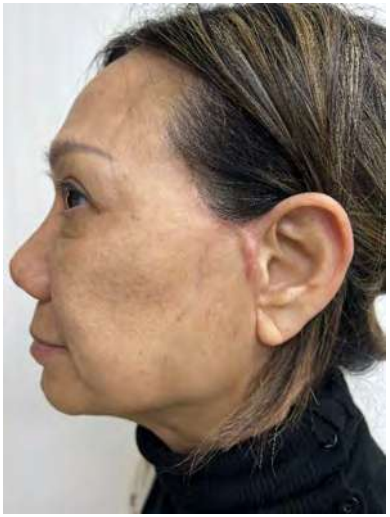
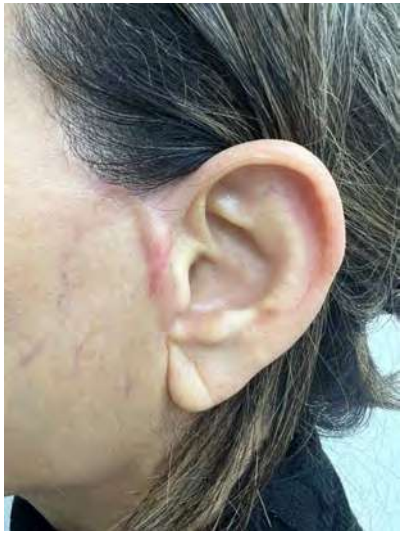
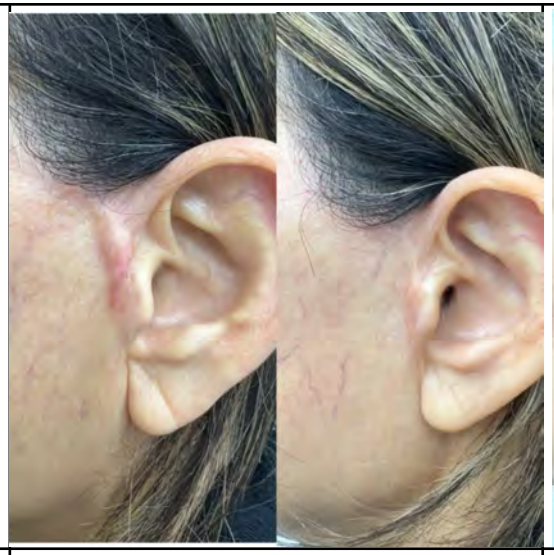
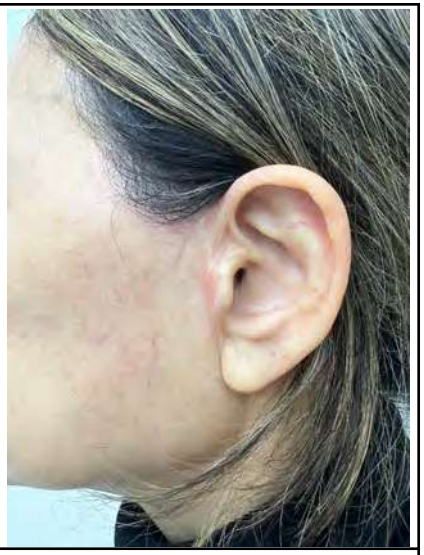
Clinical Case (Dr. Ruri Pamela)

			
Before 1	**Before 2**	**After 1**	**After 2**
• A patient with vitiligo affecting the vulvar region underwent narrowband ultraviolet B (NB-UVB) therapy for 4 months. Despite consistent treatment, the patient demonstrated minimal repigmentation in the affected area.	• vitiligo lesion at the vulvar area	• Visible repigmentation observed one month after the first treatment, utilizing topical adipose-tissue exosome application assisted by fractional picosecond 755 nm laser therapy.	• More significant repigmentation was observed six weeks after the second treatment using topical adipose-tissue exosome application assisted by fractional picosecond 755 nm laser.

- **Age of the patient** : 36
- **Treatment type** : Laser fractional 755 nm picosecond assisted topical delivery of adipose-tissue exosome
- **Treatment duration** : 2 sessions one month apart
- **Procedure description :** A 36-year-old female presented with vulvar vitiligo refractory to NB-UVB phototherapy. The patient had undergone NB-UVB (Waldmann™ UV Therapy System 7002, Villingen-Schwenningen, Germany) for four months but achieved minimal repigmentation. A novel combination treatment involving fractional picosecond 755 nm laser (Picosure™, Cynosure Lutronic, Masschusetts, USA) and topical adipose tissue-derived exosomes (ExoCoBio™ Inc., Seoul, Republic of Korea) was explored as a potential approach to influence melanocyte activity and migration. The sessions were spaced one month apart, and clinical assessment occurred six weeks following the second session.
- **Products utilized (brand and type) :** Combination treatment involving fractional picosecond 755 nm laser (Picosure™, Cynosure Lutronic, Masschusetts, USA) and topical adipose tissue-derived exosomes (ExoCoBio™ Inc., Seoul, Republic of Korea)
- **Result description :** Significant repigmentation was observed six weeks after the second session, with hyperpigmented areas in the previously depigmented regions.

Best Complication (Dr. Alicia Hann)

Post-rhytidectomy hypertrophic keloid pre-auricular scar management with combination therapy of Triamcinolone, dual-wave Radiofrequency microneedling and Exosomes

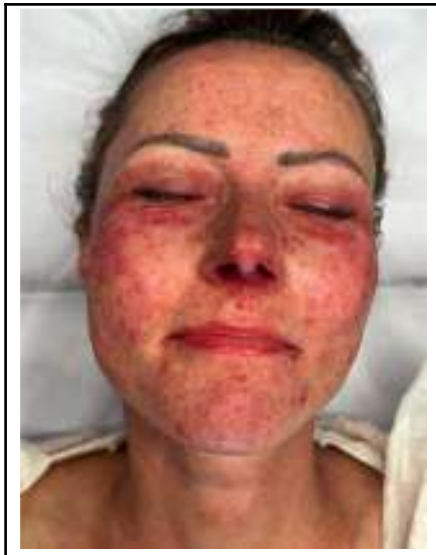
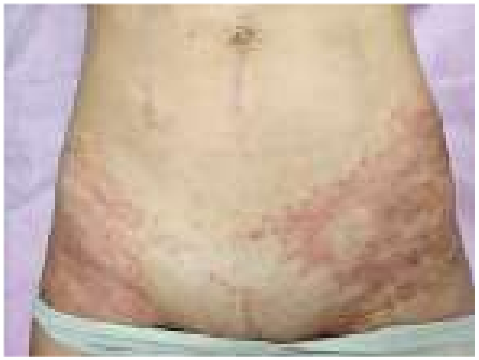
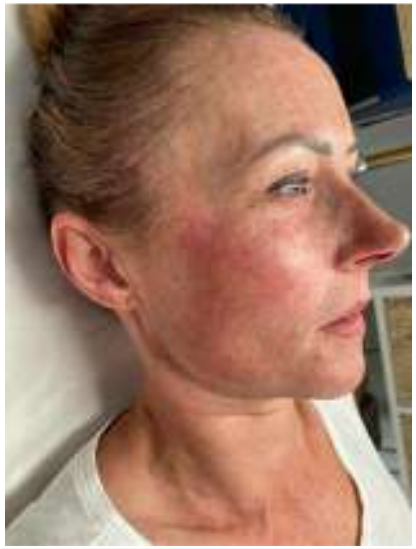
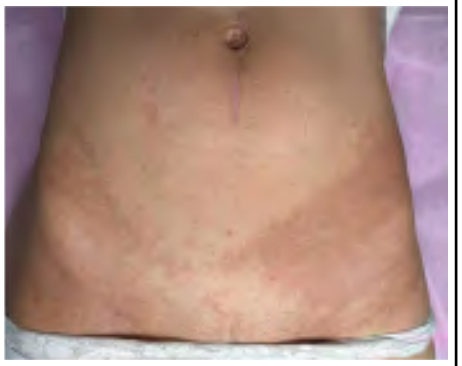
Before 1	Before 2	After 1	After 2
			
• This patient (my dearest mother) felt depressed one day in February 2024 and without much thought, walked into the nearest clinic in a busy shopping mall and asked for a face lift immediately. The plastic surgeon gave her the said face lift, immediately, with temporal and pre-auricular access. This would be her second face lift, her first one being 30 years ago. • However, after this particular surgery, likely related to poorly placed incisions, the patient developed temporal hair loss and a very conspicuous hypertrophic pre-auricular scar that was around 4cm in vertical length.	• Not only was the pre-auricular hypertrophic keloid 4cm scar unsightly, her midface nasolabial folds, marionette lines and jowls did not improve, with the addition of the scar tissue that persisted for more than half a year. There is also clear evidence of the pixie ear complication. Here, it shows that repeated forceful face lifts can cause complications such as keloids.	• After a combination therapy of Triamcinolone, dual wave Radiofrequency microneedling and Exosomes in 2+5 separate sessions, you can see that the post-repeated-rhytidectomy keloid scar is relatively undetectable in comparison.	• This combination therapy works in this rare clinical picture case.

Best Complication (Dr. Alicia Hann)

- **Age of the patient** : 68
- **Treatment type** : Intralesional Triamcinolone, Pulsed Wave RF microneedling and Exosomes.
- **Treatment duration** : 4 months
- **Procedure description :**
  - Treatment plan was split into 7 sessions. The 1st session was to purely inject 0.5mL of Triamcinolone mixed with Lignocaine first to decrease the bulk of the pre-auricular hypertrophic keloid surgical scar along with Exosomes via microneedling. The 2nd session was repeated of the above. Dual-wave RF microneedling was not commenced in the 1st and 2nd session due to Physics - skin hydration / injected solutions such as tumescent anaesthesia significantly lowers impedance therefore the RF settings must be adjusted (the power must be lowered and pulse duration adjusted to account for the decreased resistance in the circuit and maintain precise energy delivery), which would have affected the results and may have added on unnecessary risk of burns. The hypertrophy part of the scar was completely flattened after the 2 treatment sessions.
  - The 3rd to 7th sessions were purely dual-eave RF microneedling + Exosomes microneedling per session, spaced 2-3 weeks apart. The settings of the RF microneedling were: Pulsed Wave 4 mode at 2.5mm depth, energy Level 3, with 2-3 passes along the scar until a strong erythema is achieved. 5mL of STEM CELL DERIVED LYOPHILIZED EXOSOMES (Exosome Regenerative Complex) was subsequently applied directly over the red scar with a microneedling device.
- **Products utilized (brand and type) :** Triamcinolone (full concentration) 0.5mlx2 sessions / SylfirmX 5 sessions / Benev ERC+ Exosomes x 5 sessions
- **Result description :** This complicated case recovered, and it shows that minimally invasive methods can help rare cases like these, which is a hopeful step towards the future for both physicians and patients.

Clinical Case (Dr. Lidia Majewska)

Exosome-Based Therapy for Skin Complications in Oncology Patients Treated with EGFR Inhibitors: A Case Report Highlighting the Need for Coordinated Dermato-Oncologic Care

			
Before 1	**Before 2**	**After 1**	**After 2**

- **Age of the patient** : 41
- **Clinical signs**
  - In December, 2023, the patient underwent surgery for colorectal cancer, and starting in February 2024, she received 12 cycles of chemotherapy with FOLFOX + panitumumab.
  - In May 2024, severe pustular eruptions and acneiform rash appeared on the skin of the face, accompanied by redness, burning, and a deep sensation of inflammation. The skin felt noticeably warm to the touch. Patient reported that the pain around the eyes and nose was even more pronounced, and she experienced intense itching of the skin all over her body, more pronounced in the abdominal area.
- **Diagnosis (Anamnese, lab tests, etc.)**
  - Patients who receive epidermal growth factor receptor inhibitor (EGFRi) in the treatment of metastatic colorectal cancer develop skin side effects, with approximately 10% to 20% of patients experiencing grade 3/4 toxicity. In 2007, 32% of oncology providers reported discontinuing EGFRi therapy due to a rash. Hair loss, hyperpigmentation, and dry skin are also frequently reported skin toxicities during EGFRi therapy. Because of the key role of EGFR signaling in skin, dermatological toxicities have frequently been described with EGFRIs. The resultant significant physical and psycho-social discomfort might lead to interruption or dose modification of anticancer agents. There is an urgent need for an improved understanding of these toxicities to develop adequate staging systems and appropriate therapies.

Clinical Case (Dr. Paul Han, Australia)

- **Presentation of the treatment step by step**
  - Topical application of the exosome product three times a day for three days over the face. After first application patient reported significant reduction of itching and burning. Healing process was visible 24h after first application with a significant reduction of rash. On the third day patient healed completely which was shown on the picture attached.
  - Skin changes on the abdomen were treated with moisturizing cream containing exosomes, tranexamic acid, nicotineamide, D-panthenol and madecassosid. Patient reported reduction of itching immediately after cream application. Complete recovery took three days. On the third day.
- **Why do you use this treatment approach?**
  - Following acneiform rash development, moisturising creams/balms, barrier repair creams and acne dermocosmetics with nicotinamide are recommended. The pharmaceuticals minocycline/doxycycline, systemic steroids, and TCS (where there is no local superinfection) are also recommended. Ultimately, dose adjustment of EGFR inhibitors may help overcome a difficult acneiform eruption.
  - More recently, EGF ointments have been proposed for treating EGFR inhibitor-induced skin toxicities, including acneiform rash however these products are not available on our market thus I thought about using exosome products which I already know and use in different dermatologic indications such as atopic dermatitis, acne atrophic scars, skin inflammation and improving wound healing. Rose stem cell-derived exosomes (RSCEs) offer a novel therapeutic approach in dermato-oncology due to their regenerative and anti-inflammatory properties.

- **Why do you use this treatment approach?**
  - For patients with skin cancers or those undergoing treatments that induce skin damage, RSCEs may enhance wound healing, support skin regeneration, and reduce inflammation without exacerbating cancerous processes. Their potential to promote collagen synthesis and repair damaged skin barriers could make RSCEs a supportive therapy, particularly for managing side effects from cancer treatments such as radiation or EGFR inhibitors.
  - Further research is needed to fully understand their impact in oncological settings, but initial findings are promising for integrative care in dermato-oncology. Recent studies have demonstrated that RSCEs can enhance the proliferation of human dermal fibroblasts and promote collagen synthesis, indicating their potential in skin regeneration and anti-aging treatments.
  - Additionally, RSCEs have been shown to reduce melanin production in melanocytes, suggesting applications in managing hyperpigmentation disorders. Their anti-inflammatory properties, evidenced by the downregulation of pro-inflammatory cytokines like IL-6, further support their use in treating inflammatory skin conditions.
- **Products or devices utilized (brand and type)**
  - For face: ASCE+Skin Rejuvenation Lyophilized Vial (SRLV)-S, ExoCoBio Inc., Seoul, Republic of Korea
  - For abdominal skin: ASCE+ EXOBALM, ExoCoBio Inc., Seoul, Republic of Korea
- **Result description**
  - Cutaneous side-effects are found in 100% of patients treated with EGFRIs for more than 6 months and have a significant effect on patients' QoL. The clinical spectrum of skin manifestation varies over time. As the use of EGFRIs rapidly increases, it is critical for us to improve our knowledge in the understanding and managment of these skin manifestations. Further research is needed to fully understand exosomes' impact in oncological settings, but initial findings are promising for integrative care in dermato-oncology.

ASCEplus + Morpheus8

Lichen Planus & Lip Rejuvenation (Microneedling)

어제 10:54 오후

Byong- I did the Exosome on the Lichen Planus on the lips and I saw him 3 days later and he said in 5 years this is the first time his lips aren't cracking and uncomfortable!! He is so happy we are going to do another one in 2 weeks 🥰 life changing!!

오늘 9:47 오후

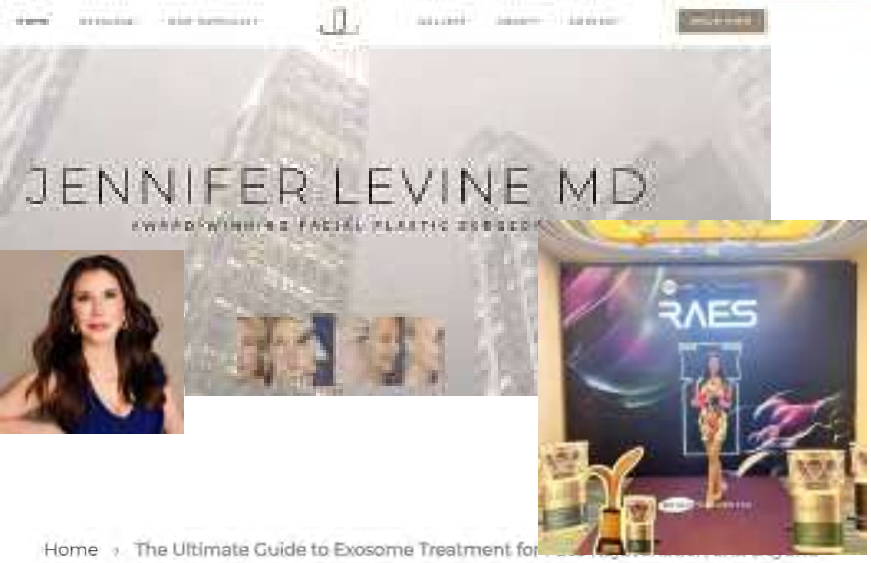
Hello so happy to hear that !!

Please share the photos before and after.

Let's try to publish 🥰🥰🥰🥰

메시지 보내기...

The Combination of Ultherapy and ASCEplus



Home › The Ultimate Guide to Exosome Treatment for

The Ultimate Guide to Exosome Treatment for Face Rejuvenation and Beyond

by Dr. Jennifer Levine

Exosome therapy is a pioneering technique that has garnered significant attention in the realm of regenerative aesthetics – and for good reason!

As research advances, the potential of exosomes in enhancing facial rejuvenation, hair restoration and skin challenges is proving to be a reality – see our incredible patient results below!

- Frax Laser Resurfacing with Exosomes

The Frax laser targets the skin's surface, initiating a healing response to reduce scars and fine lines. When combined with exosomes, the skin's recovery is not only expedited, but the resultant texture and tone improvements are markedly enhanced.

TIP: *This combination treatment can also be used on the body to reduce the appearance of stretch marks, skin laxity and cellulite!*

- Ultherapy with Exosomes

Ultherapy uses ultrasound energy to lift and tighten the skin. Introducing exosomes into the treatment augments the skin's natural response, promoting a firmer, more uplifted appearance with benefits that are more profound and longer-lasting.

TIP: *This combination treatment can also be used on the body to tighten and improve skin texture on arms, knees, elbows and more!*

- Microneedling or PRP with Exosomes

Source: https://www.drjenniferlevine.com/the-ultimate-guide-to-exosome-treatment-for-face-rejuvenation-and-beyond/

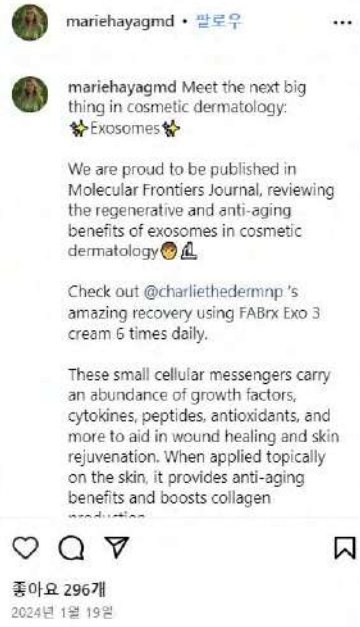
The Combination of Ultherapy and Exosome

Ultherapy + Exosomes Treatment

In New York, NY

By Marie V. Hayag, MD, FAAD

Marie V. Hayag, M.D., FAAD is the leading authority in the burgeoning area of topical exosomes. Her innovative product, FABrx EXO3 Exosomes, not only aids in immediate, visible results post Ultherapy treatment but enhances the long term effects for wrinkle reduction and lax skin for a younger, refreshed appearance.



Exosomes Skincare Product FAQs:

Can Exosomes be used in conjunction with Ultherapy?

Yes, using Exosomes alongside Ultherapy can complement the skin's rejuvenation process, promoting enhanced results and supporting overall skin health.

Souce: https://mariehayagmd.com/pages/ultherapy?srsltid=AfmBOorewOYFjCAoXJAJm6SerS3FWcL4HpzwNmjyrf3AekMwmifrXiR-

The Combination of Ultherapy and ASCEplus

Priming & Post-care

Better skin quality & Faster recovery

- Redness
- Swelling
- Bruising
- Tingling
- Temporary numbness