Journal of Clinical & Experimental Dermatology Research

OPEN ACCESS Freely available online

Short Communication

Gene Expression Changes Following Solar Skincare Protection and Repair Strategies in a 3-Dimensional Reconstructed Human Skin Model

Yohei Tanaka[1*], Keely Marsh[2], Amaryllis Aganahi[2], Richard Parker[2]

[1]Department of Plastic Surgery, Reconstructive Surgery and Anti-aging Institute, Matsumoto, Japan; [2]Department of Dermatology, Rationale Institute, Kyneton, Australia

DESCRIPTION

In this study, we investigated to find out how a skincare regimen consisting of formulations that target solar protection and repair (the rationale essential six) can positively influence the expression of genes responsible for skin health, resilience and vitality [1,2]. It is now commonly accepted in human dermatologic research that at least 80% of facial ageing is caused by the sun [1-10].

Even though many people use sunscreen and are aware of the importance of sun protection, skin damage from the sun remains a significant concern for skin health and beauty worldwide.

Despite this, very few studies examine the critical changes in gene expression and our skin's ability to repair itself on a holistic level after using solar protective and reparative skincare.

The overarching objective of such strategies is to offer a comprehensive protection and repair solution against all of the sun's energy, which comprises not only UV A and B, but also Visible Light (VL including blue light) and Near Infrared Radiation (NIR). This will allow for a better understanding of how the skin is able to defend itself against solar damage and also to highlight effective solutions to assist the skin in this endeavor. In order to achieve these results, several studies focused on different biochemical and biomechanical markers may be required. A major area of inquiry is the need to identify and document which specific genes are being up and downregulated following a solar protective and repair skincare regimen daily [1,2]. In previous in-vivo research, we assessed the efficacy of several of the solar protective and repair skincare formulations used in the below study. This research was conducted by a leading European laboratory assessing each formulation on panels of 20 to 25 subjects at a time for periods ranging from 28 to 56 days. The results obtained via skin physiological, dermatological and subject self-assessments, showcased significant visible skin improvements in tone and texture, which are the major visible hallmarks of cutaneous solar damage.

Typically, solar-specific formulations would not be used in an isolated manner but would be strategically combined in order to create an optimized skincare regimen focused on enhancing daytime skin protection and nighttime repair. From this research, a hypothesis was born. If each individual product provides significant improvement on an *in-vivo* level, what would be the synergistic outcomes on the skin when the formulations were applied in combination with this focus on targeted daily protection and nightly repair? This approach most realistically represents what patients would do "in real life". In order to validate this hypothesis, we partnered with a leading US genomics and gene sequencing laboratory to initiate an *in-vitro* study using a 3-dimensional reconstructed human skin model containing dermal fibroblasts and epidermal keratinocytes [1,2]. This study was carried in two parts to better identify the results of each day/night regimen (Table 1).

Solar protection formulations			Solar repair formulations		
#1 Serum	**#2 Serum**	**#3 Tinted serum**	**#4 Cream**	**#5 Serum**	**#6 Night cream**
Vitamin B, E	Vitamin A, C, E	Vitamin B, E, D precursor	Vitamin C, E	Alpha and beta hydroxy acids	Vitamin A, E

Correspondence to: Yohei Tanaka, Department of Plastic Surgery, Reconstructive Surgery and Anti-aging Institute, Matsumoto, Japan, E-mail: info@clinicatanaka.jp

Received: 02-Jan-2024, Manuscript No. JCEDR-24-29335; **Editor assigned:** 05-Jan-2024, Pre QC No. JCEDR-24-29335 (PQ); **Reviewed:** 19-Jan-2024, QC No. JCEDR-24-29335; **Revised:** 26-Jan-2024, Manuscript No. JCEDR-24-29335 (R); **Published:** 02-Feb-2024, DOI: 10.35841/2155-9554.24.15.656.

Citation: Tanaka Y, Marsh K, Aganahi A, Parker R (2024) Gene Expression Changes Following Solar Skincare Protection and Repair Strategies in a 3-Dimensional Reconstructed Human Skin Model. J Clin Exp Dermatol Res. 15:656.

Complex and essential fatty acids	Complex and essential fatty acids	Complex and essential fatty acids	Complex and essential fatty acids	Complex of lactic, citric, tartaric and salicylic acids	Complex and essential fatty acids
15 Amino acids	15 Amino acids	15 Amino acids	15 Amino acids	15 Amino acids	15 Amino acids
Humectants and penetration enhancers	Humectants and penetration enhancers	Humectants and penetration enhancers	Humectants and penetration enhancers	Humectants and penetration enhancers	Humectants and penetration enhancers
Australian botanicals extracts	Australian botanicals extracts	Australian botanicals extracts	Australian botanicals extracts	Australian botanicals extracts	Australian botanicals extracts
Plant extracts	Plant extracts	Plant extracts	Plant extracts	Plant extracts	Plant extracts
Hydro-lipophilic delivery system	Emollients and waxes	Emollients and waxes	Emollients and waxes	Hydro-lipophilic delivery system	Emollients and waxes
Stabilizers and preservatives	Stabilizers and preservatives	Stabilizers and preservatives	Stabilizers and preservatives	Stabilizers and preservatives	Stabilizers and preservatives
Thickener and emulsifiers	Thickener and emulsifiers	Thickener and emulsifiers	Thickener and emulsifiers	Thickener and emulsifiers	Thickener and emulsifiers

Table 1: Rationale formulations used in this study categorized by day/night application. **Note:** #: The naming system of each product, i.e., "#3 Tinted serum SPF 50" means "Number 3 tinted serum SPF 50.

Each formulation has been bioengineered to be highly compatible with skin physiology and to facilitate delivery of active ingredients to their specific epidermal and dermal targets. The delivery systems of these formulations are all different and created to provide stability and bioavailability of active ingredients and synergistic activity between actives from each formulation. This involved assessing the compatibility of each of the active ingredients with each other and with skin physiology, as well as ensuring that the application and skin penetration of each active is optimal and synergistic. For example, #5 The serum has been developed with a low pH in order to optimize the penetration and efficacy of the Alpha-Hydroxy Acid (AHA) and Beta-Hydroxy Acid (BHA) complex. The thickeners, stabilizers and humectants used in this formulation as well as the humectants are all compatible with low pH and initiate acidic pH recalibration of the stratum corneum and its desirable enzymatic and non-enzymatic metabolic effects on skin barrier function.

As a first step, the laboratory assessed the cytotoxicity of each formulation and total regimen on skin tissues performing a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) viability analysis. The individual products of each regimen (photo protective and photo repair) were applied on three sets of tissues each. One tissue sample was treated with 1%Triton X-100 as a negative control and two tissues were left untreated as a positive control. 24 hours after application results revealed that tissues inoculated with each regimen displayed a cell viability percentage higher than 90% which provides confidence that any changes in gene expression were not impacted by product toxicity.

The second step was to assess gene expression changes within these tissues after inoculation with the day and night regimens.

The essential six steps 1, 2 and 3 for solar protection were applied to the reconstructed human skin tissues, then changes in gene expression were measured. Next, steps 4, 5 and 6 for solar repair were applied to another set of tissues and gene expression changes were also examined. Our research revealed that out of 107 genes assessed, 67 genes responsible for skin health were significantly up or downregulated following usage of a typical rationale essential six regimen.

The results discussed in the study have been selected out of those 67 genes as the most representative and significant (Table 2).

Photoprotection/photorepair genes upregulated	Gene functions	Details
Intercellular Adhesion Molecule 1 (1CAM1)	Skin immune protection	Regulates skin immunologic responses. Induced by environmentally stimulated proinflammatory cytokines.
Metallothionein 1A (MT1A)	Antioxidation protection	Regulates cellular anti-oxidant detoxification.

		Reduces free radical activity, oxidative damage and inflammation.
Prostaglandin-Endoperoxide Synthase 1 (PTGS2)	Environmental protection	Regulates epidermal and dermal homeostasis in response to solar and environmental damage
Late Cornified Envelope 3D (LCE3D)	Skin barrier repair	Protein coding gene. Regulates keratinization and barrier repair.
Peroxisome Proliferator Activated Receptor (PPARD)	pH recalibration	Acidic activated transcription factor of the nuclear hormone receptor family. Stimulates epidermal differentiation, regulates apoptosis, reduces epidermal proliferation and inflammation and enhances barrier repair.
Granulocyte/Macrophage Colony Stimulating Factor 2 (GM-CSF2)	DNA repair	A cytokine that regulates DNA repair processes. Upregulates expression of extracellular matrix proteins, including tenascin, fibronectin and collagen-1 in fibroblasts. Stimulates differentiation of epidermal melanocytes in response to UV exposure.

Table 2: Significantly up-regulated 6 genes and their functions.

Based on a typical rationale essential six regimen for the morning routine targeting solar protection, we recorded upregulation of genes responsible for skin immune protection by 278%, antioxidant protection by 86,000%, and environmental protection by 1389% respectively. The results for the solar repair regimen at night were equally impressive, resulting in an upregulation of genes responsible for skin barrier repair by 409%, pH recalibration by 142% and a Deoxyribonucleic Acid (DNA) repair by 1251%. In summary, we were able to demonstrate that genes responsible for solar skin protection and repair were exponentially upregulated in a 3-D reconstructed human skin model following application of rationale solar protection and repair skincare formulations (Table 3). This study suggests that there exist endogenous and exogenous mechanisms and pathways for skin protection and repair from solar radiation beyond daily sunscreen use. These findings are of great relevance in environmental dermatologic research, with implications and a call-to-action for further investigations into the role of skin immunity, antioxidants, zinc oxide UV filters, barrier lipids, skin pH and DNA repair mechanisms can play when synergistically deployed in daily solar skin protection and repair strategies and regimens.

Formulation	**Gene functions**	**Photoprotection/photorepair genes upregulated**
#1 Serum	Skin immune protection	Intercellular Adhesion Molecule 1 (1CAM1)
#2 Serum	Antioxidation protection	Metallothionein 1A (MT1A)
#3 Tinted serum	Environmental protection	Prostaglandin-Endoperoxide Synthase 1 (PTGS2)
#4 cream	Skin barrier repair	Late Cornified Envelope 3D (LCE3D)
#5 Serum	pH recalibration	Peroxisome Proliferator Activated Receptor (PPARD)
#6 Night cream	DNA repair	Granulocyte/Macrophage Colony Stimulating Factor 2 (GM-CSF2)

Table 3: Rationale essential six regimen and significantly up-regulated genes.

CONCLUSION

This study provided evidence that this targeted skincare regimen focused on daily solar protective and nightly repair processes significantly and positively influenced skin gene expression. The results obtained suggest that supplementing the skin daily with various skin identical components (such as vitamin A, B, C, D, E, amino acids) as well as with essential components that the skin is unable to produce itself (such as essential fatty acids and certain peptides and enzymes) can assist is creating desirable biochemical and biomechanical alterations that significantly impact skin health and beauty.

Understanding the complexity of the skin and its functioning, the next step would be to perform an *in-vivo* study with the same photoprotective and photorepair skin care regimen over a period of 28 to 56 days. This follow up research would establish whether *in-vivo* results correlate to *in-vitro* and clinically observed outcomes. The resultant data would also increase our knowledge of how to proactively enhance skin solar protection and repair processes and the epigenetic mechanisms involved.

REFERENCES

1. Tanaka Y, Parker R, Aganahi A. Up-regulated expression of ICAM1, MT1A, PTGS2, LCE3D, PPARD, and GM-CSF2 following solar skincare protection and repair strategies in a 3-dimensional reconstructed human skin model. Clin Cosmet Investig Dermatol. 2023:2829-2839.
2. Tanaka Y, Parker R, Aganahi A. Up-regulated expression of SOD2 and HPRT1 following topical photoprotection and photorepair skincare formulations in a 3-dimensional reconstructed human skin model. J cosmet dermatol. 2023;13(04):322-332.
3. Tanaka Y, Gale L. Beneficial applications and deleterious effects of near-infrared from biological and medical perspectives. 2013;3(4):1-9.
4. Tanaka Y, Gale L. Protection from near-infrared to prevent skin damage. Opt Photonics J. 2015;5(04):113-118.
5. Tanaka Y. Long-term objective assessments of skin rejuvenation using solar protection and solar repair shown through digital facial surface analysis and three-dimensional volumetric assessment. Clin Cosmet Investig Dermatol. 2019:553-561.
6. Tanaka Y. Three-dimensional quantification of skin surface displacement following skin rejuvenation using solar protection and solar repair. J Clin Aesthet Dermatol. 2020;13(7):47.
7. Tanaka Y. Photoprotective ability of sunscreens against ultraviolet, visible light and near-infrared radiation. Opt Photonics J. 2023;13(6):140-146.
8. Tanaka Y, Parker R, Aganahi A. Photoprotective ability of colored iron oxides in tinted sunscreens against ultraviolet, visible light and near-infrared radiation. Opt Photonics J. 2023;13(8):199-208.
9. Tanaka Y, Parker R, Aganahi A, Pedroso A. Novel low viscosity zinc oxide, iron oxides and erioglaucine sunscreen potential to protect from ultraviolet, visible light and near-infrared radiation. Opt Photonics J. 2023;13:217-226.
10. Marsh K, Coppa B, Matten K, Parker R, Tanaka Y. A non-invasive skin treatment combining led with pharmacologic and ultrasonic technologies for facial rejuvenation. J cosmet dermatol. 2023;13(04):333-344.