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Improvement of the Dermal-Epidermal Junction (DEJ) and skin appearance by a plant-derived PPAR-α agonist complex

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Highlights

1. Validation of PPAR-α as a highly relevant target for skin care products,
2. Description of a cosmetic clinical study using a botanical complex with significant PPAR-alpha activation and collagen IV stimulatory activity,
3. Presentation of the cosmetic outcomes achievable with a DEJ-targeting PPAR-alpha activator.

Opportunity

This presentation teaches a new cooperative multi-molecular approach to quantitatively improve skin aging parameters, such as roughness, wrinkles and sagging.

Rationale

PPAR-α, a nuclear receptor, has been reported to exert a homeostatic role in human skin. Traditionally, PPAR-α activators have been applied in skin care for improving barrier function by inducing synthesis of ceramides, other barrier lipids and proteins. However, given that PPAR-α analogs have been implicated in the regulation of collagen metabolism, we developed a new cooperative PPAR activator, and examined its relevance at the level of DEJ, where collagens play key structural and functional roles. This approach was further warranted by the published reports, showing that with age, the activity of the cutaneous PPAR-α decreases, while the DEJ undergoes chronological degradation marked by a decline of collagen IV and other anchoring proteins. Taken together, these observations raised an exciting question whether a PPAR-α agonist may produce an improvement in the visible signs of aging skin by acting at the DEJ.

Results

1. Derived from olive leaf and castor oil, our PPAR-α agonist complex [oleanolic acid & glyceryl monoricinolate] activated PPAR-α by cooperatively acting on its two distinct regulatory sites.

2. Collagen IV, a key anchoring protein in the DEJ, whose output decreases with age, was upped by this treatment both in skin cells and skin explants.

3. In a 45-day split-face image analysis clinical case study, a significant improvement of multiple age-related parameters was observed with the PPAR agonist complex/niacinamide cream but, interestingly enough, not with the niacinamide placebo.

Fig. 1. In silico modeling: a PPAR-α agonist complex containing oleanolic acid and glyceryl monoricinolate – docked in the active site of the PPAR-α protein (PDB ID: 2P54) at a distance criterion of 5 Å, demonstrates distinct regulatory sites and possibility of cooperative activation.

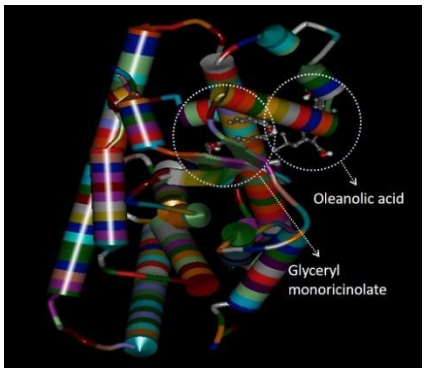

Fig. 2. Cell culture: Dose-dependent stimulatory effect of PPAR agonist complex on the synthesis of collagen type IV in human dermal fibroblasts expressed as percentage of water control wherein 50 µg/mL MAP is a positive control. Data are presented as mean values ± SEM, n = 6; **p-value < 0.01 vs. water blank.

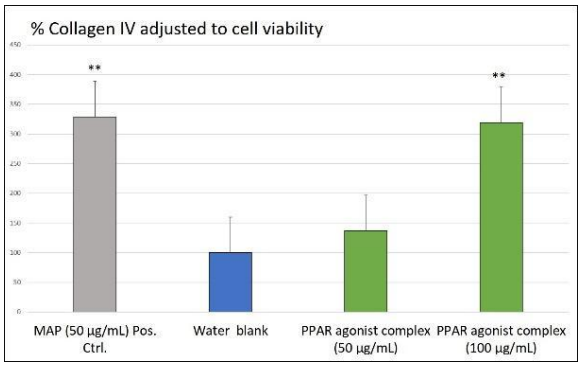

Fig. 3. Cosmetic clinical study image analysis: Mean percent (%) variation in the Rz parameter (mean depth of roughness) between niacinamide placebo and PPAR agonist complex/niacinamide cream. *p values refer to a statistically significant variation value when below 0.05.

Conclusion

Here we demonstrated that PPAR-α is a functional target for treating chronological aging, and a PPAR agonist complex is capable of stimulating type IV collagen in the DEJ. Upregulation of PPAR-α activity by plant-derived cooperative agonists, such as the olive leaf/castor oil derivative complex, improves the connectivity of skins' layers and translates into quantifiable clinical benefits such as increased skin smoothness and diminished sagginess.

References

Iriyama S, Nishikawa S, Hosoi J, Amano S. Basement Membrane Helps Maintain Epidermal Hyaluronan Content. Am J Pathol. 2021 Jun;191(6):1010-1019.

Chauvel-Picard J, Bérot V, Tognetti L, Orte Cano C, Fontaine M, Lenoir C, Pérez-Anker J, Puig S, Dubois A, Forestier S, Monnier J, Jdid R, Cazorla G, Pedrazzani M, Sanchez A, Fischman S, Rubegni P, Del Marmol V, Malvehy J, Cinotti E, Perrot JL, Suppa M. Line-field confocal optical coherence tomography as a tool for three-dimensional in vivo quantification of healthy epidermis: A pilot study. J Biophotonics. 2022 Feb;15(2):e202100236

Iriyama S, Ogura Y, Nishikawa S, Hosoi J, Amano S. Regeneration of collagen fibrils at the papillary dermis by reconstructing basement membrane at the dermal-epidermal junction. Sci Rep. 2022 Jan 17;12(1):795.

Addae A, Zahr A, Jiang L, Desai S, Kononov T. Clinical Study to Evaluate the Efficacy and Tolerability of Cosmeceuticals Targeting the Dermal-Epidermal Junction. J Drugs Dermatol. 2021 Dec 1;20(12):1314-1321. doi: 10.36849/jdd.6355. PMID: 34898162

Majewski GP, Singh S, Bojanowski K. Olive leaf-derived PPAR agonist complex induces collagen IV synthesis in human skin models. Int J Cosmet Sci. 2021 Dec;43(6):662-676.

Majewski GP, Marchesi P and Bojanowski K. Olive Leaf Complex + Niacinamide Ameliorates Crow's Feet Wrinkles and Facial Sagging in a Split-Face Image Analysis Study. Under review.

About the speaker

Krys Bojanowski *CEO, Sunny BioDiscovery, Inc.*

Dr. Krys Bojanowski is the CEO of Sunny BioDiscovery, Inc., a California lab engaged in skin aging research. Krys received his PhD cum laude in Cellular and Molecular Pharmacology at the University of Paris, France, then, for 8 years studied dermal microcirculation and cancer at the National Cancer Center in Tokyo, Harvard Medical School and Lawrence Berkeley National Laboratory. Started in 2000, his company, Sunny BioDiscovery, developed a line of award-winning products for diabetic skin and wounds with the support from 4 NIH Institutes, including the National Institute on Aging. His scientific interests focus on the importance of hypodermis and its stem cells for dermal regeneration. Krys' lab

also engages in bioactivity and contract research projects for cosmetic and biotech companies.

Dr. Bojanowski has been consultant reviewer for NIH, Lytmos and Science Foundation Arizona, as well as for a dozen of scientific journals.

He is member of the Society of Cosmetic Chemists and co-author on over sixty patents, book chapters and research publications.