P2393

Integrating metabolomics and imaging data: innovative insights into the links between molecular signatures and phenotype in wound healing

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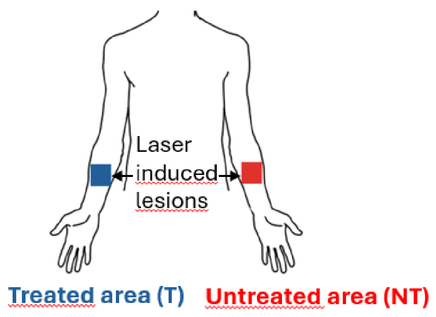
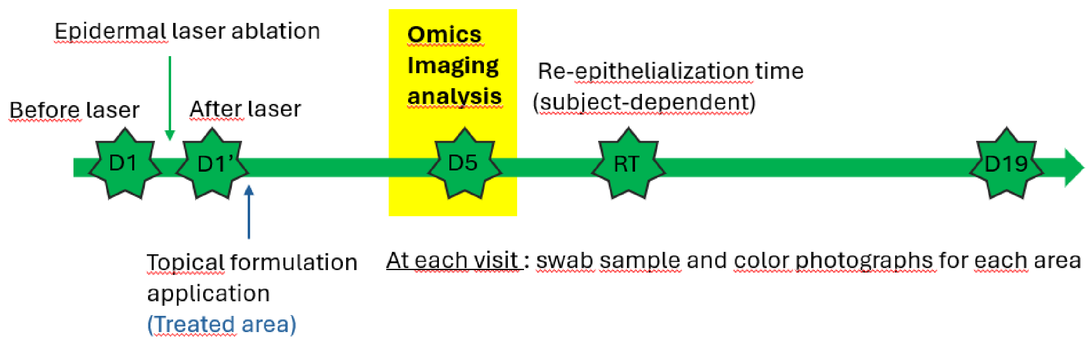
INTRODUCTION

The **integration** of Omics and imaging data (a field called "**omics imaging**") aims **to explore links between molecular signatures provided by omics technologies (at the molecular level) and phenotypic information provided by images (at the macroscopic level)**. This allows, for example, to reveal potential biological mechanisms underlying specific tissue lesions visible on biomedical images. Omics imaging, not yet used in dermo-cosmetics, was here applied in wound healing to link molecular repair signatures with **skin condition improvement after topical formulation use.**

MATERIAL & METHODS

In a clinical study involving 21 subjects [1], lesions on the forearms were induced by epidermal laser ablation. The areas were then either left untreated or treated with a topical formulation containing Rhealba oat concentrate and cicahyalumide (a mixture of Rhealba, the dipeptide L-Ala-L-Glu and hyaluronic acid). Skin swabs were taken before and at various times after ablation and were analyzed for metabolomic profiles using UHPLC-HRMS. At each sampling time, color photographs were also taken using a video dermoscope camera. Twenty **imaging features (colorimetry and Haralick texture features) were computed from these images**. For omics imaging analysis, we focused solely on **the identification of metabolites linked to imaging features that best described treated and untreated areas on Day 5 (D5)**. This integrative analysis was performed using the DIABLO [2] method.





RESULTS

Image analysis at D5

Imaging Feature: information on the visual properties of an image
- Colorimetry feature : quantification of the color characteristics in the CIELAB color space
- Texture feature : Spatial variation patterns in pixel intensity levels (grayscale values)

- Significant (D5-D1) changes between the Treated and Untreated areas for 16 imaging features highlight a **treated skin with less inflammation, fewer crusts, a milder squamous state, and less dryness, indicating a better skin barrier reconstruction compared to untreated skin.**

- Image Analysis : **quantitative assessment of the improvement of the skin condition** following the application of the topical formulation

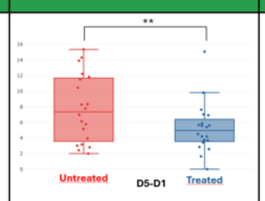
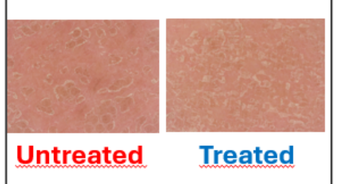
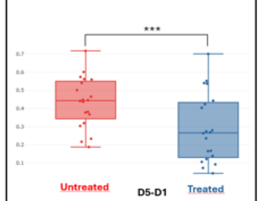
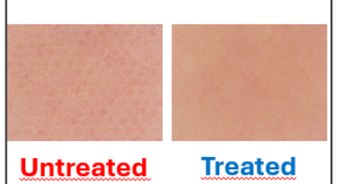
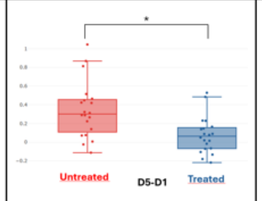
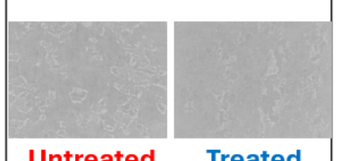
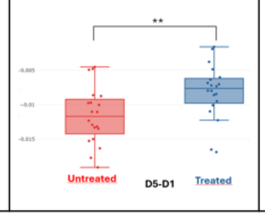
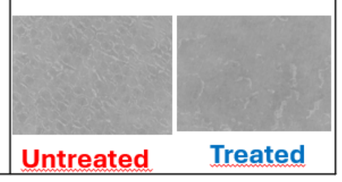
Imaging Feature Name /Type	Measure interpretation /Clinical Interpretation	Over-Expression	D5-D1 changes	Quantification of Skin condition Improvement with the formulation	Median Subject's Images (D5)
a* (mean)/ Colorimetry	**Average redness** /inflammation	Untreated		1.53 times **less redness on the T area** than on the NT area	
H76/ Colorimetry	**Color heterogeneity** /heterogeneous healing on the area	Untreated		1.51 times **less color heterogeneity on the T area** than on the NT area	
Contrast/ Texture	**Texture sharpness** /crusts, squamous state, dryness	Untreated		4.72 times **less contrast on the T area** than on the Untreated area	
ASM (Angular Second Moment)/ Texture	**Texture homogeneity**/ Skin with few or no marks (crusts, squames, ...etc)	Treated		1.4 times **more texture homogeneity on the T area** than on the NT area	

Table 1. Example of 4 imaging features with (D5-D1) changes significantly different between the Untreated (NT) and Treated (T) areas (Mean a*, H76, contrast, ASM) . Statistical significance (mixed linear models) : *p<0,05, **p<0.01, ***p<0.001

Integration of metabolomics and Imaging data at D5 (Omics Imaging)

Metabolites were associated with imaging features to describe the efficacy of the topical formulation and skin condition improvement

- **Treated area** presented a **higher intensity of sucrose and capric acid metabolites,** more homogeneous textures and colors and fewer contrasted structures compared to untreated skin. Commensal microbiota is beneficial to wound healing. **Interestingly, sucrose and capric acid promote and sustain the growth of the commensal microbiota and can be formed from the components of the formula [1]**,

- **Untreated area** exhibited a **higher intensity of uric acid metabolite,** more heterogeneous textures and colors and more contrasted structures compared to the treated area**.** Notably, **Uric acid increases oxidative stress and promotes inflammation [1]**

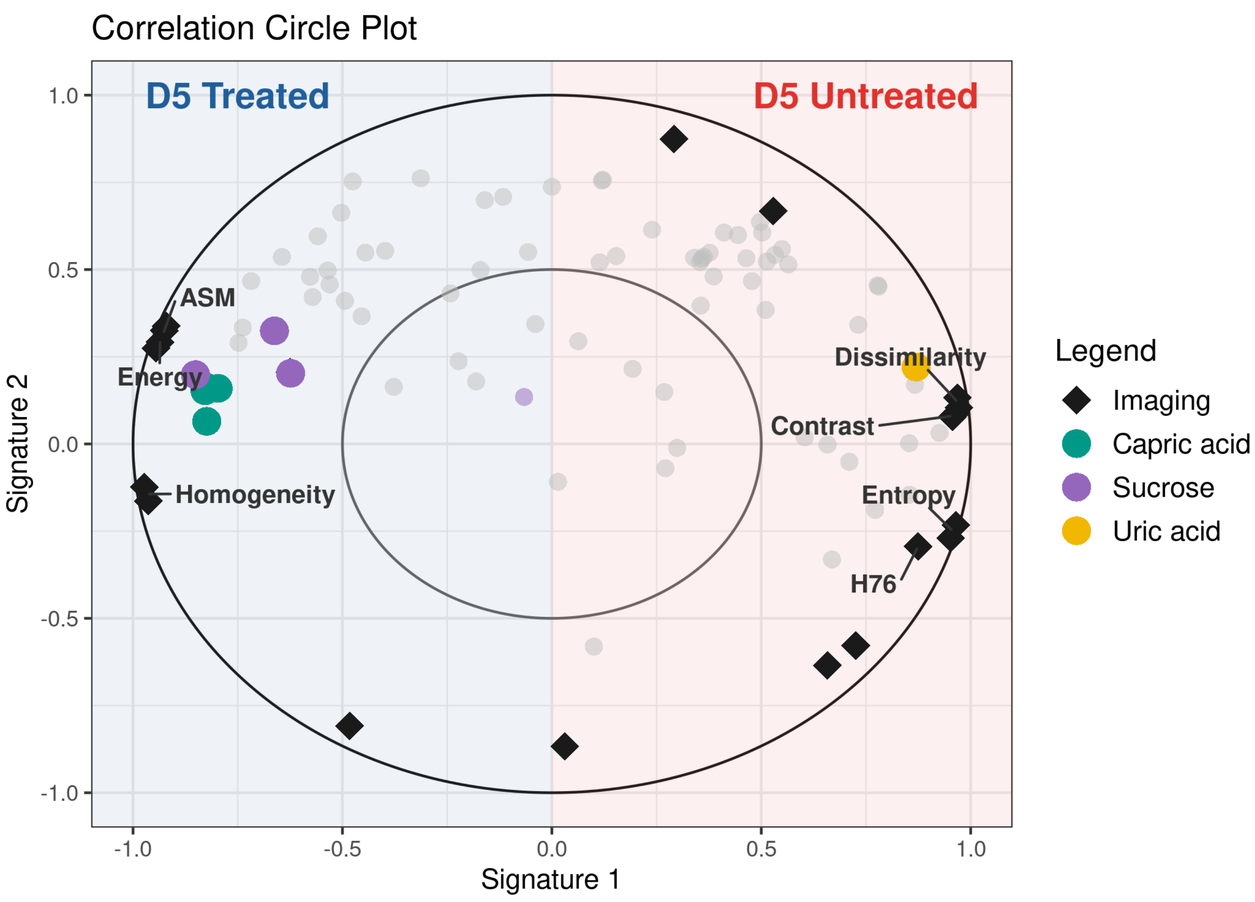


Figure 1. Correlation Circle Plot to study the correlation structure between variables (imaging features / metabolites). Variable vectors that have a close proximity to one another are positively correlated. Variables that are positioned on opposite sides of the X axis are negatively correlated.

CONCLUSION

- Integrating metabolomic data and biomedical images is an **innovative approach in dermo-cosmetics**
- Image analysis (color, texture) allows for a **quantitative assessment of the improvement in skin condition** after the application of a topical formulation containing Rhealba oat concentrate and cicahyalumide
- Omics Imaging reveals **biological mechanisms underlying visual appearance of the skin** (tissue alteration/reconstruction). It allows for a **better understanding of mechanisms of action and efficacy of the topical formulation**

[1] Bianchi, P., Jacques, C., Theunis, J. *et al.* Clinical profiling of skin microbiome and metabolome during re-epithelialization. *Sci Rep* **15**, 22282 (2025). https://doi.org/10.1038/s41598-025-07547-9
[2] Singh A, Shannon CP, Gautier B, Rohart F, Vacher M, Tebbutt SJ, Lê Cao KA. DIABLO: an integrative approach for identifying key molecular drivers from multi-omics assays. Bioinformatics. 2019 Sep 1;35(17):3055-3062. doi: 10.1093/bioinformatics/bty1054. PMID: 30657866; PMCID: PMC6735831.