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Multi-omics and integrative approach to evaluate solar exposure impact on skin ecosystem and a new SPF50+ sunscreen

INTRODUCTION

As the skin is the primary interface with the external environment, skin is an ecosystem consisting of the hydrophilic film, bacteria, viruses, and fungi and the over whole reflect the state of the skin. To evaluate the impact of external factors like sun exposure, the cutaneous ecosystem has to be studied as a whole to understand how they interact with each other and contribute to reply to external stress like sun exposure. The consequences of sun exposure have been previously documented both at genetic and proteomic levels. However, only few studies describe the contribution of sun exposure to biochemical changes that result in skin metabolome alterations, and interactions between skin and its microbiota have not been described.

IN VITRO ECOSYSTEM MODEL

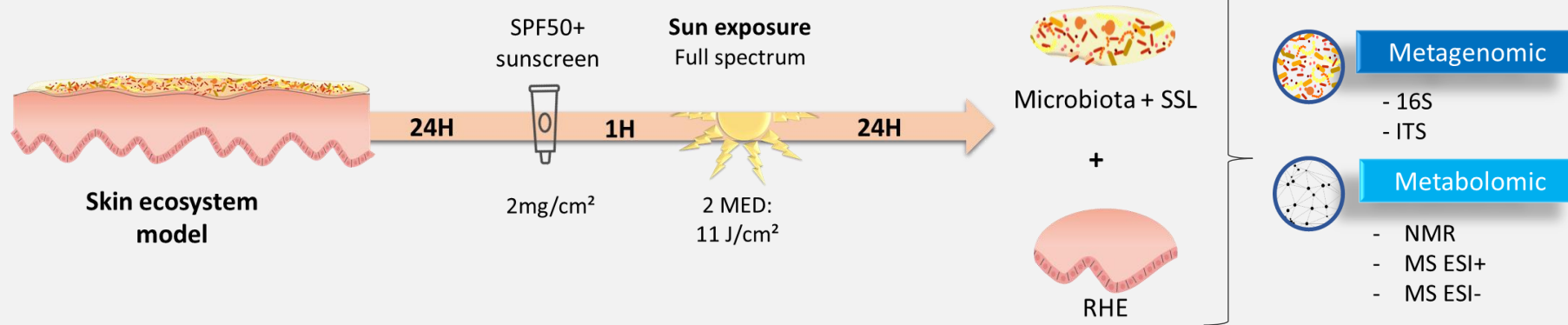


Fig.1. In vitro protocol and analysis

We developed a reconstructed human epidermal model colonized with skin microbiota and sebum (18 donors) to reproduce the complexity of the skin ecosystem. After 24 hours, the skin ecosystem model was exposed to simulated solar radiation (SSR) using a Suntest CPS+ chamber equipped with an NXE 1500 Xenon lamp. A new SPF50+ photoprotective system containing a specific combination of 4 sunfilters (TriAsorB, Tinosorb S, Uvinul T150 and Uvinul A+) and affording a broad spectrum UVB+A photoprotection (patented association WO581; WO984), was evaluated on this *in vitro* model.

METABOLOMIC STUDY

Metabolomics profiles were performed with NMR and UHPLC-HRMS. Data were processed with XCMS using W4M and filtered using quality control samples. Identified discriminant metabolites according to in-house databases were mapped on metabolic pathways using MetExplore software.

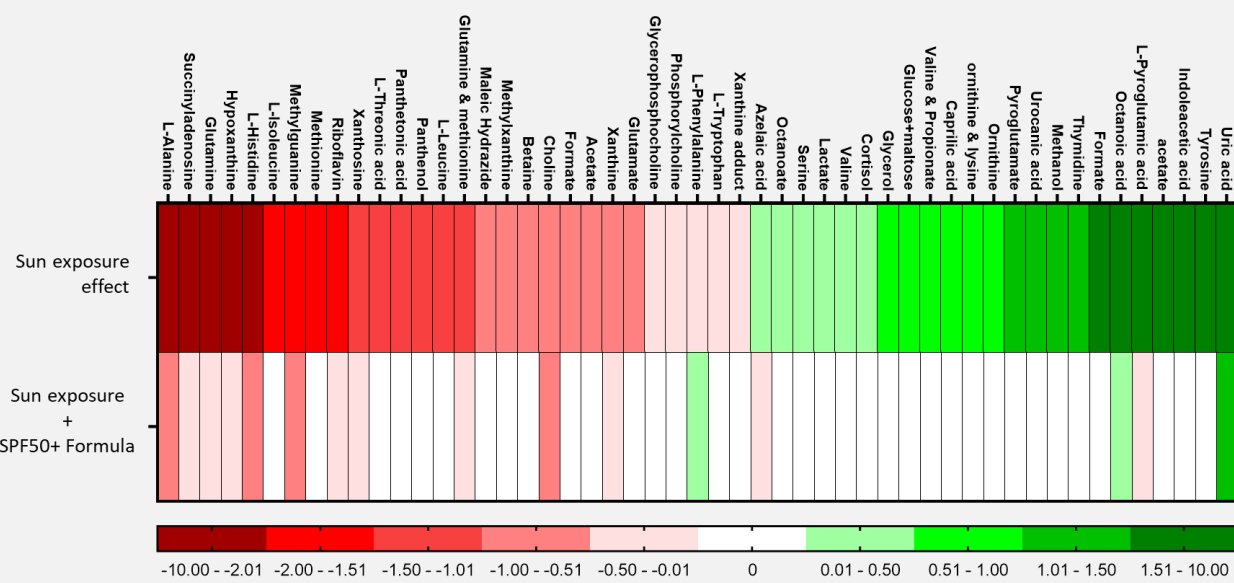


Fig.2. Heatmap of discriminant and significant metabolite (VIP > 1, p-value < 0.05) between unexposed and sun-exposed skin

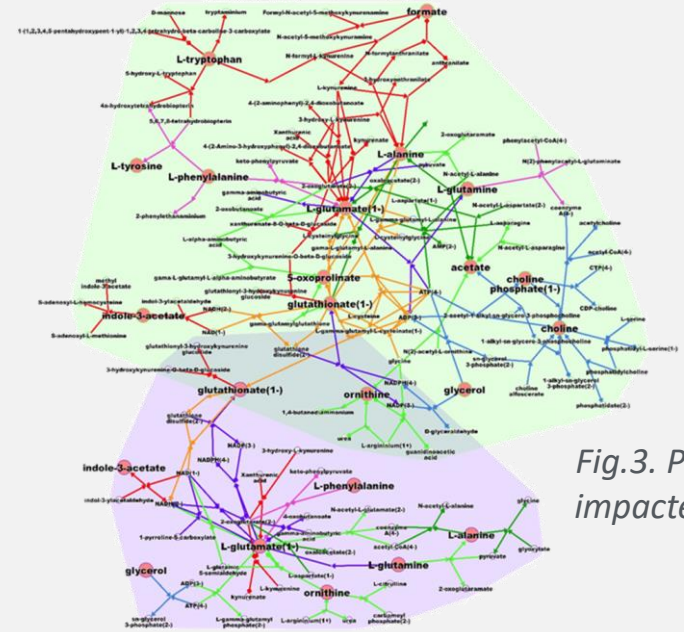


Fig.3. Pathways significantly impacted after sun exposure

Several pathways were modulated after sun exposition. The skin is under high oxidative stress with modification of glutathione, purine pathway and urea cycle. Other pathways have been highlighted, linked to skin microbiota, like BCAAs cycle, lipid metabolism and tryptophan pathway.

When the new SPF50+ photoprotective system is applied on skin ecosystem, metabolome of the skin was preserved and the interactions between skin and its ecosystem were protected from sun exposure deleterious effects.

METAGENOMIC APPROACH

Metagenomics analyses were performed from genomic DNA extract samples. Intergenic spacers 1 (ITS1) of the ribosomal RNA gene, or of the V1-V3 region of 16S gene was sequenced by high-speed sequencing. Analysis of the sequences by comparison with international data bases and differential analysis was used to identify genus or species more abundant in one group than the other.

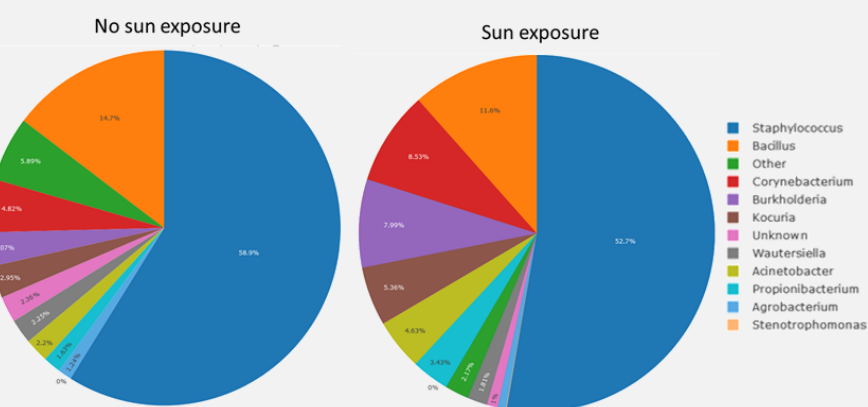


Fig.4. Bacteria population diversity without and with sun exposure

- From 16S analysis, two main bacterial genera were significantly modified by SSR irradiation: *Burkholderia* and *Cutibacterium* genus. Both genera were significantly more abundant on microbiota.
- From ITS analysis, *Malassezia* and *Cladosporium* genus are impacted by irradiation without photoprotective system while *Candida* and *Clitocybe* genus seem to be favored.
- Photoprotective system permits to avoid major modification on the microbiota

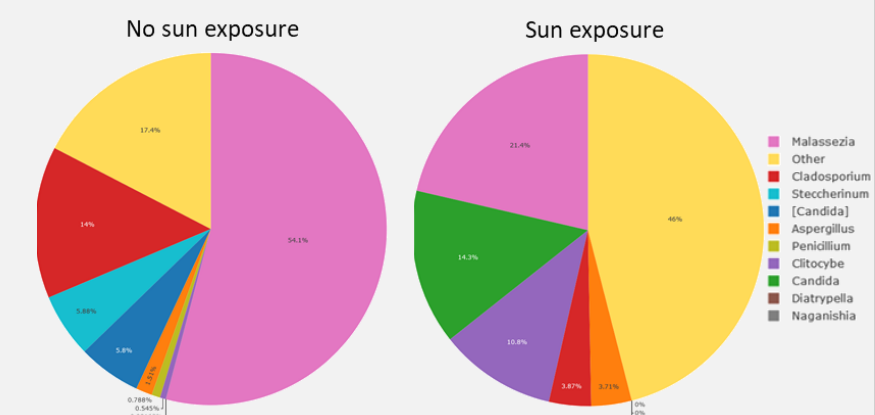


Fig.5. Fungi population diversity without and with sun exposure

CONCLUSION

This study is the first which profiled a wide range of metabolites and identified a highly accurate metabolomic signature of sun exposed skin in an *in vitro* model with complete skin ecosystem. Metabolomic signature was correlated to the metagenomic analysis of skin microbiota and explain interactions between skin and microbiota.

Data obtained show the performance of the new SPF50+ photoprotective system in order to preserve skin ecosystem from negative impact of sun exposure.