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## **Interactome expertise: an integrative approach to evaluate solar radiation impact on skin ecosystem and a new SPF50+ sunscreen efficacy**

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## INTRODUCTION

For a deeper understanding of sun exposure impact, we propose a new global and integrative vision, called Interactome expertise. We consider the skin as a complex ecosystem composed of the skin tissue, its skin surface lipids, its microbiota; and all these elements are linked and interdependent. Submitted to endogenous and exogenous factors, this ecosystem reacts to maintain skin equilibrium. To evaluate the impact of external factors like solar radiation, 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. The consequences of solar radiation have been previously documented both at genetic and proteomic levels. However, only few studies describe solar radiation contribution to biochemical changes that result in skin metabolome alterations, and interactions between skin and its microbiota have not been described.

## MATERIALS & METHODS

We developed an innovative *in vitro* model with RHE colonized with microbiota and sebum (N=18) to reproduce skin ecosystem complexity. This skin ecosystem model was exposed to simulated solar radiation (SSR) with and without application of a new SPF50+ sunscreen.

A multi-omics approach was used to evaluate SSR effect and SPF50+ sunscreen protection. 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 (MetExplore). Metagenomics analyses were performed from genomic DNA extract samples. Intergenic spacers 1 (ITS1) of the ribosomal RNA gene, or VI-V3 region of 16S gene was sequenced by high-speed sequencing. Sequences were compared to international data bases and differential analysis was used to identify differences of genus abundance.

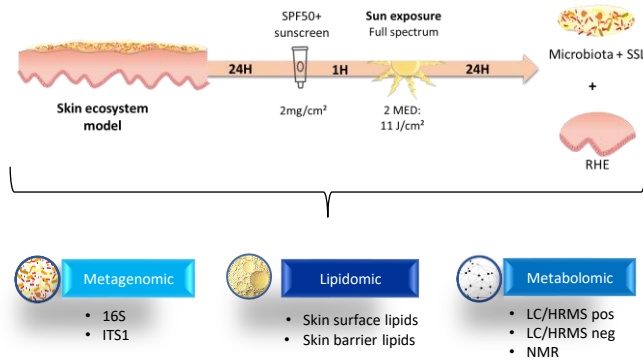


Fig.1. *In vitro* protocol and analysis

## RESULTS

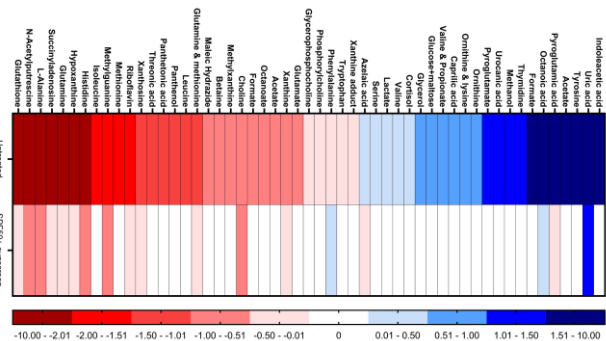


Fig.2. Discriminant and significant metabolites heatmap

Up to 50 metabolites were significantly modified (Fig.2) link to several pathways after solar radiation (Fig.3). 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. With the new SPF50+ sunscreen is applied, skin ecosystem metabolome was preserved, and interactions (Host/Microbiota) were protected from negative effect of solar radiation.

From 16S analysis, the two main anaerobic bacteria of the genus *Burkholderia* and *Cutibacterium* became more abundant after SSR exposure but not when SPF50+ sunscreen is used (Fig.4).

From ITS analysis, *Malassezia* was the most abundant genus and became less abundant after SSR. These modification were significantly reduced when SPF50+ sunscreen is used (Fig.4).

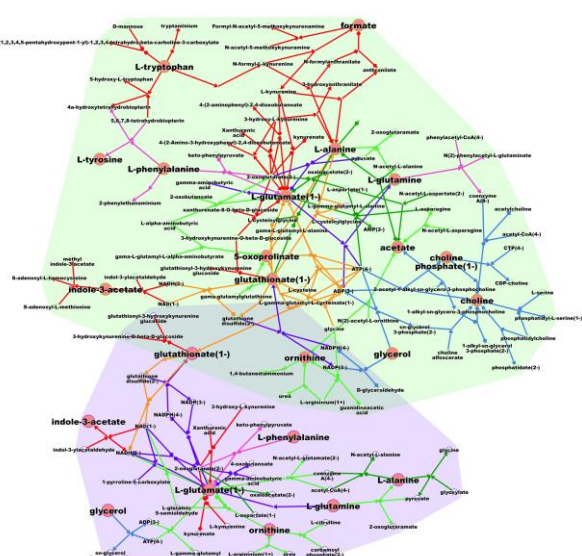


Fig.3. Pathways significantly impacted after SSR exposure

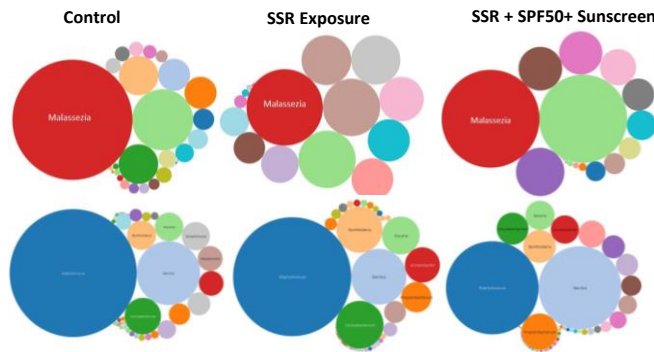


Fig.4. Bacteria and fungi population diversity

## CONCLUSION

This multi-omics approach identified a highly accurate metabolomic signature of the skin ecosystem after solar radiation and the interactions between the skin and cutaneous microbiota leading to oxidative stress/inflammation, immunosuppression and modification of microbial diversity.

**The SPF50+ sunscreen, in addition to protecting against the common negative effects of sun exposure, also preserved host-microbial interactions and microbial diversity from the deleterious effects of solar radiation.**