SKIN MANIFESTATIONS OF INTERNAL DISEASE

FIRST ASSESSMENT OF SKIN CIRCADIAN METABOLOMICS ON YOUNG AND AGING SUBJECTS

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Introduction: The “-omics” provide new understandings of biological processes and systems; the newest in this fast-growing field is metabolomics. Metabolomics is a comprehensive study of metabolites, which are small molecule (<1500 Da) intermediates and products of biochemical reactions. Additionally metabolomics encompasses network creation as well as holistic analysis and interpretation, which ultimately best represents the phenotype of a biological system. As such, metabolomics is rapidly gaining recognition for providing mechanistic understanding and biomarker discovery in various biological fields, from human health to agriculture. However, few reported metabolomic studies of the skin currently exist. Moreover, most studies are conducted invasively using biological fluids and tissues. Here we use non-invasive metabolomics to build on our years of skin circadian rhythm research.

Objective: To temporally define the skin metabolome via assessing circadian rhythm dynamics in the human stratum corneum using non-invasive D-squame collection methods.

Materials and Methods: Skin tape-strip samples were collected in the morning and evening from a healthy Caucasian population of young (≤ 25 years) and old (> 60 years) subjects. Collected samples were subjected to untargeted metabolic profiling via a multi-method LC/MS/MS platform at Metabolon. Results were compared to evaluate circadian- and age-related metabolomic changes in vivo.

Results: Clear circadian rhythm-dependent differences in the human skin metabolome were observed. For the young cohort: in the morning, skin barrier-associated metabolites were enriched, while in the evening, damage-associated metabolites were elevated. Strikingly, much of the natural rhythm of the metabolites was lost (or even inversed in some cases) in the older population.

Conclusion: Human skin metabolites follow a circadian rhythm, which is lost with age. This

study provides further understanding of the aging skin and defined the temporal human skin metabolome. To our knowledge, this study is the first to report on circadian rhythm-dependent changes in the human skin metabolome.