Genome Medicine

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# Differential effects of dietary supplements on metabolomic profile of smokers versus non-smokers

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## Abstract

**Background:** Cigarette smoking is well-known to associate with accelerated skin aging as well as cardiovascular disease and lung cancer, in large part due to oxidative stress. Because metabolites are downstream of genetic variation, as well as transcriptional changes and post-translational modifications of proteins, they are the most proximal reporters of disease states or reversal of disease states.

**Methods:** In this study, we explore the potential effects of commonly available oral supplements (containing antioxidants, vitamins and omega-3 fatty acids) on the metabolomes of smokers (n = 11) compared to non-smokers (n = 17). At baseline and after 12 weeks of supplementation, metabolomic analysis was performed on serum by liquid and gas chromatography with mass spectroscopy (LC-MS and GC-MS). Furthermore, clinical parameters of skin aging, including cutometry as assessed by three dermatologist raters blinded to subjects' age and smoking status, were measured.

**Results:** Long-chain fatty acids, including palmitate and oleate, decreased in smokers by 0.76-fold ($P = 0.0045$) and 0.72-fold ($P = 0.0112$), respectively. These changes were not observed in non-smokers. Furthermore, age and smoking status showed increased glow ($P = 0.004$) and a decrease in fine wrinkling ($P = 0.038$). Cutometry showed an increase in skin elasticity in smokers ($P = 0.049$) but not in non-smokers. Complexion analysis software (VISIA) revealed decreases in the number of ultraviolet spots ($P = 0.031$), and cutometry showed increased elasticity ($P = 0.05$) in smokers but not non-smokers.

**Conclusions:** Additional future work may shed light on the specific mechanisms by which long-chain fatty acids can lead to increased glow, improved elasticity measures and decreased fine wrinkling in smokers' skin. Our study provides a novel, medicine-focused application of available metabolomic technology to identify changes in sera of human subjects with oxidative stress, and suggests that oral supplementation (in particular, commonly available antioxidants, vitamins and omega-3 fatty acids) affects these individuals in a way that is unique (compared to non-smokers) on a broad level.

## Background

Cigarette smoking is well-known to associate with accelerated skin aging [1,2] as well as cardiovascular disease and lung cancer, in large part due to cellular damage from oxidative stress. Metabolites are downstream of genetic variation, transcriptional changes and post-translational modification of proteins. Hence, metabolites can most accurately capture the status of disease processes or reversal of disease processes [1]. Further, the identification of specific biomarkers has recently shed light on alterations that can occur in the metabolome due to disease and environmental changes [2,3].

The adverse health effects of cigarette smoking are well documented, and the basis of these effects is the generation of free radicals. It has been estimated that smoking a single cigarette can introduce about $10^{16}$

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