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The KarMeN-Study: Biomarkers of age, sex, and diet

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Introduction
Metabolomics is a promising tool to investigate the effects of diet on human health. However, background variation of the metabolome has to be taken into account.

Objectives
The goal of this study therefore was to investigate in healthy humans whether age and sex are associated with metabolite patterns, and if food intake is reflected in the metabolome.

Method / Design
KarMeN (Karlsruhe Metabolomics and Nutrition) is a cross-sectional study that was performed at the Max Rubner-Institut in Karlsruhe, Germany. 301 healthy male and female participants (age range 18 – 80 years) were thoroughly characterized based on anthropometric, physiological, functional and biochemical parameters. Fasted blood and 24h urine samples were collected and analysed by targeted and untargeted GC×GC-MS, GC-MS, LC-MS and NMR. Food intake was recorded using a 24h dietary recall, capturing the same 24h for which urine was collected. Predictive modelling was applied to find associations between age or sex and the metabolite profile using the following machine learning algorithms: SVM, glmnet and PLS. Principal component analysis was used to derive a dietary pattern based on data from the 24h dietary recall. Correlation between current diet and 24h urine metabolome was investigated using Kendall correlation analysis adjusted for age, sex, body mass index and energy intake. The Bonferroni method was used to correct for multiple testing.

Results
Based on metabolite profiles from plasma obtained with different analytical platforms, it was possible to identify metabolite patterns which can predict age in men and women. These patterns include ornithine, hippuric acid, and choline. Additionally, in women, classification according to age (based on their menopause status) was possible from plasma metabolome data. Besides a number of unknown analytes, some metabolites important for this prediction could be identified, such as ornithine, serine, or glucuronic acid. Classification of participants according to sex was possible with >95% accuracy based on plasma metabolite profiles. Metabolites important for correct classification included creatinine and branched-chain amino acids. Furthermore, we identified a dietary pattern representing a "Western diet" for high positive loadings or representing a "prudent diet" for high negative loadings, respectively. "Western diet" was associated with high consumption of e.g. meat, potatoes, animal fats and alcohol accompanied with low consumption of e.g. fish, cereals and cereal products, fruits, vegetable fats and whole meal bread; the "prudent diet" showed opposite associations. We observed 17 metabolites as being significantly correlated with this pattern pointing in particular to the tyrosine metabolism.

Conclusions
Age and sex are associated with metabolite patterns in healthy humans. This needs to be considered in studies looking for the effect of food and diets on the human metabolome. Independent of age and sex, prudent and Western dietary habits are associated with variations in urinary metabolite patterns.