Metabolomics applied to nutritional epidemiology to identify biomarkers of food intake in the framework of the Metabo-Breast cancer project, SU.VI.MAX cohort

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SESSION 1 - EPIDEMIOLOGY - NUTRITIONAL PREVENTION AND CANCER RISK

Claudine Manach - Poster - N°5

June, Thursday 22, 2017 - 10.00-10.45am for the posters presentation

Abstract title: Metabolomics applied to nutritional epidemiology to identify biomarkers of food intake in the framework of the Metabo-Breast cancer project, SU.VI.MAX cohort

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The abstract: The work presented is part of the Metabo-Breast cancer project (2015-2017, INCa, P.I. M. Touvier), which aims at 1) discovering predictive biomarkers of breast cancer using metabolomics 2) identifying biomarkers of the quality of the usual diet and of specific foods with putative health effects and 3) relating these biomarkers to enhance our understanding of the role of nutrition and specific dietary factors on breast cancer. Here we focus on the objective of discovering biomarkers of food intake by the exploration of the food metabolome in serum samples from the SU.VI.MAX cohort, using high-resolution mass spectrometry. Untargeted metabolomics is a holistic, data-driven approach that has proved efficient to discover dietary biomarkers through the comparison of the comprehensive profiles of plasma or urine metabolites from subjects differing according to their dietary habits or recent food consumption (Scalbert et al., AJCN 2014).
SU.VI.MAX female subjects who filled at least ten 24h dietary records during the first 2 years of follow-up were stratified in deciles according to their level of adherence to the guidelines of the Programme National Nutrition Santé, assessed by the score PNNS-GS previously described (Estaquio et al., JADA 2009) but not taking into account the physical activity component. A total of 80 women, aged 48±6.4 years old was randomly selected in the 10th decile of the PNNS-GS distribution and 80 women matched for age, baseline menopausal status, BMI, smoking and season of blood draw were selected in the 1st decile.
Plasma samples collected at baseline in the SU.VI.MAX study were analyzed using Ultra Performance Liquid Chromatography (UPLC) coupled with a quadrupole time of flight mass spectrometer (QToF, Impact II Bruker), equipped with an electrospray ionization source. Metabolic profiles were acquired in both positive and negative modes with a scan range from 50 to 1,000 mass-to-charge ratio. Data were pre-processed using Galaxy workflow4metabolomics.
A total of 1575 and 601 signals (ions) were detected in positive and negative mode, respectively. Metabolomics profiles were compared using univariate and multivariate statistical methods (ANOVA with Benjamini-Hochberg (BH) correction, PCA, HCA, PLS, correlation analyses adjusted for energy intake) to determine the ions associated with the PNNS-GS, some specific components of the score and with the level of consumption of 58 foods/food groups assessed with the FFQ.
84 ions in positive mode and 30 ions in negative mode were found correlated with specific foods/food groups ($r>0.3$, p-value with BH <0.1). A few of them were expected such as trigonelline, paraxanthine, actractyligenin glucuronide, known as candidate biomarkers of coffee intake and proline betaine for orange intake discovered in previous metabolomics studies. This demonstrates the relevance of our strategy. The identification of the other candidate biomarkers is ongoing. It is based on search in various in-house and online databases and literature as well as on complementary analyses with MS/MS fragmentation using a ultra-high resolution LTQ-OrbiTrap mass spectrometer and analysis of the standard when available. This work will provide a range of new candidate biomarkers of food intake that are crucially needed to improve the quality of dietary assessment in epidemiological studies.
This project was supported by the French National Cancer Institute (grant n° INCa_8085 for the project, PhD grant n° INCa_11323 for L. Lecuyer), and received the label of the French network for Nutrition And Cancer Research (NACRe, www.inra.fr/nacre).