Title: FOOD METABOLOMICS APPLIED IN COHORTS TO ACCELERATE THE DISCOVERY OF NUTRITIONAL BIOMARKERS

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Abstract: The purpose of dietary assessment is to estimate usual and recent intake of foods, nutrients, bioactive compounds and food contaminants for exploration of associations with health outcomes and monitoring of population nutritional status. These data are still extremely difficult to obtain. Methods currently used are based on dietary questionnaires which have inherent limitations linked to self-reporting. A complementary approach to questionnaires is the use of biomarkers. However, only a few biomarkers have been properly validated, which do not cover the wide range of foods consumed. Metabolomics has emerged as a promising approach to discover nutritional biomarkers. Typically, plasma or urine samples collected before and after acute intake of a specific food are profiled using NMR or high resolution Mass Spectrometry (MS) and compared using multivariate statistics to pinpoint the signals reflecting the consumption of the target food. In a proof-of-concept study on citrus, we showed that urine profiling of cohort subjects stratified by consumption could be a more effective strategy for discovery of sensitive biomarkers of intake[1].

As part of the ANR PhenoMeNEp project, we tested the approach on 20 selected plant foods. Using dietary questionnaire data (1994-2009), 144 high and 66 low consumers of fruit and vegetables (F&V) were selected from the SU.VI.MAX2 cohort. Morning spot urine samples were analyzed in positive and negative ion mode by LC-QTof MS. Subgroups of low and high consumers were selected for each of the 20 foods on the basis of questionnaire data, excluding from each selection any subject declaring high intake of other foods. For ten target foods, the urine metabolomes from low and high consumers were strongly discriminated by both univariate and multivariate statistics. The number of significant ions ranged from 133 for coffee to 428 for apple (p-value<0.05 ANOVA BH). Study of marker specificity showed that some, although highly discriminant for the target food, were not specific enough to make good candidate biomarkers. The long-term low and high consumption of F&V were also clearly reflected in the urine metabolomes, mainly through endogenous metabolites variations. Of the 39 exogenous markers having a higher intensity in the urine of high F&V consumers, 69% were recognized to be potential biomarkers of apple, tea, citrus and root vegetable intake. The study provided useful insights on the conditions for success and the limitations of the approach of applying metabolomics to cohort samples for rapid discovery of a wide range of nutritional biomarkers.

[1]Pujos-Guillot et al., J Proteome Res. 2013, DOI: 10.1021/pr300997c