Measuring small molecules for nutrition research?

Metabolomics is the study of small molecules that are present in biological samples. These small molecules include amino acids, fatty acids, organic acids and sugars, and are referred to as metabolites. These metabolites reflect the downstream activity of genes and proteins, so measuring their levels can often reveal more about a person's disease risk or health status. Over the last number of years it has become clear that certain metabolites play a key role in the development of diseases. Environmental factors such as diet, physical activity, and environmental agents can influence metabolite levels, meaning that assessment of metabolic profiles can play a major role in a range of disciplines. One such discipline is nutrition research, which has seen a rapid rise in the use of metabolomics.

Fig. 1. Metabolomic overview; from biofluid collection to data analysis. Once the samples are collected the data is acquired using one or more metabolomics platforms. For example data can be acquired using NMR , LC-MS or GC-MS. Application of multiple platforms will increase the coverage of the metabolome. Data analysis is the next step which involves use of multivariate techniques such as PCA and PLS-DA.

Metabolomic Workflow

The metabolomics workflow generally consists of the following steps (1) sample/biofluid collection and extraction (2) data acquisition; where samples are analysed using an analytical method such as nuclear magnetic resonance (NMR) spectroscopy or a mass spectrometry (MS)-based method (3) data analysis and interpretation; advanced statistical methods are applied to make sense of the data (Fig. 1).

Briefly, metabolomics is applied to a range of biofluids, including serum, plasma and urine. Attention should be given to sample collection procedures for e.g. when collecting urine, storage on ice immediately following collection is important and recommended in order to prevent any metabolite losses. The metabolites in the biofluid samples are then measured using an analytical

method. Different analytical methods include NMR spectroscopy and MS based methods, which are the most common. Once the metabolites are measured, statistical analyses are applied to understand the data. These include unsupervised methods such as Principal Component Analysis (PCA), which gives a visual overview of the measured metabolites to see if there are any trends in the data. Supervised techniques require *a priori* knowledge of the class membership and are used to identify spectral signals or metabolites that are different between groups. Examples of such techniques include Partial Least Squares Discriminant Analysis (PLS-DA), Random Forests and Genetic algorithms.

Nutrition Applications
Our food contains thousands of metabolites which contribute to and impact on the human metabolome; as a result metabolomics has huge potential in the nutrition field. Broadly speaking, the areas where metabolomics has played a key role include (1) identification of new dietary biomarkers related to the food intake (2) application to intervention studies to understand the potential role of the diet in health promotion (3) examining the relationship between diet and disease and (4) precision nutrition. In the case of dietary biomarkers, metabolomics is playing a major role in the identification of new dietary biomarkers that reflect food intake which in turn can be used to aid dietary assessment. Work in our research group is underway to develop and validate biomarkers for a range of foods. With regards intervention studies, application of metabolomics pre and post nutrition interventions can help in identifying underlying mechanisms by which the intervention is working and in turn can lead to substantiation of health claims. Application in the context of diet related diseases allows researchers to identify metabolic signatures related to diet related diseases and thus potential underlying causes. In the field of precision nutrition, application of metabolomics has the potential to identify responders and non-responders to various interventions and thus in the long term will pave the way forward for precision nutrition. This review article gives an overview of the technologies available in metabolomics, the data analysis approaches and applications in nutrition research.

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