DEVELOPMENT OF METABOLOME-BASED PREDICTORS OF LIVER DISEASES

INTRODUCTION

Metabolomics is a rapidly expanding discipline in the group of ‘omics’ sciences and has gained increasing attention in the biomedical research. Comparisons of different metabolic profiles let us distinguish between different physiological stages of an individual, or different individual stages. A detailed analysis of serum metabolome can be used as unbiased approach to obtain an assessment of whole-body metabolic response to disease states and their progression, or to monitor response to therapies.

The high-throughput approaches in metabolomics studies allow measuring simultaneously thousands of metabolites from complex samples in a large set of samples, obtaining a snapshot of their metabolic state. Despite the potential of these high-throughput technologies, the success of a metabolomics study relies on careful sample selection and some basic considerations about the experimental design.

LIVER & SERUM CORRELATION

For tissues whose primary physiological role is metabolic, such as the liver, metabolites are the best indicators of organ function.

Metabolic alterations of the hepatic function can be reflected in the circulating metabolome. We have observed a correlation (R²=0.45, p<0.0001) between the serum and the liver metabolomes. This is relevant since serum and not liver will be the base for any noninvasive diagnostic test.

METABOLIC PROFILING

In metabolic profiling, there is no single platform or method to analyze the entire metabolome of a biological sample mainly due to the wide concentration range of metabolites coupled to their extensive chemical diversity. Metabolite extraction is usually accomplished by fractionating the serum samples into pools of species with similar physicochemical properties, using appropriate combinations of organic solvents. We use multiple UHPLC-MS platforms optimized for extensive coverage of the serum metabolome.

DATA HANDLING

Metabolomics in biomedical research depends on its capability to find biomarkers. The task of extracting the hidden meaningful information buried in the data is essential but one of the biggest bottlenecks of the metabolomics workflow and remains challenging.

STUDY DESIGN

Recruitment of the patients
Collect serum (fasting) Perform liver biopsy Histopathological evaluation

METABOLITE EXTRACTION

Random ordering of the samples
Add internal standard spiked extraction solvent Collect metabolite extract
Dry and resuspend for UHPLC-MS analysis

UHPLC-MS ANALYSIS

Random ordering of the extracts
Analysis in multiple UHPLC-MS platforms

REFERENCES: