
Title: Understanding Human Health and Disease With LC/MS Based Metabolic Phenotyping

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Abstract

The MRC-NIHR National Phenome Centre, Imperial College London, is the first of its kind facility. Born out of the UK Olympic Legacy its mandate is to provide “high throughput, forensic quality, metabolic phenotyping to support large scale epidemiological studies as well as basic medical research into disease understanding and patient stratification”. As global life-styles change we are seeing increasing cases of obesity, diabetes, and mental health issues. This not only affects a person’s quality of life but also places increased strain on the health-care systems to provide the right treatment whilst managing costs closely.

Metabolic Phenotyping offers a valuable and unique insight into the underlying biochemistry of diseases as well as the patients individual biochemistry “phenotype”, diet, health status, age and stress. To deliver this information the analytical data generated is processed via a variety of chemometric modelling and analysis methodologies to deliver the relevant biochemical information. These chemometric platforms employed vary from simple multivariate analysis to highly complex model based analysis and is presented in a format ready for interpretation by medics.

This facility comprises of high field NMR instruments, accurate mass LC/MS instruments, tandem quadrupole LC/MS systems as well as dedicated training facility. In this presentation we will discuss the development of analytical platforms both LC/MS and NMR as well as a detailed discussion on the workflow, validation, reporting and decision making process. The presentation will cover the development and validation of the “discovery” screening methods for polar, non polar metabolites and lipid profiling using LC/MS methodology, as well as describe the use of proton NMR as an initial screen to eliminate contaminated samples. The quantitative targeted LC/MS assays will also be discussed the various compounds classes such as bile acids, amino acids, eicosanoids, and acyl carnitines.