

## Quantified Metabolomics for the Determination of Phenotypes and Biomarkers across Species in Health and Disease

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**Abstract :** Metabolic changes are one of the major factors in the development of a variety of diseases in various species. Metabolism of agricultural plants is altered the following infection with pathogens sometimes contributing to resistance. At the same time, pathogens use metabolites for infection and progression. In humans, metabolism is a hallmark of cancer development for example. Quantified metabolomics data combined with other omics or clinical data and analyzed using various unsupervised and supervised methods can lead to better diagnosis and prognosis. It can also provide information about resistance as well as contribute knowledge of compounds significant for disease progression or prevention. In this work, different methods for metabolomics quantification and analysis from Nuclear Magnetic Resonance (NMR) measurements that are used for investigation of disease development in wheat and human cells will be presented. One-dimensional <sup>1</sup>H NMR spectra are used extensively for metabolic profiling due to their high reliability, wide range of applicability, speed, trivial sample preparation and low cost. This presentation will describe a new method for metabolite quantification from NMR data that combines alignment of spectra of standards to sample spectra followed by multivariate linear regression optimization of spectra of assigned metabolites to samples' spectra. Several different alignment methods were tested and multivariate linear regression result has been compared with other quantification methods. Quantified metabolomics data can be analyzed in the variety of ways and we will present different clustering methods used for phenotype determination, network analysis providing knowledge about the relationships between metabolites through metabolic network as well as biomarker selection providing novel markers. These analysis methods have been utilized for the investigation of fusarium head blight resistance in wheat cultivars as well as analysis of the effect of estrogen receptor and carbonic anhydrase activation and inhibition on breast cancer cell metabolism. Metabolic changes in spikelet's of wheat cultivars FL62R1, Stettler, MuchMore and Sumai3 following fusarium graminearum infection were explored. Extensive 1D <sup>1</sup>H and 2D NMR measurements provided information for detailed metabolite assignment and quantification leading to possible metabolic markers discriminating resistance level in wheat subtypes. Quantification data is compared to results obtained using other published methods. Fusarium infection induced metabolic changes in different wheat varieties are discussed in the context of metabolic network and resistance. Quantitative metabolomics has been used for the investigation of the effect of targeted enzyme inhibition in cancer. In this work, the effect of 17  $\beta$  -estradiol and ferulic acid on metabolism of ER+ breast cancer cells has been compared to their effect on ER- control cells. The effect of the inhibitors of carbonic anhydrase on the observed metabolic changes resulting from ER activation has also been determined. Metabolic profiles were studied using 1D and 2D metabolomic NMR experiments, combined with the identification and quantification of metabolites, and the annotation of the results is provided in the context of biochemical pathways.

**Keywords :** metabolic biomarkers, metabolic network, metabolomics, multivariate linear regression, NMR quantification, quantified metabolomics, spectral alignment

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