High throughput metabolomics using ultra high resolution detection and chemometric tools to address health monitoring

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Abstract

Concern for public health involves evaluation of population exposure to toxicants. To do this, robust and high-throughput approaches are required to perform analyses of a large number of samples collected from subjects enrolled in cohort studies. The targeted methods enable detection of only predetermined compounds, but do not search for new or unknown markers. Global approaches such as metabolomics which aim to reveal metabolic changes due to environmental stress or diseases can detect even those metabolic biomarkers that are unknown.

Direct introduction mass spectrometry (DIMS) characterized by a significant reduction in analysis time is more appropriate for large scale high throughput analyses such as for phenotyping large cohorts [1]. Additionally, its combination with high resolution mass spectrometry (DI-HRMS) improves the efficiency of the DIMS approach. Nevertheless, DI-HRMS generates complex data containing several thousands of peaks.

Therefore, the objective of my work was to develop a rapid, high-throughput workflow, including the development of chemometric tools, in order to highlight metabolomic perturbations induced by exposure to toxicants.

First, DIMS approach was performed on urine of farmers professionally exposed to two pesticides using an Orbitrap instrument and a new chemometric tool called Independent Component - Discriminant Analysis was developed for supervised analysis of the DIMS data [2]. The developed methodology was then applied to five types of exposure and two analytical approaches DIMS and LC/MS were examined in order to validate the DIMS approach as well as the developed chemometric data analysis tool [3].

Second, DIMS approach was applied to an instrument of higher performances the FT-ICR, to improve the quality of the DIMS data [4]. The procedure was applied to a large number of samples to test the robustness of the approach [5].

All these works demonstrated the feasibility and effectiveness of our high-throughput metabolomic approach for metabolic phenotyping of large populations.

References

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