New computational solutions to improve metabolic profile interpretations

Fabien JOURDAN[1]
[1] INRA Toxalim (Research Centre in Food Toxicology) MetaboHub, Toulouse, France
E-mail: Fabien.Jourdan@inra.fr

1. Introduction

List of discriminating identified metabolites (according to the studied disease between two groups), known as "metabolic profiles", are the observable outcomes of metabolic modulations. Those lists of identified compounds are of great value to better understand the underlying biochemical shifts induced during a disease. Nevertheless, those lists are incomplete mainly due to the nature of LC/MS and the ability to identify compounds. Moreover, the analysis of human biofluids only represents the modulations of metabolites exchanged between the tissue and its environment, overshadowing potential metabolites of interest which are involved in intracellular metabolic processes and not released nor uptaken by the tissue/cell.

2. Approach

We propose an approach combining metabolic networks (union of all metabolic reactions) and medical text mining to propose metabolites which may expand the biological interpretation by "filling the gaps" of metabolic profiles. The network strategy is inspired from social network recommendation engines such as the ones used by twitter or media broadcasters. It allows finding upstream and downstream metabolites biochemically related to the ones in the profile. The text mining approach consists in automatically mining the literature to retrieve metabolites that are significantly associated with the perturbation under study.

3. Results

The approach had been successfully applied to high resolution LC/MS metabolomics data obtained on Cerebrospinal fluid (CSF) of patients affected by hepatic encephalopathy. The proposed methodology combined with interactions with analysts allowed increasing the metabolic profile size by 40%. Some of the metabolites suggested by our recommendation system were confirmed using standards. Other propositions were confirmed as metabolites of interests when analyzing patient clinical data.

References

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