BBB Seminar (BMED380)

SCAN ME

Thursday, February 15. 14:30 at the BBB, Auditorium 4

Untargeted metabolomics in body fluids and tissues - from the bench to the bedside

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Untargeted metabolomics aims at providing an holistic view on metabolism by analyzing a vast array of metabolites in body fluids or tissue-extracts. To this end we have used liquid chromatography in combination with QToF mass spectrometry. From plasma samples we obtain more than 10.000 metabolite signals. The sensitivity of the technique is low nanomolar. In clinical practice we use it to diagnose patients with metabolic diseases. As such the technique has largely replaced the traditional targeted techniques that were used for decades. A bioinformatics pipeline enables easy interpretation of the >10.000 signals in body fluids of patients with known metabolic diseases.

As expected most metabolic diseases cause more perturbations than the substrate accumulation and the product depletion of the defective enzyme. Mostly an array of metabolites is present in abnormal concentrations; we see a characteristic fingerprint of that specific disease. A limitation of the technique is that a significant percentage of the signals deriving from a body fluid sample cannot yet be identified. If a specific unusual signal is consistently present in samples of one patient MS/MS fragmentation, but also advanced infrared spectroscopy in the Nijmegen Felix Facility may help to identify the causative metabolite.

Examples will be given on the performance of the technique in the diagnosis and follow-up of metabolic patients. Also will be shown how the technique enabled us to find novel biomarkers for a disease that in some cases were relevant for understanding its pathophysiology. For pyridoxin dependent epilepsy (PDE) biomarkers were found that were stable in Guthrie cards thus enabling the introduction of the disease in neonatal screening. By further identification of relevant “unknowns” we could delineate NANS deficiency as a novel metabolic disease.

The most recent innovation is the untargeted metabolomics profiling of MALDI-MS imaging on tissue slices. An example will be shown of the untargeted analysis of brain slices from a PDE KO-mouse. In this way we can use the technique as a molecular microscope providing spatial information on the brain localization of the metabolite. Untargeted metabolomics will find its way as a novel and useful tool in clinical practice as well as in research for metabolic- and other diseases.

Chairperson: Jan Haavik, Department of Biomedicine