BBB Seminar (BMED382)

SCAN ME

Thursday, October 30. 14:30 at the BBB, Auditorium 4

Functional tracer proteo-metabolomics: a toolbox to study cellular metabolism and the regulatory interplay between hub molecules and protein modifications

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Biological systems are highly dynamic and strive to maintain cellular homeostasis. This process is regulated by cellular metabolism and signaling, particularly through the modification of proteins. Hub molecules, such as acetyl-CoA, play a pivotal role in cellular metabolism and signaling by acting as direct substrates for protein modifications. Alterations in cellular metabolism and protein modifications are associated with diseases such as cancer and metabolic disorders.

Our work centers on the development of innovative bioanalytical methods that combine proteomics, metabolomics, and stable isotope-based fluxomics. These methods allow us to study the regulatory interactions between cellular metabolism and signaling at a molecular level. We have developed a mass spectrometry (MS)-based, multiplexed metabolic phenotyping approach that uses multiple metabolic tracers simultaneously. Compared to the conventional metabolic phenotyper, this multiplexed tracer metabolomics approach enables the rapid metabolic phenotyping of cells and tissue samples with metabolite, and thus molecular, resolution. In addition, we have developed an analytical systems approach for the simultaneous determination of the turnover of hub molecules, such as acetyl-CoA and S-adenosylmethionine (SAM), and the resulting protein and histone modifications (acetylation and methylation) by combining tracer proteomics and metabolomics (tracer proteo-metabolomics). Using the example of acetyl-CoA and histone H3 acetylation, we were able to show that our approach makes it possible to distinguish between effects on metabolism and histone modification. Without integrating acetyl-CoA and histone acetylation dynamics, metabolic alterations induced by AKT inhibition would be erroneously interpreted as changes in histone acetylation dynamics, rather than as alterations in metabolic flux from glucose to acetyl-CoA.

Chairperson: Thomas Arnesen, Department of Biomedicine