BIOCHEMISTRY SEMINAR SERIES

"The Power of Proteomics to understand Mechanisms of Senescence during Aging – and other Applications of Data-Independent Acquisitions as Novel Tool for Biology"

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Cellular senescence is a striking example of a prime driver of aging phenotypes and pathologies across multiple tissues. This complex stress response causes an essentially irreversible arrest of cell proliferation and the development of a multi-component senescence-associated secretory phenotype (SASP). We hypothesize that, via the SASP, senescent cells exert cell non-autonomous effects that can disrupt cells and tissues locally and at a distance and contribute to neurodegeneration, thrombosis, and multiple age-related pathologies. Using quantitative SILAC workflows as well as more comprehensive data-independent acquisitions approaches, we have assessed the composition and functions of the SASP in aging and disease contexts. Recently, our proteomic screens have identified a novel role for senescent cells and SASP in hemostasis and blood coagulation. Since senescent cells accumulate with age, we speculate that the SASP is at least partly responsible for thrombotic events that increase with age. The general role of senescent cells as driver of age-related diseases has moved forward potential therapeutics (senolytics) to remove senescent cells to improve health span. Overall, it will be of key importance to identify senescence markers, both as biomarkers for aging and age-related diseases, in order to monitor any therapeutic interventions to eliminate senescent cells.

Additional recent work is presented using data-independent acquisitions to identify and quantify PTM containing peptides in a high-throughput format. Several projects will be shown assessing protein acylation, such as acetylation and succinylation in liver and brown adipose fat tissues, and other PTMs. We will discuss the relevance of succinylation during acute kidney injury, the role of succinylation as part of brown adipose tissue function and the extremely dynamic and massive remodeling of the acylome and succinylome in liver upon dietary supplementation. Simultaneous enrichment of multiple PTMs using antibody enrichment DIA-MS workflows are performed to assess PTM crosstalk and to obtain comprehensive coverage. PTM site localization is determined using various software tools, such as Skyline and Spectronaut. Acquiring PTM samples in DIA mode provides capabilities to identify multiple different site localization isomers from peptides with the same peptide sequence and precursor ion m/z. Thus DIA acquisitions for PTM profiling and quantification provides unique opportunities to overcome challenges that are associated with protein PTM workflows.

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