Maria Wahle
Title: Decoding the Soluble Immunopeptidome in Alpha-1 Antitrypsin Deficiency

Simon Davis

Title: Mapping Tumour Complexity using Single-Cell and Spatial Proteomics
Abstract:
Mapping Tumour Complexity using Single-Cell and Spatial Proteomics

Brain tumours exhibit complex, heterogeneous microenvironments and diverse cell populations. Understanding these microenvironments is critical for investigating disease pathology and function. To address this, we used a glioblastoma (GBM)-immune cell spheroid model to investigate immune-cancer interactions. Using spatially resolved, mass spectrometry-based single-cell proteomics, we analysed GBM and immune cells within the spheroids, complemented by bulk proteomics of the individual cell lines. On average, 1,500–2,000 proteins were detected per cell. Our analysis revealed distinct spatial localization patterns corresponding to different cell lineages within the spheroids.

Additionally, we performed spatially resolved proteomics measurements of an Atypical Teratoid/Rhabdoid Tumor using laser capture microdissection. This approach achieved resolutions up to 40 µm in gridded patterns and identified thousands of proteins. Unbiased spatial clustering highlighted clusters co-localised with prominent pathologies visible in H&E-stained sections, as well as subtler features such as immune-cell infiltration and oxygen/nutrient gradients.

Proteomic measurements with spatial and single-cell resolution, profiling thousands of proteins, will advance our understanding of tissue biology and pathology at the molecular level. Recent developments in mass spectrometry technology were key to achieving this throughput and depth, and these approaches stand to benefit from further technological improvements.

Julia Chamot-Rooke

Title: **Case Studies of Proteoforms in Human Health and Disease**
Abstract:
Case Studies of Proteoforms in Human Health and Disease

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Proteins are the central intermediaries between genotype and phenotype. It is not possible to understand the functioning of a biological system if one does not know what protein molecules are present, as well as the nature and abundances of their proteoforms. In a recent paper[1], the Consortium for Top-Down Proteomics has highlighted five important disease areas illustrating the critical role of proteoforms in disease and health: neurodegeneration, cardiovascular health, infectious disease, cancer and immunology.

In the first part of this talk, the concept of proteoforms will be introduced and simple pipelines allowing the analysis of these proteoforms, from sample preparation to data analysis will be described[2]. Challenges associated with the different steps of these pipelines will be discussed.
In a second part, a few examples showing how disease-driven research can be advanced by discovery of proteoforms and their post-translational modifications will be highlighted. These examples fall into the field of infectious diseases[3, 4] and immunology[5].

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Bryan Gonzales

Title: Proteomics without Borders: understanding the pathophysiology of childhood severe malnutrition

Noemi Procopio

Title:
Unconventional Proteomics: Where Proteins can be Used in Criminal Investigations

Eduard Sabido
Title::
Quality control in mass spectrometry-based proteomics

Magnus Palmblad
Title: AI in Mass Spectrometry and Proteomics: Fascinating Past, Exciting Present and Promising Future
Abstract:

AI in Mass Spectrometry and Proteomics: Fascinating Past, Exciting Present and Promising Future

The history of computing and the history of mass spectrometry are intertwined, going back at least to the work of Sibyl Rock at Consolidated Engineering Corporation (CEC) compiling the first computing manual for mass spectrometry in 1946, and together with Clifford Berry developing the first, or one of the first, commercially available electronic computers, the CEC 30-103. This work was driven by the need to solve computational problems in mass spectrometry. Another intersection is the development of an early expert system, Dendral, by Joshua Lederberg and colleagues at Stanford, for identifying chemical structures from mass spectra, representing a major milestone not only in mass spectrometry, but also in the development of artificial intelligence (AI). Even a conversational AI “chatbot” to search through mass spectrometry data and identify molecules was pioneered in the early 1970s.

After two “AI winters”, the field has now thawed, with machine learning and in particular deep neural networks trained on thousands to millions of spectra, significantly improving our ability to identify peptides and small molecules by predicting their observability, chromatographic behavior and fragmentation in tandem mass spectrometry. The integration of machine learned models can be used to generate realistic synthetic data. This has many potentially beneficial applications in system suitability testing, experimental design and method optimization, and providing ground truth for algorithm and computational workflow benchmarking. It also has some significant risks, which must also be addressed.

Beyond predicting behavior of analytes, AI is also used in multiomics data integration to find patterns in highly dimensional but noisy data, developing protein language models to predict structure, interactions and functions of proteins and large language models for interpreting results. With this presentation, I will focus on the history and recent developments in an attempt to put ongoing work in this rapidly developing field in context.