Advancing Single-Cell Multi-Omics: Multimodal Technologies for Functional Analysis and Therapeutic Discovery

Abstracs

Tim Welsink	**InVivo** https://www.invivo.de/, https://brukercellularanalysis.com/products/instruments/the-beacon-optofluidic-system/

Discover novel opportunities in antibody discovery, cell line development and functional single-cell analysis with Beacon® optofluidic technology

InVivo BioTech Services will present innovative applications of the Beacon® platform to accelerate biologics development. We will demonstrate how the technology enables us to expand our B-cell-based antibody discovery and efficient cell line development CRO service, as well as showcasing collaboration opportunities in functional single-cell analysis to advance single-cell Omics.

Leif Ludwig	**MDC – BIMSB / BIH** https://www.mdc-berlin.de/de/ludwig

Mitochondrial DNA mosaicism and clonality through the lens of single-cell multi-omics

Single-cell multi-omics approaches capturing mitochondrial genetic variation across individual cells have enabled new avenues for clonal tracing and studying fundamental aspects of mitochondrial genetics. Here, we will discuss our advances surrounding tracking somatic mitochondrial DNA (mtDNA) mutations toward attaining a more quantitative understanding of the clonal dynamics underlying human hematopoiesis. In the context of mitochondrial disorders, we resolve the dynamics and purifying selection of pathogenic mtDNA variants in human T cell subsets, suggesting cell-type-specific metabolic vulnerabilities.

Guido Uhlenbrock	**Bruker Biosensors** https://www.dynamic-biosensors.com/dynamic-biosensors/, https://www.dynamic-biosensors.com/helixcyto/

Characterizing membrane-associated molecular interactions directly on cells using single-cell Interaction Cytometry

Binding kinetics of molecules binding to membrane receptors are often investigated using isolated proteins, neglecting the membrane context of the target. However, the cellular membrane constitutes a complex microenvironment for embedded receptors, with factors like target mobility, co-receptors, and transmembrane domain folding affecting their behavior. Thus, understanding the influence of the cell membrane context on the interactions of molecules with membrane receptors is pivotal for understanding receptor-ligand interactions and for developing targeted therapies. In this study, we investigated how the native receptor environment influences the kinetic rates of therapeutic antibodies binding to different cell lines. By measuring real-time association and dissociation on cells, we aimed to identify predictive parameters for guiding future antibody engineering. To this end, single-cell Interaction Cytometry (scIC) was employed. In scIC measurements, single cells are captured in polymer cages on the surface of a microfluidic chip, enabling the real-time measurement of fluorescently labelled analytes. We first investigated the binding behavior of anti-CD3-antibodies to Jurkat cells and detected differential binding behaviour on living versus fixed cells. Living cells showed an increase in avidity-based binding, which could be ascribed to the maintained mobility of the target receptors within the membrane. Next, we examined the binding of two therapeutic antibodies, pertuzumab and trastuzumab, which target distinct HER2 epitopes in HER2-overexpressing breast cancer cells and exhibit different clinical efficacies. We detected differences in their binding behavior with pertuzumab exhibiting faster association to the HER2 receptor compared to trastuzumab. Furthermore, we compared breast cancer cell lines with high and low HER2 expression levels, showing that target expression levels influence the residence time.
Together, these case studies indicate that different microenvironments within the cellular membrane have direct effects on the kinetics of antibodies binding to membrane receptors. These effects need to be characterized in more detail now to elucidate the predictability of kinetic rates for example regarding the clinical efficacy of antibody candidates.

Agnieszka Ryback	**MDC – BIMSB** **https://www.mdc-berlin.de/organoids-platform**

Brain organoid technologies to model human brain diseases

Understanding how the human brain function in both health and disease remains one of the greatest challenges in modern science, yet hindered by limited availability of human samples and ethical restrictions. In recent years, 3D human brain organoids have emerged as a groundbreaking experimental system that overcomes many of these limitations. Derived from human pluripotent stem cells, brain organoids are genetically tractable and capable of recapitulating key aspects of early brain development, including cellular diversity, spatial organization, and functional properties reminiscent of the fetal brain. In my presentation, I will provide an overview of recent advances in the brain organoid field and showcase several exemplary projects that illustrate how this technology can be leveraged to model human brain diseases. These include applications in the study of neurodevelopmental disorders, neurodegenerative diseases, and brain infections, highlighting the potential of organoids to transform our understanding of brain pathology and support the development of novel therapeutic strategies.

Silvia Würtenberger	**PreOmics** **https://www.preomics.com/, https://www.preomics.com/products/beatbox**

Triple insight: Unified tissue homogenization enables in-depth proteomics, metabolomics, and glycomics from low-input samples

Originally developed for proteomics, the BeatBox® has emerged as a versatile and unified tissue homogenization platform for diverse omics applications. It enables rapid and homogeneous lysis of 1–96 samples within 10 minutes, delivering up to 2.5× higher reproducibility than traditional methods. Even challenging low-input materials—like FFPE tissue and tiny biopsies of only a few milligrams—are processed with ease. I will present applications in proteomics, metabolomics, and glycomics to highlight how BeatBox can support a broad range of research topics