Marta Carroni

Title of talk:
Structural basis for bacterial protein disaggregation and proteolysis

Abstract:
Protein homeostasis is meticulously maintained across all cells, spanning from archaea to humans. Any deviation from the equilibrium of the proteome, induced by stress or cellular aging, leads to the accumulation of misfolded proteins, contributing to cellular toxicity. A complex proteostasis network actively manages misfolded proteins through processes such as refolding, degradation, or sequestration into intracellular inclusions. Integral to this protein quality control system are ATPases from the AAA+ superfamily (ATPases Associated to a variety of cellular Activities).

These AAA+ proteins, universally present in organisms, share a common structural fold for ATP hydrolysis, but each possesses distinct function-specific domains, enabling specialization in particular cellular activities and interactions with regulatory protein partners.

Our work focuses on the structural investigation of bacterial Hsp100 AAA+ chaperones involved in protein quality control. We aim at understanding their fine-tuned regulation, which is absolutely required by the bacterium to survive harsh environment conditions and useful for us in the effort of killing pathogenic bacterial strains. Using cryo-EM in combination with biochemical functional assays, we can describe the molecular tuning mechanisms used by bacteria to assure the disaggregation or proteolysis of toxic protein species only, while leaving intact functional protein molecules.

Jan Ellenberg

Title of talk:
Quantitative Imaging of Protein Networks and Genome Structure in Single Human Cells and an Outlook on Alpha Cell

Abstract:
The rapid development of new imaging technologies allows unprecedented insights into the molecular machinery inside living cells and organisms. For the first time, light and electron microscopy have molecular sensitivity and resolving power in situ, and, if used together, can connect structural detail with molecular dynamics of the whole cell. Aided by machine learning driven image analysis powered by open sharing of image data, this provides unprecedented opportunities for new insights into the molecular mechanisms that drive life's core functions at the scale of the cell.

I will present the progress we have made to study one of life's most fundamental functions, cell division, by mapping the dynamic protein network, assembly of individual protein complexes and genome re-folding that drive it. Our work has studied cell division in human cancer cells and early mammalian embryos using advanced cross-scale imaging methods, including light-sheet, quantitative fluorescence correlation spectroscopy (FCS)-calibrated, super-resolution and correlative light and electron microscopy. The quantitative integrated molecular data that these new technologies deliver, allow us to better understand how the molecular machinery functions in space and time to ensure faithful cell division and prevent the errors that underlie congenital disease, infertility and cancer.

Anja Hauser

Title of talk:
Functional, multidimensional optical microscopy to analyze the function of myeloid cells during bone regeneration

Abstract:
Focusing on bone regeneration after injury, we aim to understand how the tissue microenvironment affects the metabolism of myeloid cells in the bone marrow over time, and how that impacts on cell function. We previously demonstrated that CX3CR1+ myeloid cells act as trailblazers for osteogenic type H vessels in the bone marrow. In order to analyze this process in 3D, we developed a tissue clearing, staining and light sheet fluorescence microscopy imaging pipeline called MarShie, optimized to image the entire intact femur at subcellular resolution down to the deepest bone marrow regions. To analyze the three-dimensional dataset, we applied a machine learning approach, enabling us to segment thousands of cells. We find that during homeostasis CX3CR1+ myeloid cells localize in perivascular niches, whereas CD169+ myeloid cells are dispersed in the parenchyma. After injury, CX3CR1+ myeloid cells relocate and sequester the injury site prior to vascularization. Analysis of the femur after full osteotomy reveals that vessel sprouting is initiated at periosteal regions.

Phenotypes and functions of immune cells are tightly linked to their metabolic profiles, which in turn is affected by changes in the tissue microenvironment. We developed a lens implant for longitudinal intravital imaging of the mouse femur, to enable micro-endoscopic fluorescence lifetime imaging (FLIM) for metabolic profiling at the same tissue region over the whole time course of bone healing. Using a reference system of fluorescence lifetimes derived from the ubiquitous metabolic co-enzymes NADH and NADPH (NAD(P)H), we can determine enzymatic activities in vivo. This approach allows us to identify a high degree of dynamics in dominant metabolic pathways for energy production. Additionally, we distinguish pathways associated to cellular function and cellular state, i.e. oxidative burst (NADPH oxidase activity) and dormancy or death. Under in vivo conditions, myeloid cells with various metabolic profiles, i.e. using other pathways for energy production than the anaerobic pathway associated with pro-inflammatory cells, perform the oxidative burst necessary for phagocytosis. This demonstrates that a high metabolic flexibility of myeloid cells in vivo.

Sverker Holmgren

Title of talk:
National Data Services for Imaging in Cell and Molecular Biology

Abstract:
The Gothenburg DDLS Data Science Node is developing and deploying national services for managing and analyzing images in CMB. The node works together with the SciLifeLab Data Center, and the areas covered are selected jointly with the DDLS Expert Group in CMB. Currently, a national Open Microscopy Environment service (OMERO) for image data management and storage is being deployed, and this will be connected to High Performance Computing resources for analysis, using e.g. AI models, and later also to image repositories for preservation and open sharing. In the next phase, the underlying work setting up this national service is used to develop and deploy two other sets of prioritized services.

Rasmus Krogh Norrild

Title of talk:
High-throughput experimental approaches for quantifying the thermodynamics of biomolecular condensate formation

Abstract:
Biomolecular condensates (BMCs) are phase-separated and membraneless compartments enriched in specific biomolecules, playing key roles in biological function and disease. Understanding how BMC formation depends on solution conditions, amino acid sequence, and nucleotide sequence is crucial, particularly for applications in drug discovery. High-throughput methods are therefore highly valuable for large-scale screening and for elucidating the fundamental driving forces of condensate formation.

In this seminar, I will present Condensate Partitioning by mRNA-Display (CPmD), a novel high-throughput approach based on mRNA display (Norrild et al., bioRxiv 2024). CPmD enables the simultaneous analysis of partitioning behaviour for tens of thousands of peptides and their corresponding synthetic mRNAs within BMCs, offering new insights into the thermodynamics of condensate formation. To validate CPmD, we employed two microfluidics-based methods, Capflex (Stender, Ray, Norrild et al., Nat. Commun. 2021) and TDIPS (Norrild et al., Angew. Chem. Int. Ed. 2024), both leveraging the commercially available FIDA1 microcapillary system. These methods demonstrate how proteome-scale CPmD data on peptide partitioning can directly inform on biomolecular condensate formation of the proteins from which the peptides originate.

Wei Ouyang

Title of talk:
Unleash the Power of Generative AI for Data-Driven Cell Biology

Abstract:
This talk presents the ongoing work of AICell Lab (https://aicell.io) focusing on developing generative AI, diffusion models for human cell modeling, and AI-driven automation in microscopy and robotics. We focus on the development of the REEF Microscopy Imaging Farm, which aims to create fully automated imaging systems that generate high-quality datasets for cell simulation. We are also building scalable platforms like ImJoy and Hypha, which power the BioImage Model Zoo—a community-driven repository enabling easy AI model testing. Additionally, our BioImage Chatbot, an AI agent built on a bioimaging knowledge base, is being extended for automated scientific discovery. These efforts converge in the Hypha platform, connecting hardware, AI models, and users to advance whole-cell modeling and redefine in-silico research and drug discovery.

Erdinc Sezgin

Title of talk:
Physical properties of cells and nanoscale bioparticles as new biomarkers of health and disease

Abstract:
Remodelling of our cells as response to environmental changes is essential for their survival and function. Although numerous studies aimed at finding protein markers during such cellular processes, there is a major gap in our understanding of how collective biophysical properties of the cells (such as stiffness, membrane fluidity, viscosity etc) alter during these crucial biological processes. Similarly, our understanding of how biophysical properties of cells change in diseases is also limited. To gain a thorough mechanistic perception of cellular processes and diseases, it is essential to fill this gap and have a clear and quantitative picture of biophysical remodelling of the cells.

We and others have made extensive effort to unravel the biophysical aspects of cells in a quantitative manner. To achieve this, we developed advanced imaging approaches that could reveal the molecular details with very high spatiotemporal resolution. These technologies allowed us to see how biophysical properties of cells play crucial roles for signalling from molecular to cellular level. Although these technologies were extremely useful to study biophysical aspects of cellular life at the molecular level, their low sampling (one cell at a time) has been a major obstacle to apply them to medical problems that require measuring thousands of cells. This can be overcome with high throughput methodologies that can robustly report on the ensemble biophysical properties of cells which require reliable reporters and instruments. Thus, while developing advanced instrumentation, we also develop reliable probes to quantify different biophysical properties of cells. Here, I will discuss our approach from probe development to high throughput biophysical analysis

Eduardo Villablanca

Title of talk:
Unraveling the Molecular Architecture of the Intestinal Barrier: Insights from Spatial Transcriptomics

Abstract:
The complex cellular network that constitutes the intestinal barrier is crucial for maintaining health and preventing diseases. In this talk, I will present the remarkable capabilities of spatial transcriptomics (ST) in unveiling the molecular organization of the entire colonic tissue during mucosal healing and tumorigenesis. By leveraging ST, we revealed a previously undiscovered regionalization of the colon's transcriptomic landscape under steady state conditions, which undergoes dramatic changes during mucosal healing. We identified spatially organized transcriptional programs that define compartmentalized mucosal healing, including regions exhibiting dominant wired pathways. Furthermore, I will discuss the translational potential of our findings by mapping transcriptomic modules associated with human diseases.