Contribution ID: **1** Type: **not specified**

Integration of live-imaging with single-cell genomics to dissect spatiotemporal gene regulation and its impact on cell behavior in the developing zebrafish embryo

Wednesday 25 June 2025 09:05 (13 minutes)

Morphogenesis during embryonic development relies on the continuous integration of complex spatiotemporal cues into gene regulatory consequences. Our lab uses zebrafish embryos as an optically accessible and genetically manipulatable model to investigate the link between gene regulation and dynamic cellular behaviors in vivo. We combine live-imaging with advanced genomics—including spatial transcriptomics, single-cell RNA sequencing, and epigenetic sequencing techniques—to dissect how cell-intrinsic programs are shaped by extrinsic cues.

The core expertise of our lab lies in the development of single-cell and spatial genomic sequencing methods, a technical repertoire that is inherently disruptive to the biological sample. Traditionally, transcriptomic readouts provide static snapshots of RNA expression, lacking both spatial and temporal resolution. A central aim of our research is to overcome these limitations by capturing space and time in genomic data. Lineage-tracing approaches allow us to reconstruct cell specification trajectories and quantify clonal diversity. Slam-seq timestamps newly transcribed RNA molecules, encoding temporal information into transcriptomes. In parallel, we are advancing spatial RNA sequencing techniques to achieve increasingly refined spatial resolution of gene expression. While it remains technically impossible to continuously observe transcription in vivo, our long-term goal is to bridge this gap by integrating live-microscopy with genomic profiling.

One of these newly-initiated projects will focus on neural crest cells, a highly migratory, multipotent cell population that travels through diverse environments before integration to various, distinct tissues. By combining live-imaging approaches with time-resolved spatial transcriptomics, we will map their migratory paths alongside their changing transcriptional landscapes. This allows us to understand how transient interactions of the cell with surrounding microenvironment drive gene regulatory changes that will influence fate decisions and differentiation.

A second research direction investigates how cells sense and integrate mechanical inputs to drive morphogenic outcomes. We are interested in how distinct or converging mechanosensitive pathways are activated by external stimuli, translated into gene expression programs that influence cell morphology, migration and proliferation. To dissect these processes at a single-cell level, we use transplantation-based chimeric embryos and will in future also incorporate optogenetic tools to perturb signaling pathways with high spatial and temporal control. This approach will enable us to distinguish cell-autonomous effects from those driven by the tissue environment.

A major challenge across both projects is the analysis and integration of the complex imaging data with our genomic analyses. The segmentation and tracking of populations and/or single cell across time points in the growing environment of the developing embryo, is our current bottleneck. Therefore, we are actively seeking collaborations in computational image analysis and further modeling after integration of the multimodal datasets.

Presenter: KLAUS, Anna

Session Classification: Talks 1-5