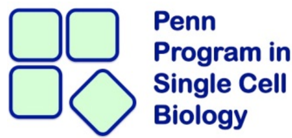

Single Cell Biology Symposium 2018

November 13, 2018, 9:00AM – 5:00PM
Arthur H. Rubenstein Auditorium
University of Pennsylvania

ABSTRACTS
Listed alphabetically by speakers' last name (underlined)

Tumor and immune single cell heterogeneity and evolution during therapy

Andrea Bild
Department of Medical Oncology and Therapeutics Research, City of Hope

My research program focuses on cancer, and uses genomic and pharmacological studies to interrogate and treat cancer. As a member of NCI's Cancer Systems Biology Consortium, our Center of HoPE (Heterogeneity of Phenotypic Evolution) is developing a suite of systems-based methodologies to understand how genomic diversity, clonal evolution, and phenotypic change interact in the progression toward chemoresistant cancer. Our studies show that selective pressures from therapy and the tumor microenvironment can propel subclones from a patient's tumor along an evolutionary trajectory that leads to resistance. In particular, we use single cell RNA and whole genome DNA sequencing to identify tumor subclones and their phenotype as tumor cells acquire resistance to chemotherapy. We have also examined the dynamics of immune cell populations during cancer treatment and progression in a clinical trial with immunotherapy and chemotherapy. Ultimately, by integrating broad disciplines centered on translational sciences, and ensuring that we include multiple ethnicities in our research, we promote innovative scientific exploration and enable scientists to tether clinically impactful results to the enhancement of an individual patient's care.

Building proteins to peek and poke at signaling circuits in vivo

Klaus Hahn
Department of Pharmacology, UNC Chapel Hill School of Medicine

This presentation will focus on new approaches to visualize and manipulate signaling networks in living cells, including what we believe are broadly applicable methods to control proteins with light, and to visualize signaling with reduced cell perturbation for multiplexing. We are probing the role of Rho family GTPase circuits in immune cell function, using engineered allosteric switches to photoinhibit or photoactivate guanine exchange factors, kinases, and GTPases as we visualize effects on downstream signals in real time. A new approach to study the conformational changes of individual molecules in live cells will be highlighted.

Generating cell diversity in the mouse and human kidney

Andrew McMahon
Department of Stem Cell Biology and Regenerative Medicine, USC Keck School of Medicine

The mammalian kidney is a complex multifunctional organ system essential for maintaining homeostasis of body fluids, removal of nitrogenous waste, and regulating the pressure and cellular

composition of the blood system. To develop new insights into mouse and human kidney organization and its developmental underpinnings, we have performed a variety of scRNA-seq studies. I will discuss approaches to generate cell resolution maps to visualize developmental patterning of the nephron anlagen, and sex and region-related variability in gene activity and cell diversity within distinct cell lineages of the mature kidney.

Single-cell dissections of a dynamic cell lineage commitment process

Ellen Rothenberg
Department of Biology, Caltech

Multilineage hematopoietic progenitors become programmed to develop into T cells in the thymus. We have shown that the "point of no return" for T-lineage choice is when *Spi1* is silenced and *Bcl11b* is activated. Control depends on GATA-3, TCF-1, and RUNX1 as well as Notch signaling, but the timing is not explained by the expression patterns of these factors alone. In this presentation, we combine results from live imaging of cell clones undergoing commitment in real time and single-cell transcriptome analysis to reveals a complex gene network as well as a slow epigenetic process that together determine commitment timing.

Quantifying proteins in single cells by high-throughput single-cell mass-spectrometry

Nikolai Slavov
Department of Bioengineering, Northeastern University

A major limitation to applying quantitative mass-spectrometry to small samples, such as single cells, is the losses during sample cleanup. To relieve this limitation, we developed Minimal ProteOmic sample Preparation (mPOP). mPOP obviates cleanup, and thus eliminates cleanup-related losses. Bulk SILAC samples processed by mPOP or by conventional urea-based methods indicated that mPOP results in complete cell lysis and accurate relative quantification. Combining mPOP with cell-sorting and liquid handling of U-937, HEK293 and Jurkat cells, we can prepare hundreds of Single Cell ProtEomics by Mass Spectrometry (SCoPE-MS) samples per day and can process 12 such samples, thus quantifying thousands of proteins in 96 single cells, per day per instrument.

Single-cell atlas of the mouse kidney reveals unexpected cellular plasticity

Katalin Susztak
Perelman School of Medicine, University of Pennsylvania

Our understanding of kidney disease pathogenesis is limited by an incomplete molecular characterization of the cell types responsible for the organ's multiple homeostatic functions. To help fill this knowledge gap, we characterized 57,979 cells from healthy mouse kidneys by using unbiased single-cell RNA sequencing. On the basis of gene expression patterns, we infer that inherited kidney diseases that arise from distinct genetic mutations but share the same phenotypic manifestation originate from the same differentiated cell type. We also found that the collecting duct in kidneys of adult mice generates a spectrum of cell types through a newly identified transitional cell. Computational cell trajectory analysis and in vivo lineage tracing revealed that intercalated cells and principal cells undergo transitions mediated by the Notch signaling pathway. In mouse and human kidney disease, these transitions were shifted toward a principal cell fate and were associated with metabolic acidosis.