Emerging Technologies in Single Cell Biology Symposium 2017
May 10, 2017, 9AM – 5:00PM
Arthur H. Rubenstein Auditorium
University of Pennsylvania

ABSTRACTS
Listed alphabetically by speakers’ last name (underlined)

Single-Neuron Methylome Analysis Reveals Epigenomic Diversity in the Mammalian Brain
Maria Margarita Behrens
Senior Staff Scientist, Computational Neurobiology Lab, Salk Institute for Biological Studies

Epigenomic marks, such as cytosine DNA methylation (mC), show characteristic cell-type and region-specific patterns that are highly dynamic during brain development. Human and mouse cortical neurons accumulate high levels of non-CG methylation (mCH) as the brain matures, and more than 200,000 differentially methylated regions are found between the main neuronal populations present in cortex. Extending cell-type specific mC analysis to all brain cell types requires unbiased single cell mC profiling. To meet the need of large-scale single-cell methylome profiling, we developed a new method for the preparation of single-cell methylome libraries. The strategy generates libraries with greater complexity than commercially available methods and allows the pooling of single cells for high-throughput library preparation. Single-cell methylomes generated from over 6,000 single neuronal nuclei, isolated from human and mouse frontal cortex, produced robust cell type classification, readily separating excitatory and inhibitory populations and identifying distinct inhibitory cell types. Single-cell methylation patterns further allowed accurate classification of pyramidal neurons in superficial versus inner layers of mouse frontal cortex.

Microfluidics-Free and WGA-Free Single-Cell Genomics
Paul Blainey
Assistant Professor, Department of Biological Engineering, Broad Institute, Massachusetts Institute of Technology

Microfluidics and whole-genome amplification are enabling single-cell genomics. At the same time, these technologies limit single-cell genomic studies by imposing cost and complexity (microfluidics) and limiting data quality (whole-genome amplification). Here I will present two new methods for single-cell genome analysis, one that requires no microfluidics or specialized equipment for direct single-cell genome amplification and another that leverages culture-based amplification rather than biochemical amplification to enable studies of de novo mutations in single cells.
The NIH Common Fund HuBMAP Initiative
Richard Conroy
Program Leader, Office of Strategic Coordination, National Institutes of Health

This presentation will give a brief overview of the NIH Common Fund's Human Biomolecular Atlas Program (HuBMAP) due to start in the fall of 2017. The goal of HuBMAP is to catalyze the development of a comprehensive atlas of cellular organization in solid, normal human tissues that will elucidate the principles of organization-function. If successful, the program will lead to new insights into inter-individual variation and tissue organizational changes across the lifespan and health/disease continuum.

Nanoscale Microfluidics for Clinical Diagnostics: Applications in Pancreatic Cancer and Traumatic Brain Injury
David Issadore
Assistant Professor of Bioengineering and Electrical & Systems Engineering, University of Pennsylvania

Circulating exosomes contain a wealth of proteomic and genetic information, presenting an enormous opportunity for diagnosis and monitoring of a wide range of diseases. While microfluidics have been used to precisely isolate cells from complex samples, scaling these approaches for exosome isolation has been limited by the low throughput and susceptibility to clogging of nanofluidics. To address these challenges, we developed a new platform, wherein millions of nanofluidic devices operate in parallel, increasing throughput by a million fold and eliminating clogging from clinical samples. To demonstrate the power of this approach, I will share two recent examples of collaborations, where we use this approach to diagnose pancreatic cancer and traumatic brain injury.

From Cell States to Cell Fates by Single Cell RNA-Seq: Examples in Developing and Adult Tissues
Allon Klein
Assistant Professor of Systems Biology, Harvard University

Can we predict future behavior from the state of cell? We explore approaches linking cell states and fates using scRNA-Seq. One “first principles” approach invokes a conservation law to predict fate probabilities from static molecular profiles. We apply this approach to study hematopoiesis, recovering the hematopoietic progenitor cell hierarchy, and identifying several novel fate regulators. A second "brute force" approach simply traces molecular states over time. We apply this approach to map differentiation in early embryos, and to explore how divergent differentiation protocols in vitro can nonetheless converge onto the same mature cell type.
Understanding Cellular Heterogeneity
Sarah Teichmann
Head of Cellular Genetics, Wellcome Trust Sanger Institute

From techniques such as microscopy and FACS analysis, we know that many cell populations harbor heterogeneity in morphology and protein expression. With the advent of high throughput single cell RNA-sequencing; we can now quantify transcriptomic cell-to-cell variation. I will discuss technical advances and biological insights into understanding cellular heterogeneity in T cells and ES cells using single cell RNA-sequencing.

Somatic Mutation and Genomic Diversity in Human Cerebral Cortex
Christopher Walsh
Chief of Genetics and Genomics, Boston Children's Hospital; Bullard Professor of Pediatrics and Neurology, Harvard Medical School

The role of somatic mutations arising during brain development in human disease, is not well understood, nor is the potential role of genomic variation between neurons as a source of normal neuronal diversity. Hemimegalencephaly (HMG) and focal cortical dysplasia are developmental brain malformations characterized by enlarged, malformed cerebral lesions typically causing epilepsy that requires resection. Direct analysis of tissue reveals causative somatic mutations that focus on mTOR activation. In parallel experiments we have developed methods for systematically comparing the genomes of single human neurons, by isolating single neuronal nuclei from human postmortem brain, and amplifying and sequencing the genomes at a single cell level. Our data suggest that normal and pathological genetic variation in neural cells are very common, and represent an intrinsic map of the cell lineage of the human brain.