Speaker: Cole Trapnell

Title: MASSIVELY MULTIPLEXED, WHOLE-EMBRYO DEVELOPMENTAL GENETICS AT SINGLE-CELL RESOLUTION

Abstract:

Vertebrate genomes encode programs of development that are remarkably robust to intrinsic and environmental noise. However, our understanding of mechanisms underlying this developmental robustness is limited. Recent advances in high-throughput genomics and single-cell RNA-sequencing now allow for comprehensive views of the molecular- and cellular-state of cells in whole developing embryos. To resolve the variation between embryos, we adapted single cell combinatorial indexing (sci)-RNA-seq with oligo-hashing to barcode a cell's embryo of origin. We deployed this technology to characterize developmental variability during (1) normal zebrafish embryonic development, and (2) development consequent to genetic knockout of 22 essential developmental genes. Together these datasets comprise ~1,700 barcoded embryos across 15 timepoints and nearly 4 million cells. These atlases of wild-type and mutant zebrafish development establish the baseline range of variation in cellular states observed during normal embryonic development and demonstrate how genetic knockouts result in specific alterations in cell-type abundances, cell state changes, and increased variance in specific cell types over time. We expect that the scale and resolution afforded by multiplexed sci-RNA-seq will transform our ability to phenotype developmental processes and necessitate new statistical and quantitative models to describe them, together enabling a mechanistic understanding of developmental robustness across cell types and organisms.