CBDS Special Single Cell Seminar Series

"Computational approaches for CRISPR/Cas9-based single-cell lineage tracing to study the drivers of metastasis and dynamics of tumor evolution"

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Host: Yariv Aizenbud, Gibbs Assistant Professor, Applied Mathematics

Special Date: Wednesday, April 21, 2021
4 p.m. to 5 p.m. Seminar

Recent advances in CRISPR/Cas9-based engineering and massively parallel single-cell sequencing have enabled the profiling of single-cell lineages. However, the rapid increase in the complexity of the data has outpaced our ability to accurately infer phylogenetic relationships. To address this, we developed Cassiopeia - an end-to-end pipeline for reconstructing phylogenies from these single-cell lineage tracing assays. I will first introduce the Cassiopeia algorithms which address the scale and nuance of this data by utilizing perfect phylogeny-based heuristics and Steiner Tree optimization. Then, I will demonstrate Cassiopeia's improved performance over traditional algorithms on both simulated trees and the largest and most complex dataset to date -- 34,557 human cells undergoing continuous CRISPR/Cas9 lineage tracing over 21 days *in vitro*. Next, I will share two vignettes that demonstrate how we can use these high-resolution phylogenies to study evolutionary aspects of cancer. First, I will discuss how we applied Cassiopeia and this technology to investigate the rates, routes, and drivers of metastasis in a mouse model of non-small-cell lung cancer (NSCLC). Next, I will share ongoing work in which we are studying the dynamics and determinants of tumor evolution from a single transformed cell in a genetic model of NSCLC. In both cases, we show that integrating our rich phylogenies with scRNA-seq information grants us novel insights into these well-studied problems. Cassiopeia and all related computational tools are publicly available on Github at https://github.com/YosefLab/Cassiopeia.

Matthew Jones is a Ph.D. Candidate at the University of California, San Francisco working in the labs of Jonathan Weissman (UCSF / MIT) and Nir Yosef (UC Berkeley). He holds a degree in Computer Science from UC Berkeley. Currently, his work focuses on developing algorithms for single-cell lineage tracing technologies and using these approaches to learn new biology about non-small-cell lung cancer tumor development and metastatic behavior. Previously, he has worked on developing computational tools for analyzing high-dimensional single-cell RNA-seq assays and simulating complex population genetic events. Recently, he spent time as a research intern at Google Health where he created deep learning models to predict patient disease risk with Electronic Health Record data. He is currently a UCSF Discovery Fellow.

Lab name: Weissman & Yosef Labs

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