ABSTRACT:

Recent progress in single-cell assays and CRISPR/Cas9-based genetic engineering has enabled the development of single-cell resolution lineage tracing technologies. While these technologies hold promise for unraveling dynamic processes across biological systems and scales, the complexity of the data presents several analytical challenges. In this seminar, I will first describe our algorithmic developments for the inference of single-cell lineages and our end-to-end computational pipeline, Cassiopeia. In the second part of the seminar, I will present our recent work using this technology and computational framework to trace tumor evolution from a single transformed cell in a mouse model of Kras;p53-driven lung adenocarcinoma. With this application, I will illustrate how these approaches and this model enable rich insights into the phylodynamics and plasticity of tumor evolution, while simultaneously highlighting the current analytical limitations that can be addressed with future work.

Suggested reading:

* Chan et al, Molecular recording of mammalian embryogenesis. Nature 2019 [This paper describes the lineage tracing technology that our group uses]
* Jones et al, Inference of single-cell phylogenies from lineage tracing data using Cassiopeia. Genome Biology 2020 [This paper describes the first iteration of Cassiopeia]
* Yang, Jones et al, Lineage Recording Reveals the Phyldynamics, Plasticity and Paths of Tumor Evolution. bioRxiv (accepted in principle to Cell). 2021 [This paper describes the lung cancer lineage tracing system and the findings of our work].