

DSICCR Tuesday Seminar Series

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Phylogenetic inference and metastatic dissemination of breast cancer from single-cell RNA-Seq

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The end-stage of breast cancer is characterized by prevalence of metastatic and chemoresistant tumors, and much effort has been devoted to understanding, preventing, and treating these phenotypes. However, studying them has been complicated by the observation that tumors are heterogeneous, and that the genotypes and phenotypes of cells within a tumor can vary widely. Nevertheless, the dissemination patterns of cancer cells have been reconstructed on the single-cell level using barcoding and DNA profiling. In contrast, chemoresistance, which is a cellular phenotype not revealed in the DNA, has been profiled using single-cell RNA sequencing. This leaves unanswered the question of whether metastasis and chemoresistance are driven primarily by genotypic or phenotypic changes in human tumors. To address this, we are currently developing an algorithm, PhylinSIC, to reconstruct the phylogenies of cancer cells from single-cell RNA-Seq data so that we can characterize the evolutionary trajectory of the cells and relate them to phenotypic changes. We are applying this algorithm to data that we previously generated from metastatic tumors from five breast cancer patients in a rapid procurement program.

