“Single-cell paired RNA & ATAC: Surveying broad multi-modal coordination in development and cancer resistance”

Single-cell paired multi-omic data, such as jointly sequenced RNA and ATAC via 10x Multiome, has been widely adopted to study the regulatory mechanisms in different biological systems. However, there are still open questions on how to broadly measure the coordination between these two modalities within individual cells and account for the changing coordination over time. In this talk, we discuss two different lines of work with similar themes that model the RNA-ATAC coordination holistically. In the first half of the talk regarding cortical development, we present the Tilted-CCA, a new statistical decomposition that uncovers the common and modality-unique geometric relations among cells. This decomposition gives us a new perspective for studying development since a gradual increase and decrease of RNA-ATAC coordination can mathematically quantify the poised chromatin state. In the second half of the talk regarding cancer resistance, we present a cell-wise lineage imputation score. This statistical regression method uses static lineage barcoding data that our collaborators have developed to work with the 10x Multiome. Our method offers new insight into cancer resistance mechanisms, as our statistical method can assess how many progenies each cancer cell is likely to produce at a future time. This method allows us to quantify how a cancer subclone's lineage size, its RNA+ATAC profile, and its plasticity contribute towards said subclone's resistant behavior.