

**Imaging and Sequencing Analysis of Cellular Regulation and Communication within Spatial Context in Cancer Tissue**

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# Thesis abstract:

Cellular interaction is a mechanism that one cell secretes signalling molecule to influence the behaviour of itself of other cells to coordinate higher biological processes. Studies have shown that cancer cells can develop the mutations to supress immune responses through cellular interaction to foster tumorigenesis and metastasis. By studying cell-cell interactions in cancer, we can systematically understand the behaviours of cancer cells and unravel the complexity of the crosstalk between cancer-immune cells. Besides, there are thousands of cells signalling molecules that have been identified as the possible communication tools. Experimentally iterate through each individual signalling molecule is prohibitively expensive. Therefore, this thesis will specifically focus on developing and implementing the computational approaches to study cellular communication in cancer.

Due to the heterogeneity in cancer, malignant tumours often comprise of multiple layers of cell-cell interactions. Besides, tumour growth and cancer metastasis are a location-dependent events. The heterogeneity of the cancer tumour is the central issues that hinders successful cancer treatment. The ability to capture the genes and/or proteins expression of the cells within the spatial context is essential in studying cell-cell communication in cancer. The past few years have witnessed a significantly rapid growth of the state-of-the-art spatial-omics technologies including spatial transcriptomic and proteomic. In this light, I will review about the past and current development of spatial transcriptomic and proteomic technologies in Chapter 1. Subsequently, we establish the hypothesis that many cellular interactions in cancer can be identified through spatial-omics data.

Significant progress has been made to developed cell-cell interaction inference using single-cell RNA sequencing data. However, there are limited number of computational packages developed to identify the interaction between cells spatial transcriptomic technologies. To address the challenges, I developed STRISH, a computational analysis framework that scans across the whole tissue section for cell colocalization through pairs of ligand-receptor. Chapter 2 is going to describe about the development of STRISH and its application to identify the local co-expression of the cells from the skin cancer tissues using the RNAscope and multiplexed protein immunofluorescence Polaris data.

Multimodal spatial-omics measurement can offer a holistic view of cells in their nature context. The current development of spatial proteomic technologies is separated into two main categories including multiplexed fluorescence and mass spectrometry imaging technologies. In Chapter 3, a representative of spatial proteomic data for each approach is applied to capture the protein expression from specimens of human skin cancer and colorectal cancer with Opal Polaris 6-plex PD1-PDL1 panel and 16-plex Hyperion Imaging Mass Cytometry (IMC), respectively. By leveraging the spatial analysis, we illustrate the capability to study tumour microenvironment through community detection and co-occurrence analysis.