

3D Imaging and Cellular Barcoding: Novel Spatial Tools for Exploring Cancer Heterogeneity

Breast cancer affects 1 in 7 women, and the risk of death from metastatic (stage 4) disease remains high. In recent years, chemotherapy and mastectomy have improved the overall survival of breast cancer patients and reduced the incidence of breast cancer in at-risk individuals. However, these treatments are non-specific, and do not eliminate the risk of cancer development, patient relapse, or progression to advanced metastatic disease. Understanding the interactions between heterogeneous lesions and the blood vessels that facilitate their spread, will enable better characterisation of these metastasis-initiating cells. New methodologies and technologies are required to facilitate such discoveries and are rapidly developing in the fields of microscopy, spatial omics and cancer. Here, we have developed two novel protocols for the detection of cancer lesions in a murine model of metastatic breast cancer. First, we use light-sheet microscopy and optical barcoding to locate metastases and blood vessels within whole mount organs. Next, we use spatial transcriptomics to detect clones that are labelled with genetic barcodes, in their original spatial context. Here, we reveal the value of spatial information for insight into the behaviour of aggressive breast cancer clones.

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