1303 SPATIAL TOPIC MODELING OF TUMOR MICROENVIRONMENT WITH MULTIPLEXED IMAGING

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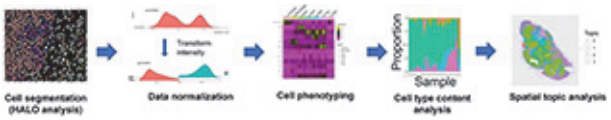
Background Multiplexed imaging technologies enable the comprehensive examination of tumor tissue at the cellular level, while preserving spatial details. However, gaining a deep understanding of complex tumor tissue organization and dynamic immune-tumor interactions from multiplexed imaging data remains challenging, primarily due to the lack of robust statistical and computational methods. Hence, we propose a novel spatial topic model that integrates cell phenotype and spatial information, inspired by the application of topic models in computer vision. Our model aims to decipher the intricate tumor tissue architecture and reveal hidden patterns in slide-based multiplexed fluorescence imaging data.

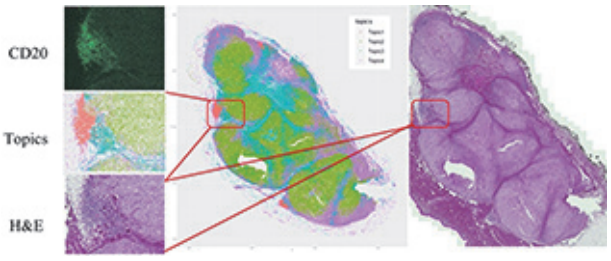
Methods We analyzed tumor tissue samples obtained from melanoma patients who received immune checkpoint blockades. The multiplexed immunofluorescence images were preprocessed using HALO (Indica Labs), which involved cell segmentation, classification of tumor/stroma region, and cellular annotation. The subsequent statistical analyses were conducted on the single cell data that were extracted and obtained from HALO. To overcome the limitations of binary gated data, a novel normalization method was developed to transform marker intensity values to probabilities of positive staining on a scale of [0,1], thereby maximally retaining information for subsequent cell phenotyping. Each cell was assigned to its most likely cell phenotype and then fractions of cell phenotypes were calculated per image. To explore the complex architecture within the tumor tissue, we employed a spatial topic model to encode spatial structure among cell phenotypes. Figure 1 illustrates the computational workflow we developed in our study.

Results Our proposed spatial topic model is an adaptation of a language model for the analysis of tumor microenvironments (TMEs) within images. In this model, spatial information is integrated into the design of documents, which represent densely overlapped regions within each image. By establishing a flexible relationship between cells and documents, the model identifies TME topics by considering co-occurring and spatially adjacent cells. We demonstrate the application of this method by analyzing whole-slide multiplexed images of melanoma samples. As a proof-of-principle, we illustrate that the spatial topic model can effectively capture Tertiary Lymphoid Structures (TLSs)-like topic representation in tumor tissue images (figure 2).

Conclusions The spatial topic model we propose offers a data-driven method for uncovering tissue architecture in multiplexed imaging data. By combining cell phenotype and spatial information, the model allows for the analysis of complex spatial tissue architectures, thereby identifying distinct TMEs across different samples. This approach facilitates the discovery of TME features that possess both biological and clinical relevance.



Abstract 1303 Figure 1 Computational workflow for TME analysis with multiplexed imaging



Abstract 1303 Figure 2 Tumor-stroma tissue architecture revealed by spatial topic model. A TLSs-like topic is identified and highlighted in a whole-slide image of a melanoma sample

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