
Spatial predictors of progression and therapeutic response in human cancers

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Abstract:

The focus of our work is to understand how normative pathways for immune tolerance are hijacked in disease. Progression to metastatic cancer, delivery of a healthy full-term infant, and pulmonary tuberculosis (TB) each occur when the immune system acquires tolerance to foreign antigens. These programs are mediated through a spatiotemporal network involving dozens of cell types and multiple organ sites. Consequently, understanding them requires technical approaches to identify these cell types and their functions within intact human tissue. To unravel this connection between tissue structure and function, in 2017 we created a new type of ion microscope for high-dimensional subcellular protein imaging of intact archival human tissue from medical center biobanks. Combining this technology with new reagents, statistical tools, and deep learning algorithms permitted us to generate the first comprehensive spatial representations of human tissue where the lineage and functional state of every cell was mapped and quantified. We have since expanded to a multimodal framework that integrates spatial proteomics with spatial transcriptomics and glycomics to understand how immune function is conserved across cancer (TNBC, DCIS, GBM), infectious disease (HIV, TB), and pregnancy. Just as red, green, and blue can be mixed to create any color, we think the vast spectrum of tissue immune responses can be broken down into weighted combinations of a much smaller set of regulatory programs. Our long-term goal is to enable a new era of anatomic pathology where unified spatial representations can be used to discover regulatory pathways that can be targeted for diagnostic and therapeutic purposes.

Reading list:

- https://www.dropbox.com/scl/fi/415fyz2ram1u2ahe9mmf/Annual-Review_MIBI.pdf?rlkey=ps9jx5xac8xbrz5b2ub0dt1ml&e=1&dl=0
- <https://www.dropbox.com/scl/fi/sv87jqw08r2pspemvamnr/Greenbaum-Nature-2023.pdf?rlkey=6j651y69m7uikm8quva5yjhrl&e=1&dl=0>
- https://www.dropbox.com/scl/fi/hx5mznnvbwu4w7jlbkh5y/Risom_Cell-2022.pdf?rlkey=kcho64mt963dgcagssrl8pplh&e=1&dl=0
- <https://www.biorxiv.org/content/10.1101/2025.01.06.631548v1>