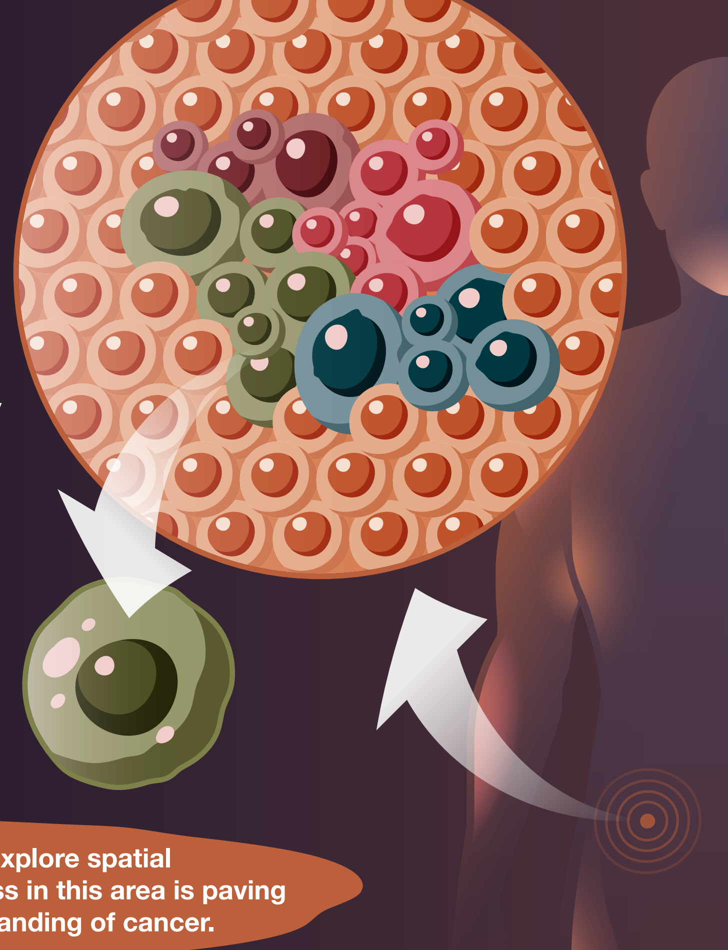
Technology Networks

Spatial Transcriptomics in Cancer



Cancers can exhibit a vast degree of intratumor heterogeneity, with different subpopulations of cells in a single tumor having distinct genetic and phenotypic characteristics. This heterogeneity can impact a patient's diagnosis, prognosis and treatment response.

Uncovering and understanding the differences between tumor cells is incredibly beneficial to cancer research, helping clinicians to diagnose and treat patients more effectively.

Single-cell approaches have been fundamental in studying tumor heterogeneity, offering a means of identifying resistant cells and providing insights into tumor progression.

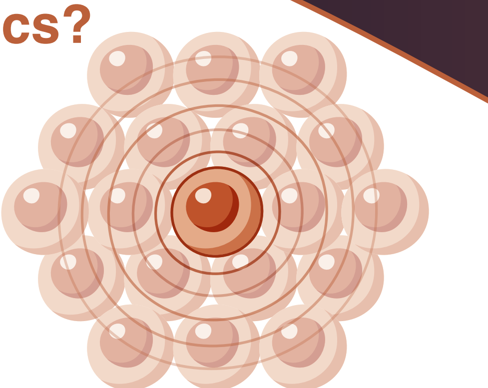
But to truly understand the function of individual cells within a tumor and its microenviroment, spatial context is needed.

In this infographic, we explore spatial transcriptomics and how progress in this area is paving the way to a better understanding of cancer.

What is spatial transcriptomics?

Spatial transcriptomics involves the use of methods that provide positional context for gene expression data.

This provides a more holistic study of cell biology by considering a cell's position and the influence of its environment.



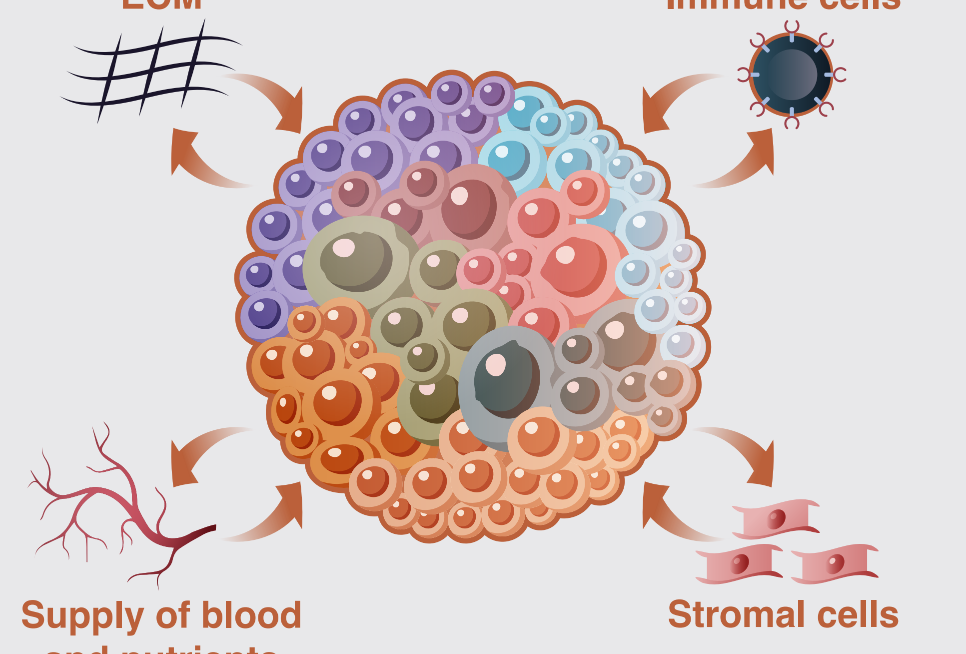
Why does spatial context matter?

Studying individual cells in isolation provides an incomplete picture; cells are heavily influenced by the surroundings in which they reside, including complex interactions with other cells, molecules and mechanical forces.

In cancer, the tumor microenvironment (TME) – a complex and dynamic mixture of non-cancerous cells and molecules that surround and interact with a tumor – contributes to intratumor heterogeneity and influences several processes including:

- Tumor growth
- Metastasis
- Immune evasion
- Therapeutic response and resistance

The TME is made up of several different components, including extracellular matrix (ECM) protein, diseased cells, various types of immune cells and secreted factors.



TME composition in one area can be completely different from an area only 100 microns away.

These differences in the TME and the dynamic interactions between tumor cells and the microenvironment cause genotypic and phenotypic changes to the cancer cells within.

Analyzing cells with spatial context can help to provide deeper insights into a tumor, its prognosis and response to treatment that may otherwise be missed.

Applications in cancer

Spatial transcriptomic methods have been used to study a variety of types of cancer, including:

Breast cancer

Spatial transcriptomics was used to examine intra- and interpatient heterogeneity in HER2-positive breast cancer patients and identify shared spatial expression signatures.

Lung cancer

Larroquette et al. used spatial transcriptomics to reveal sensitivity and resistance of non-small cell lung cancer to anti-PD1/PD-L1 antibodies.

Skin cancer

Single-cell RNA sequencing was combined with spatial transcriptomics to define the cellular composition of cutaneous squamous cell carcinoma.

Colorectal cancer

Profiling of 54,103 cells from tumor and adjacent tissues enabled the potential origin of tumor-enriched cell types in colorectal cancer to be identified.

Brain cancer

Ravi et al. used spatial transcriptomics to reveal insights into the mechanisms contributing to the immunosuppressive environment found in glioblastoma.

Prostate cancer

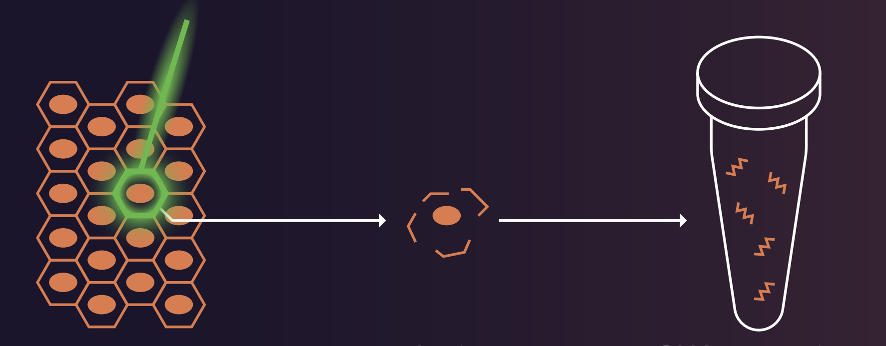
Spatial transcriptomics was used to investigate tissue-wide gene expression heterogeneity in prostate cancer.

Spatial transcriptomic technologies

There are several spatial transcriptomic approaches available, varying in complexity, throughput and resolution:

Microdissection

Regions of interest are isolated from a sample, placed in individual test tubes and the RNA is extracted and sequenced.

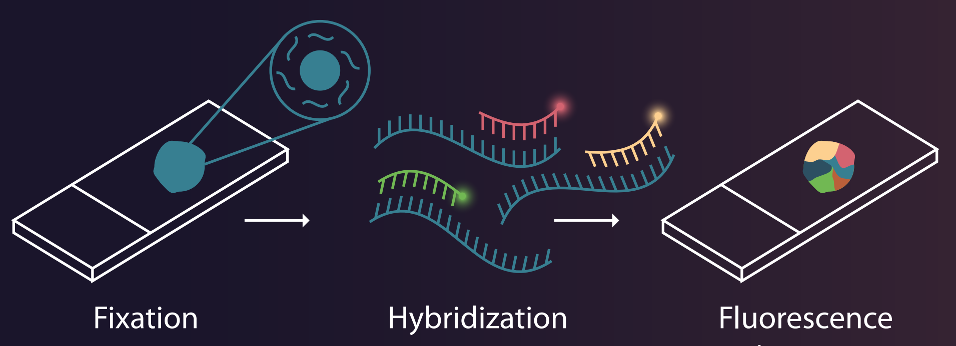


Examples include:

- Laser capture microdissection
- Transcriptome *in vivo* analysis
- Tomo-seq RNA tomography
- Geo-seq

Fluorescent *in situ* hybridization (FISH)

Fluorescently labeled probes (typically complementary RNA riboprobes) are hybridized to transcripts of interest within the sample. Binding of the probe to the complimentary transcript triggers a signal that can be visualized.

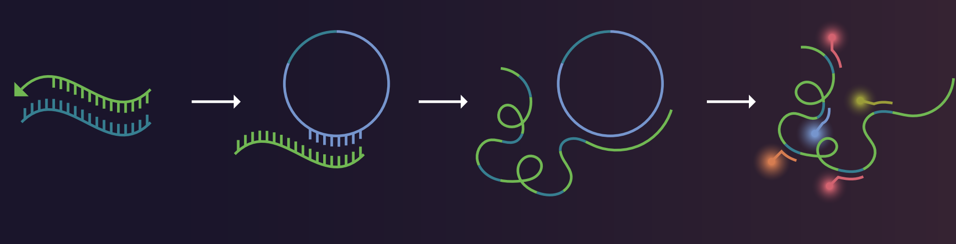


Examples include:

- Single molecule FISH
- Sequential hybridization FISH

In situ sequencing (ISS)

RNA is sequenced in a cell that remains in its original tissue sample, preserving its morphology. Originally this method was based on padlock probes targeting known RNA sequences. Over time, other variations have been developed, including the use of fluorescent probes and barcode-based methods.

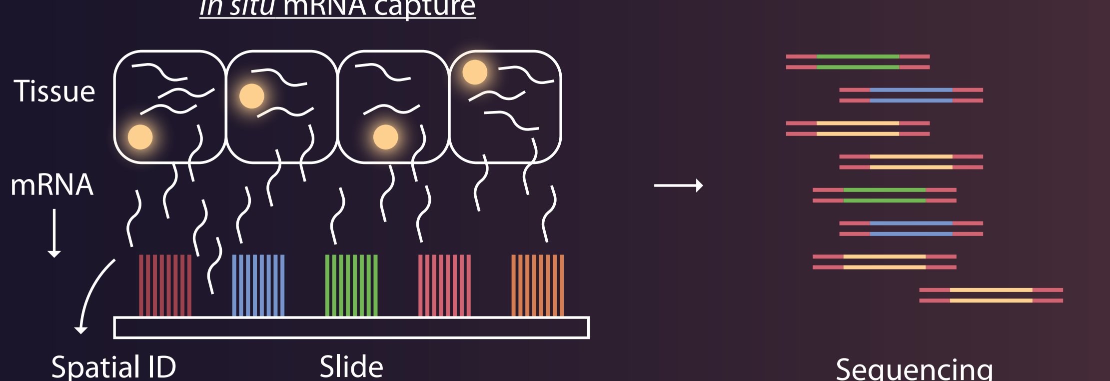


Examples include:

- Barista-seq
- STARmap

In situ capture

These methods involve capturing and barcoding transcripts within the tissue and then performing sequencing outside the tissue. This enables an unbiased analysis of the complete transcriptome.



Continual advances in methods are helping to improve the resolution, protocol run time and multiplex capacity of spatial transcriptomics, as well as the ability to work with fresh frozen tissue samples.

The future

The importance of spatial transcriptomics in oncology is expected to continue to grow and move from research to more clinical applications.

Data science improvements will be important to enable storage and analysis of big datasets.

Advances in throughput and resolution will increase accessibility.

Combining spatial data from multiple omics will provide further insights.