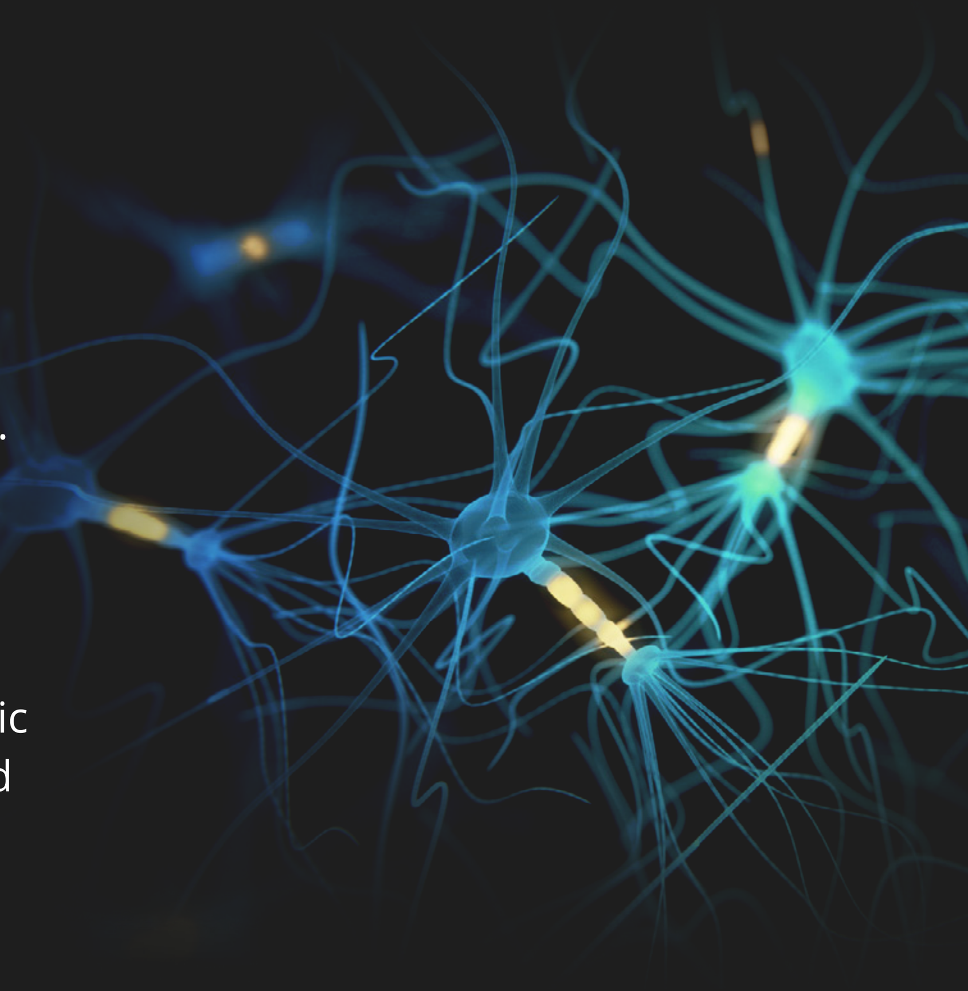
Lunaphore technologies

Navigating neuroscience through spatial biology

Neuroscience is a multidisciplinary field that focuses on the structure, function, development, and pathology of the nervous system. Thus, it has far-reaching applications from basic brain functions to the development of novel treatments for cancer, neuro-degenerative diseases, and psychiatric disorders. Spatial biology brings new tools to the field, revealing the arrangement of molecules in space and the relationships between spatial organization and various cellular and tissular functions.

Understanding brain architecture



The brain is a complex organ that exhibits cellular and molecular heterogeneity within and between brain regions. Spatial biology techniques, such as multiplex immunofluorescence (mIF), enable the identification and characterization of cell subpopulations and molecular patterns *(Figure 1)*. This level of spatial resolution allows scientists to explore how different brain regions and specific cell types interact and organize, and how these are affected by various physiological or pathological conditions.

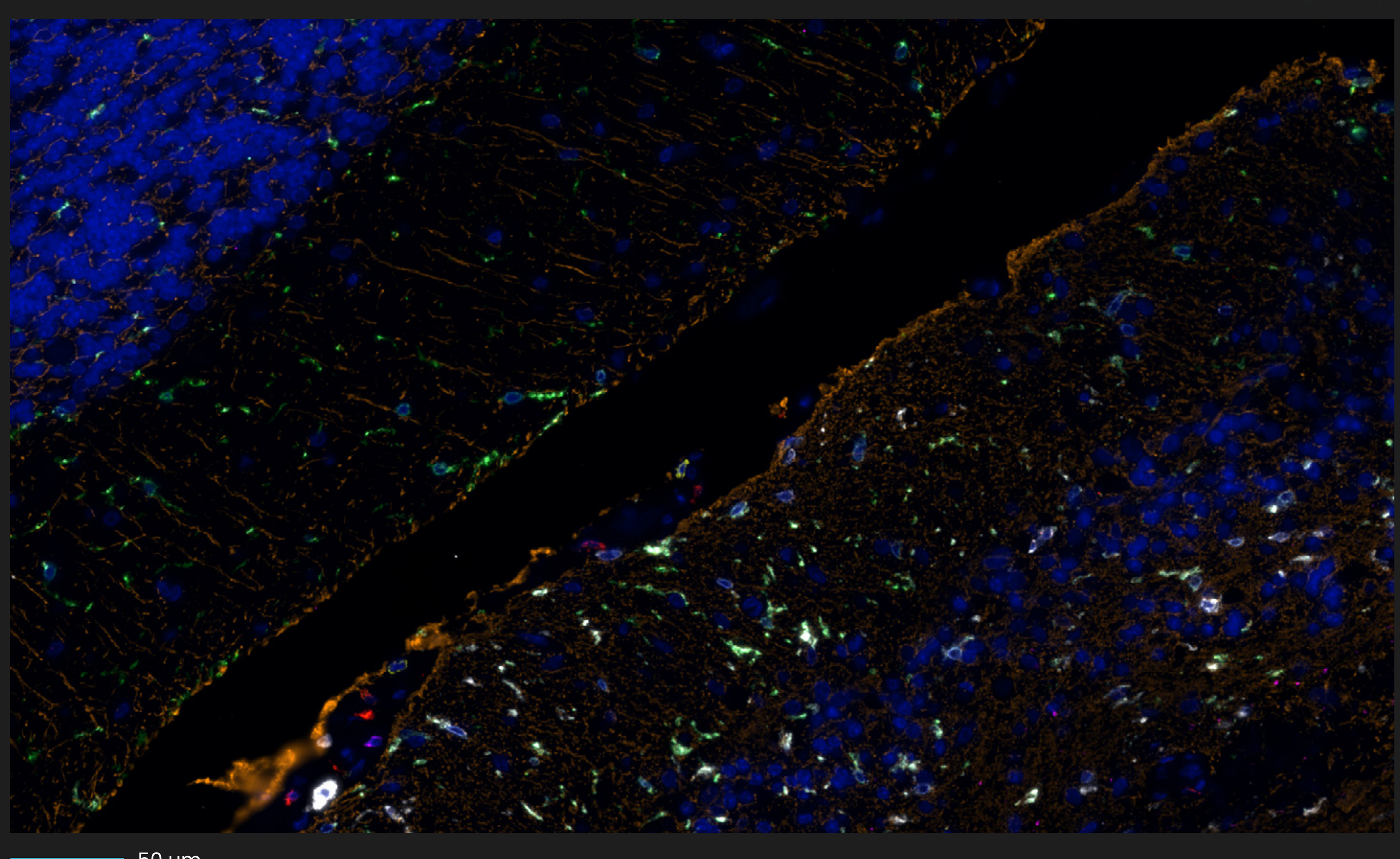


Figure 1. **Spatial composition of brain architecture in pilocytic astrocytoma.** Image generated on COMET™ by Dr. Hinda Najem from Northwestern University.

Decoding cell interactions and disease mechanisms

Spatial biology exposes spatial differences in healthy and diseased tissues, offering insights into neurological disorders' origins and progression. It has particular importance in brain tumors as it provides valuable information about the spatial organization of abnormal and healthy cells, as well as the surrounding tissue components. Malignant brain tumors present an array of complex and devastating illnesses, ranging from primary tumors like gliomas to secondary metastases, particularly from non-small cell lung carcinoma (NSCLC) or breast cancer[1]. Preclinical studies demonstrate potential for immunotherapy in treating primary brain tumors, such as glioblastoma (GBM). However, clinical trials have produced uncertain results. In contrast to treating primary brain tumors, immunotherapy has proven to be revolutionary in managing brain metastases[2]. The heterogeneity in clinical responses to immunotherapy could be attributed to an intricate interplay between molecular and genetic factors influencing T-cell-antigen recognition and immune response[3,4]. Spatial biology uncovers hidden complexities in tissue organization. It empowers scientists to deeply characterize tumor heterogeneity and correlate it with clinical benefit, leading to potentially new drug targets and applications.

Biomarker stratification: personalizing the patient journey

No two tumors are alike, and biomarker stratification acknowledges this diversity. Spatial biology techniques provide detailed tissue maps at a single-cell level through the identification and characterization of biomarkers. The spatial context highlights the key differences between different patient samples and different diseases, which aid in a better understanding of:

- Immune cell recruitment
- Level of activation of the immune system in tissue sample
- Correlation between phenotype and molecular pathways

Such molecular profiles help clinicians identify predictive biomarkers to adapt patient management, create individualized treatment plans and pave the way for new areas of drug development *(Figure 2)*.

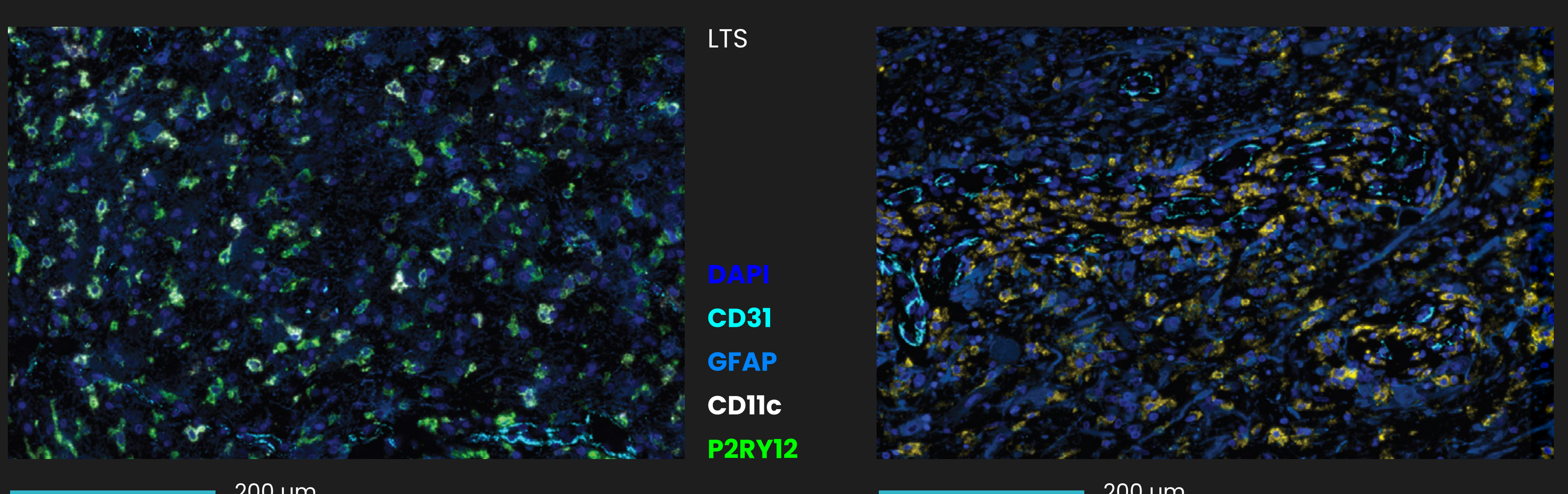


Figure 2. Studying the **immune spatial differences between long-term survival (LTS) and short-term survival (STS) glioblastoma patients by mIF** can provide insights into the immune composition of the tumor microenvironment and potentially identify factors associated with better treatment outcome. Tumors from LTS patients are enriched with P2RY12+ microglia, whereas tumor from STS patients are enriched with CD163+ macrophages. Image generated on COMET™ by Dr. Hinda Najem from Northwestern University.

Multimodal studies: a symphony of insights

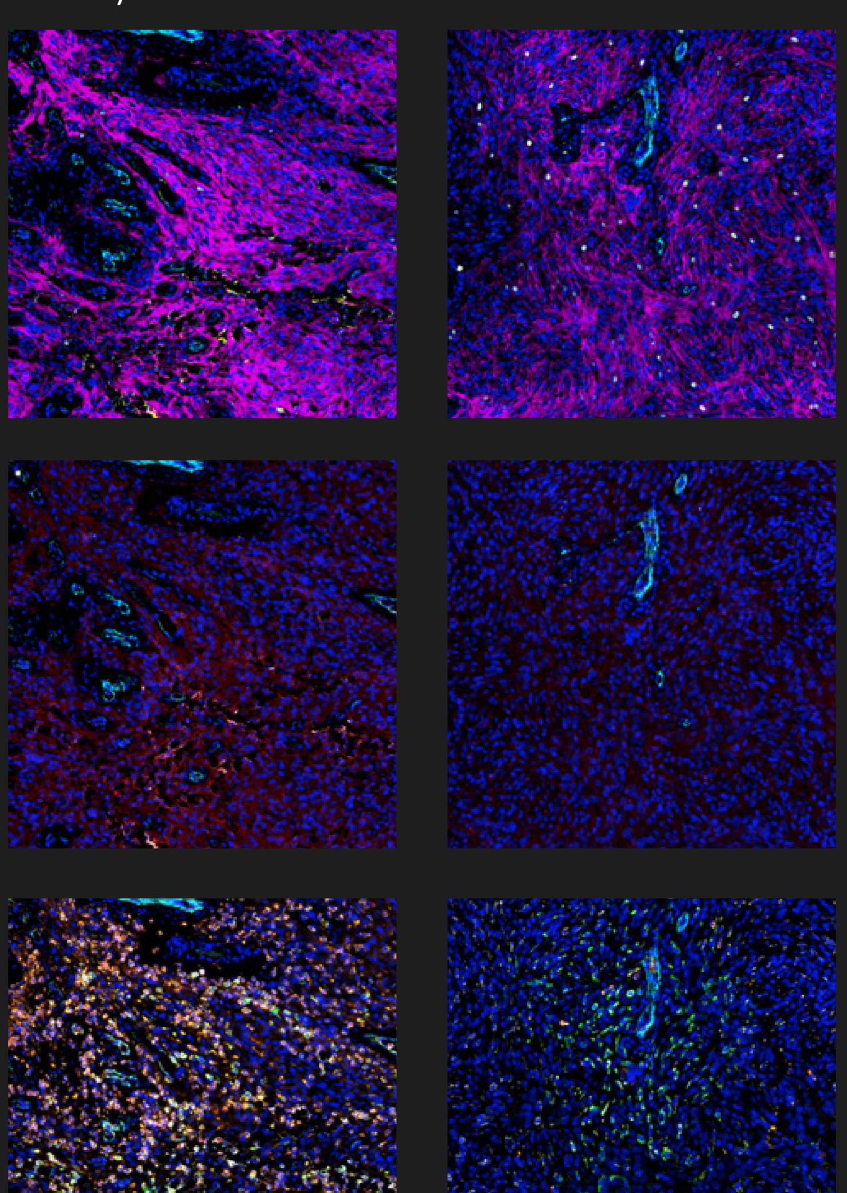
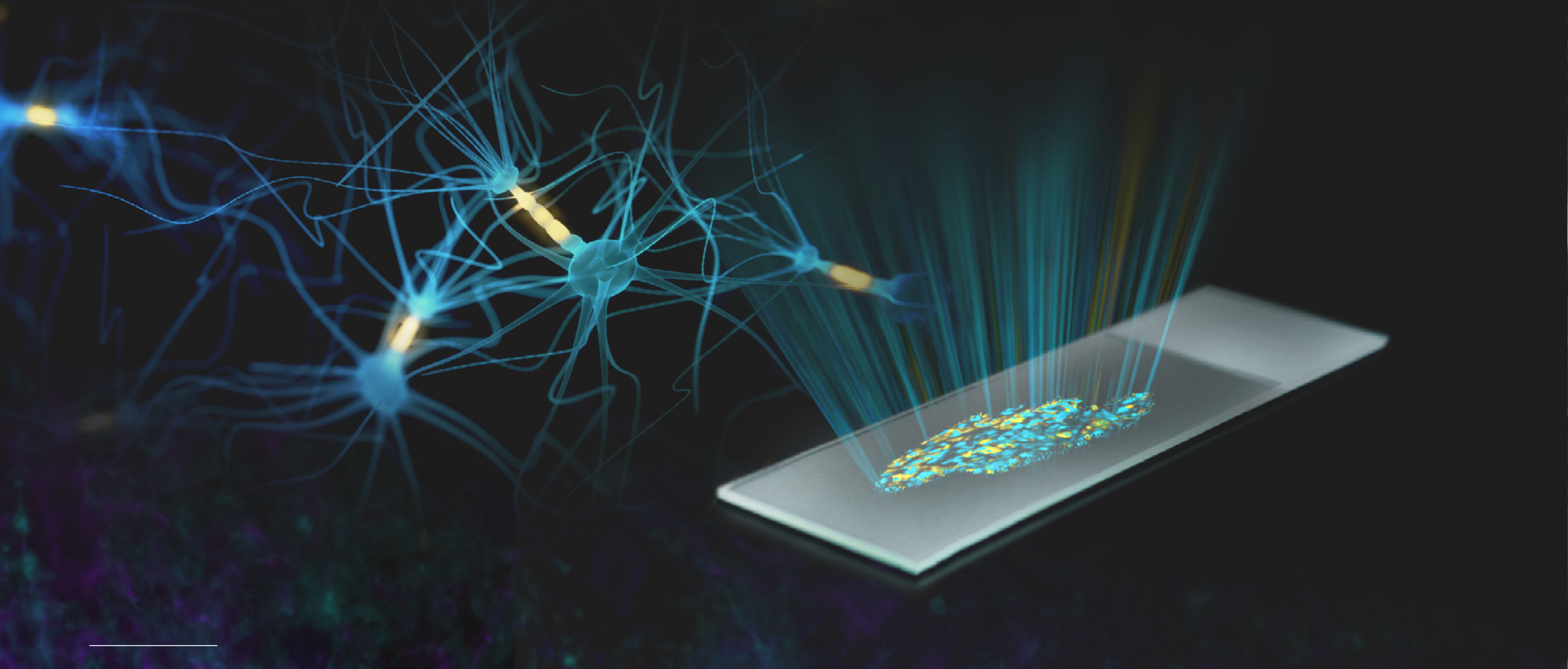


Figure 3. **Sequential immunofluorescence (seqIF™) on COMET™** highlighting the changes in pathway and cell activation in longitudinal meningioma samples at primary versus recurrent tumor stage[5]. CC license.

Multimodal approaches have the potential to transform our understanding of the brain's intricacies and unlock new avenues for addressing complex neurological challenges. Picture a symphony where each instrument contributes to a unique melody. Multimodal studies in neurosciences operate similarly by combining various imaging and analytical techniques. By integrating data from methods like spatial proteomics and single-cell sequencing, researchers gain a multidimensional perspective on brain functions, capturing both the structural and functional aspects of neuronal networks. Lucas *et al.* combined spatial transcriptomics, single-cell RNA-sequencing, and spatial proteomics, including sequential immuno-fluorescence (seqIF™) on COMET™, to characterize the intratumor heterogeneity in low- versus high-grade meningioma and primary versus recurrent tumor using matched patient biopsies[5] *(Figure 3)*.

Forging ahead

By zooming in on the brain's spatial organization, researchers are uncovering hidden insights that have the potential to transform our comprehension of brain health, development, and disease. As technology rapidly advances and interdisciplinary collaborations become more prevalent, spatial biology is poised to become a driving force behind groundbreaking discoveries in neurosciences. These progresses may lead to the development of more precise treatments and individualized therapies for a variety of neurological disorders.



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[3] Buerki RA et al. Immunotherapy of primary brain tumors: facts and hopes. *Clin Cancer Res.* 2018. 24(21):5198-5205.doi: 10.1158/1078-0432.CCR-17-2769.

[4] Friebel E. et al. Single-Cell Mapping of Human Brain Cancer Reveals Tumor-Specific Instruction of Tissue-Invading Leukocytes. *Cell.* 2020. 181(7):1626-1642.e20. doi: 10.1016/j.cell.2020.04.055.

[5] Lucas CH. et al. Spatial genomic, biochemical, and cellular mechanisms drive meningioma heterogeneity and evolution. *Res Sq.* 2023. doi: 10.21203/rs.3.rs-2921804/v1.

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