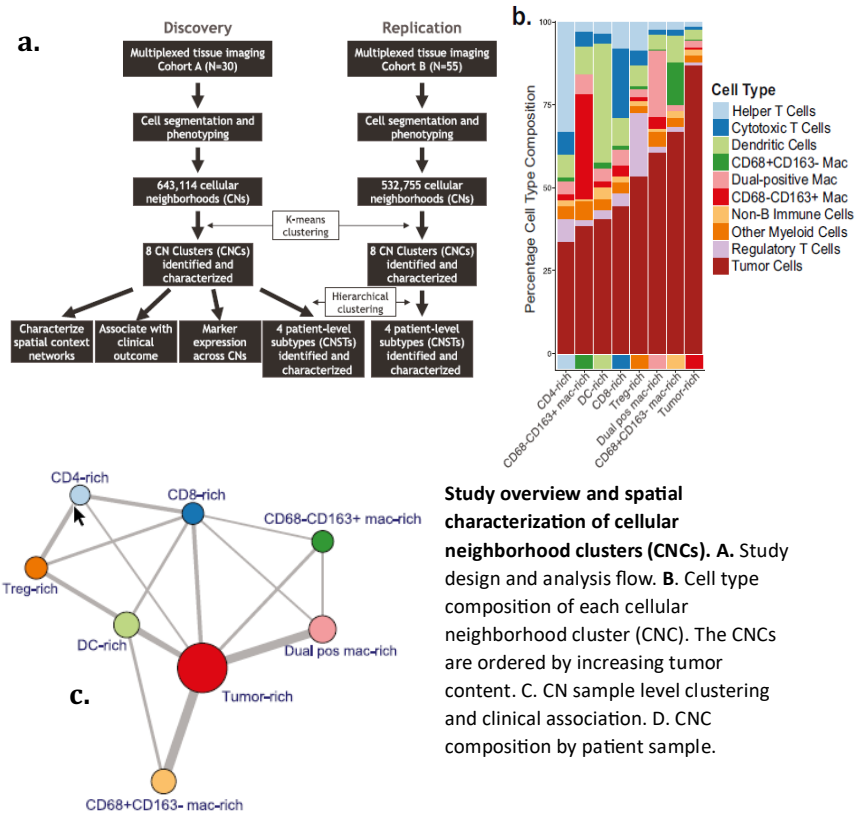
**Case Study: Uncovering Insights in Diffuse Large B-Cell Lymphoma with MIBIscope™**

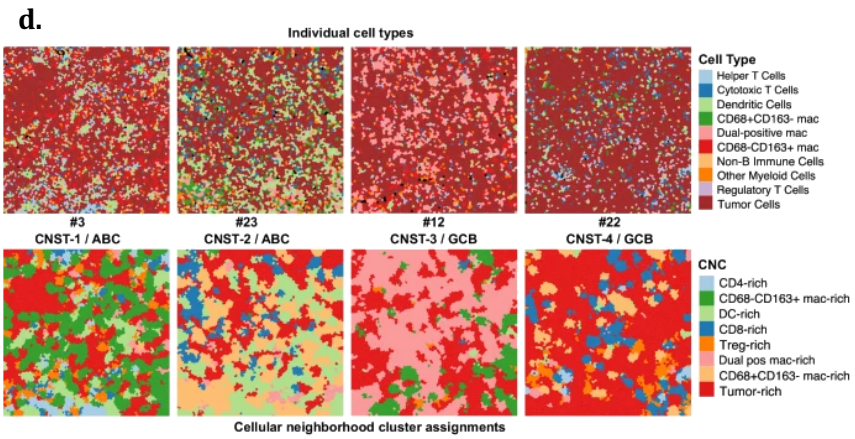
When researchers at Bristol Myers Squibb (BMS) sought to test their hypothesis that spatial relationships are key determinants in diffuse large B-cell lymphoma (DLBCL) development, they faced a significant challenge where traditional methods–fell short in providing the detailed spatial understanding of tumor and immune cell interactions. Previous analyses indicated that, despite the absence of well-defined tumor/immune compartments seen in solid tumors, the lymphoma tumor microenvironment (TME) displays organized spatial interactions between tumor and immune cells rather than a random distribution. Recognizing that these spatial relationships might be a missing piece in understanding DLBCL formation, the team turned to advanced imaging technology.

## Study overview

Using the MIBI technology, the team at BMS systematically characterized cellular neighborhood clusters (CNCs) and their spatial patterns, linking these findings to **clinical outcomes** and enhancing the understanding of DLBCL at an unprecedented level. It allowed the researchers to visualize and quantify the spatial relationships between tumor and infiltrating non-tumor cells providing a richer context than bulk transcriptomic data alone. While previous studies with imaging mass cytometry (IMC) identified cellular neighborhoods within DLBCL, they lacked detailed characterization.




**Study overview and spatial characterization of cellular neighborhood clusters (CNCs). A.** Study design and analysis flow. **B**. Cell type composition of each cellular neighborhood cluster (CNC). The CNCs are ordered by increasing tumor content. C. CN sample level clustering and clinical association. D. CNC composition by patient sample.




### Key Insights:

- Identified 31 unique cell phenotypes.
- Revealed 8 distinct cellular neighborhood clusters (CNCs).
- CD4-rich CNCs were the most segregated in tumor-rich neighborhoods.
- Discovered differences between two DLBCL cell-of-origin subtypes.
- Show in DLBCL, tumor cells show increased PD-L1 and IDO-1 expression.

## Conclusion

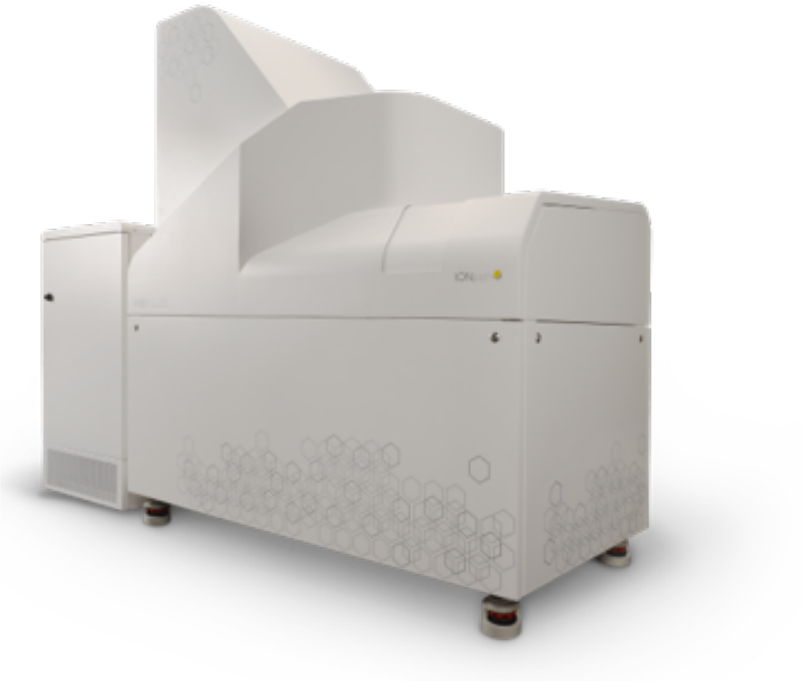
By leveraging the MIBI technology, the BMS team achieved groundbreaking insights into the spatial patterns within the DLBCL tumor microenvironment. MIBI's high-resolution imaging was crucial in uncovering and characterizing distinct cellular neighborhoods and their interactions. The team at BMS highlighted the roles of dendritic cell- and macrophage-enriched neighborhoods, with double-positive macrophages linked to poorer clinical outcomes. The work also revealed novel mechanisms of immune evasion, including physical isolation from T helper cells, clustering around immune-suppressive cells, and heightened expression of suppressive ligands. These insights pave the way for innovative approaches in immune-oncology therapies, offering a deeper understanding of tumor-immune interactions.

## MIBI technology

The MIBIscope from Ionpath is a state-of-the-art imaging platform that uses Multiplexed Ion Beam Imaging (MIBI) technology to detect and analyze over 40 biomarkers simultaneously at sub-cellular resolution.

**Key advantages include:**

- High Resolution: Sub-cellular imaging with spatial resolution down to 200 nm.
- Deep Spatial Insights: Ability to analyze the spatial distribution and interaction of proteins within the tissue microenvironment.
- In-House Bioinformatics Support: Helps researchers maximize the insights from MIBIscope's complex spatial data.



## Reference

High-plex imaging and cellular neighborhood spatial analysis reveals multiple immune escape and suppression patterns in diffuse large B-cell lymphoma.
Reiss, D.J; Leukemia (2024) 38:1164–1168;
DOI: https://doi.org/10.1038/s41375-024-02239-1