Same slide spatially resolved multi-omic profiling identifies an immunosuppressive immune checkpoint niche in nasal polyposis

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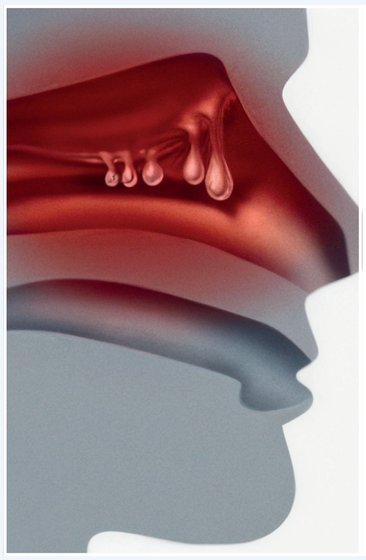
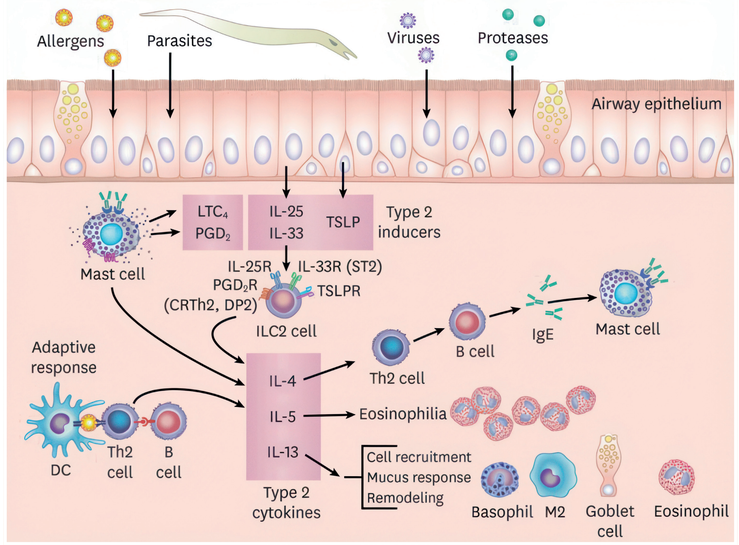


Introduction
Nasal polyps

- Nasal polyps are soft, tear drop shaped protrusions in the nasal cavity that affect ~10-15% of the population (Figure 1).
- Blocks the nasal passages and a range of symptoms, including congestion, loss of smell and pressure in the sinuses, headaches, facial pain and snoring.
- Treatments include steroid sprays and require surgery but polyps are often refractory to standard treatment and grow back.

Figure 1 Depiction of a nasal polyp



Introduction | Eosinophils and T2 inflammation

T2 inflammation is a specific immune response driven by a series of cytokines, in particular IL4, IL5 and IL13. In nasal polyps alarmins and danger signals from the epithelia are thought to drive the polarization of naïve CD4+ T-cells to a Th2 cell program and induce IgE secreting plasma cells. Th2 cytokines recruit eosinophils and mast cells with downstream activation associated with tissue damage. Eosinophils are used as a diagnostic marker in eosinophilic nasal polyps with chronic rhinosinusitis (Figure 2).

Figure 2 The T2 inflammatory cascade
K. E. Hulse, W. W. Stevens, B. K. Tan, R. P. Schleimer. Clin Exp Allergy.2015 Feb;45(2):328-46.

Aims

The aim of this pilot study was to explore multi-modal same slide imaging using a combination of CellScape multiplex immunofluorescence (mIF) and H&E staining to map immune checkpoint expression in epithelial, immune and stromal niches within polyps.

Multi-modal same slide imaging and analysis

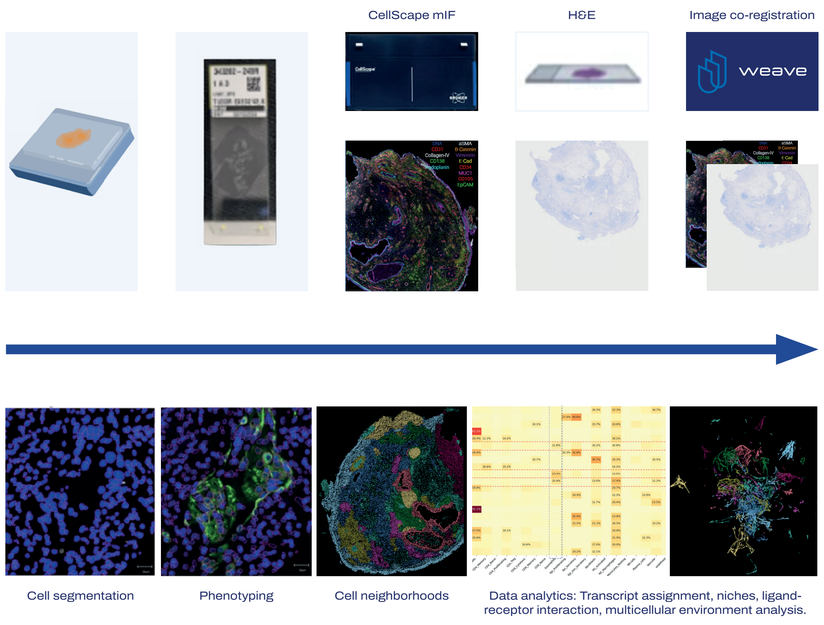
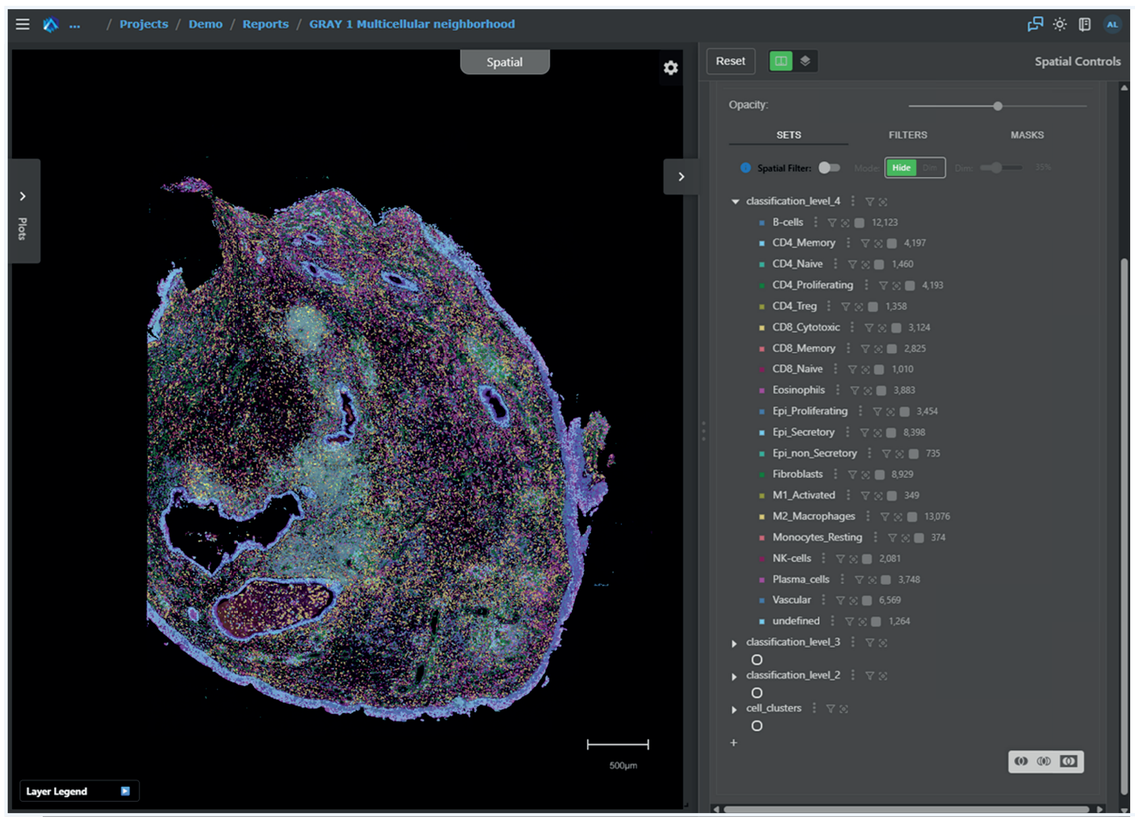


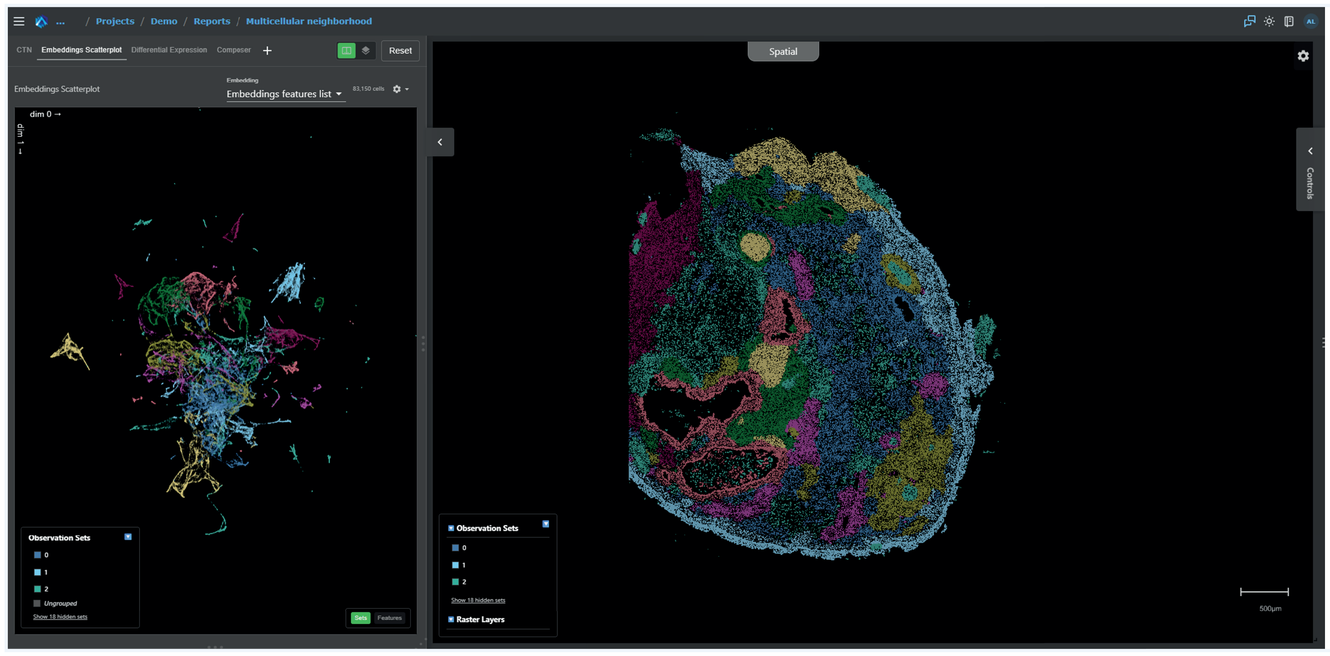
Figure 3 A schema of study design with same slide CellScape mIF and H&E staining



Multi-modal analyses identifies 19 cell types and subsets

Co-registration of the CellScape image and H&E image with Weave™ identified 19 epithelial, immune and supporting cell types in the nasal polyp, including proliferating and secretory epithelial cells, CD4+ and CD8+ cell subsets and eosinophils. Nasal polyps are characterized by a heterogenous cellular infiltrate.

Figure 4 A spatial map showing cell types across nasal polyp tissue



Multi-cellular environment analysis

Proprietary multi-cellular environment analysis in Weave was used to identify spatially recurring areas of similar cellular and molecular composition in the tissue. Weave™ identified 20 areas of tissue that had distinct cell type component and organization.

Figure 5 A spatial map showing cellular environments across the nasal polyp

Cell type compositional profiling highlights pervasive M2 macrophage infiltration

Compositional profiling of cells across multicellular environments found 20 niches within the polyp tissue (Figure 6). M2 macrophages were found in high abundance across the multicellular environments.

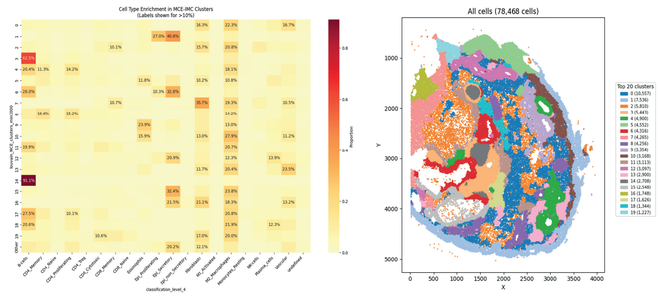
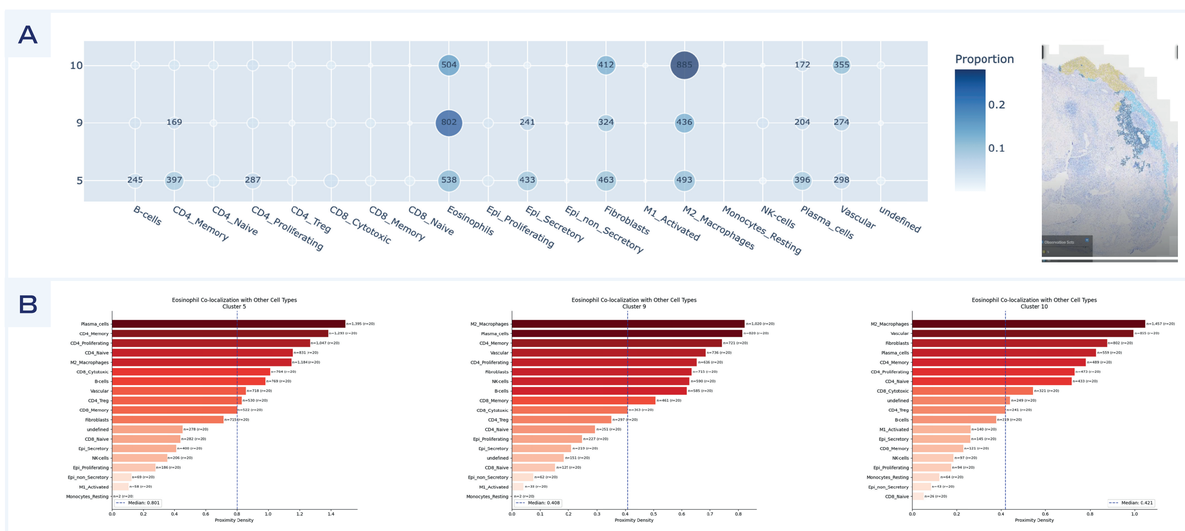


Figure 6 Neighborhood cell type composition



Three eosinophil niches identified within polyp tissue

Across the tissue, eosinophils were found in high abundance (figure 7a). Further investigation highlighted eosinophil-M2 macrophage interaction in two of the niches (Figure 7b). One niche, cluster 5, exhibited strong inflammatory activity (Figure 7c).

Figure 7 Eosinophils niches across nasal polyp tissue

Checkpoint inhibition signaling

PD-L1+ granulocytes along with PD-L1+ M2 macrophages (CD163+PD-L1+) and monocytes/macrophages (CD68+PD-L1+) were in close proximity to CD4+PD-1 and CD4+FOXP3+PD-1+ T-cells in polyp stroma.

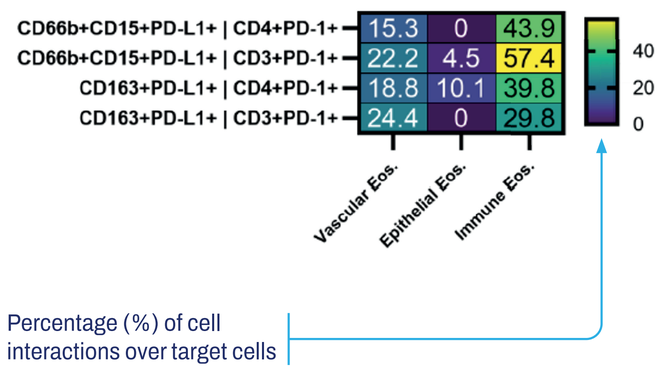
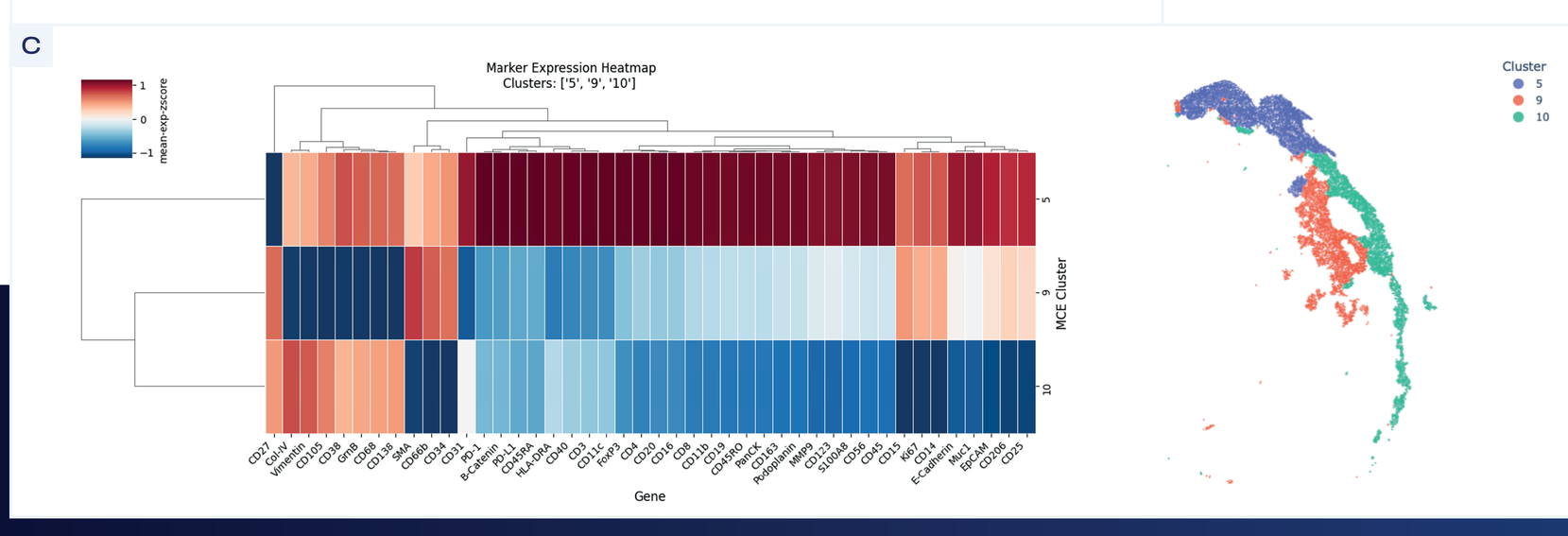


Figure 8 PD-1 and PD-L1 expression in eosinophils niches



Conclusions

Multimodal profiling identified immunosuppressive immune checkpoint niches in polyp stroma that may contribute to the aberrant inflammation of CRSwNP despite immune activation.

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