



P3.095: SPP1⁺ macrophage-CD1C⁺ DC Spatial Niches Associate With Resistance in EGFR-mutant NSCLC

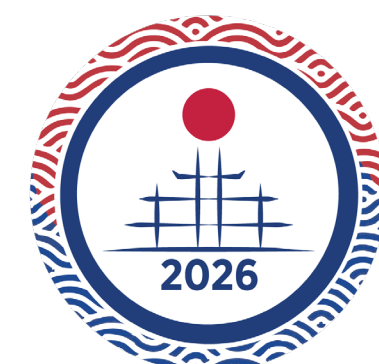
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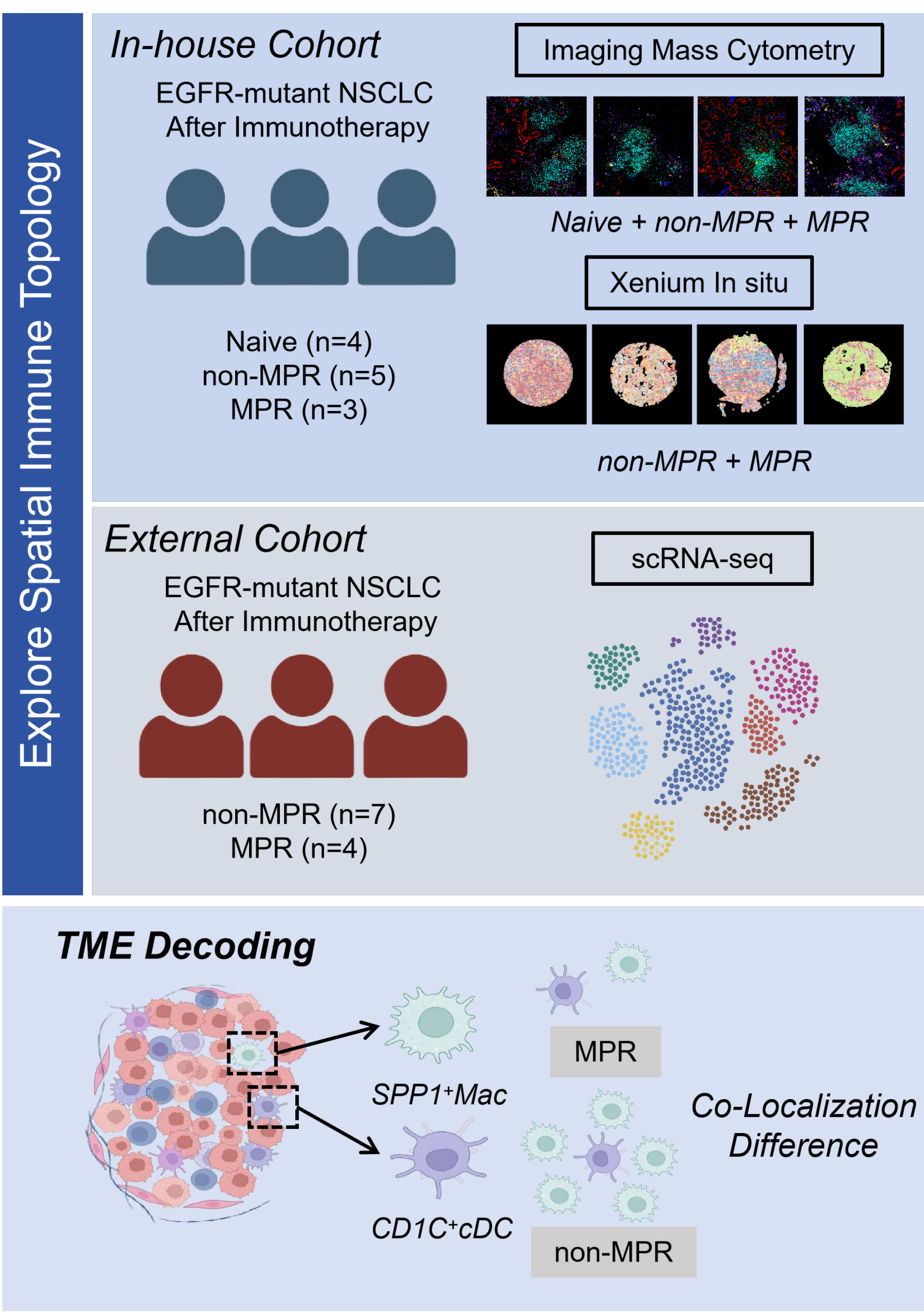
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INTRODUCTION

- EGFR-mutant NSCLC responds poorly to immune checkpoint inhibitors, yet the basis of resistance remains unclear.
- Spatial organization of the tumor microenvironment critically shapes antitumor immunity, but resistance-associated interactions remain poorly defined.
- To address this gap, we integrated scRNA-seq, IMC, and Xenium spatial transcriptomics to map immune niches linked to chemoimmunotherapy response.

METHODS



DISCUSSION AND CONCLUSION

Key Messages

- Spatial profiling identified an immunosuppressive SPP1⁺ macrophage-CD1C⁺ cDC niche linked to limited immunotherapy benefit in EGFR-mutant NSCLC.
- SPP1⁺ macrophage-CD1C⁺ cDC spatial interactions were associated with reduced DC activation and antigen-presentation capacity.
- Spatial immune features may provide novel biomarkers for predicting immunotherapy resistance in EGFR-mutant NSCLC.
- Therapeutic strategies targeting macrophage-DC crosstalk or restoring DC immunogenicity may improve the efficacy of immune checkpoint blockade in EGFR-mutant NSCLC.

Clinical Implications

REFERENCES & ACKNOWLEDGEMENTS

REFERENCES

- Shi Y, et al. Lancet Respir Med. 2022;10:1019–1028.
- Lu S, et al. J Clin Oncol. 2022;40:3162–3171.
- Piper-Vallillo AJ, Sequist LV, Piotrowska Z. J Clin Oncol. 2020.

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RESULTS

Spatial immune niches associated with chemoimmunotherapy resistance in EGFR-mutant NSCLC

- Cell neighborhood mapping revealed distinct spatial architectures associated with clinical responses.
- The SPP1⁺ macrophage-DC-enriched neighborhood (CN8) was preferentially enriched in non-MPR tumors and showed increased macrophage-DC proximity.

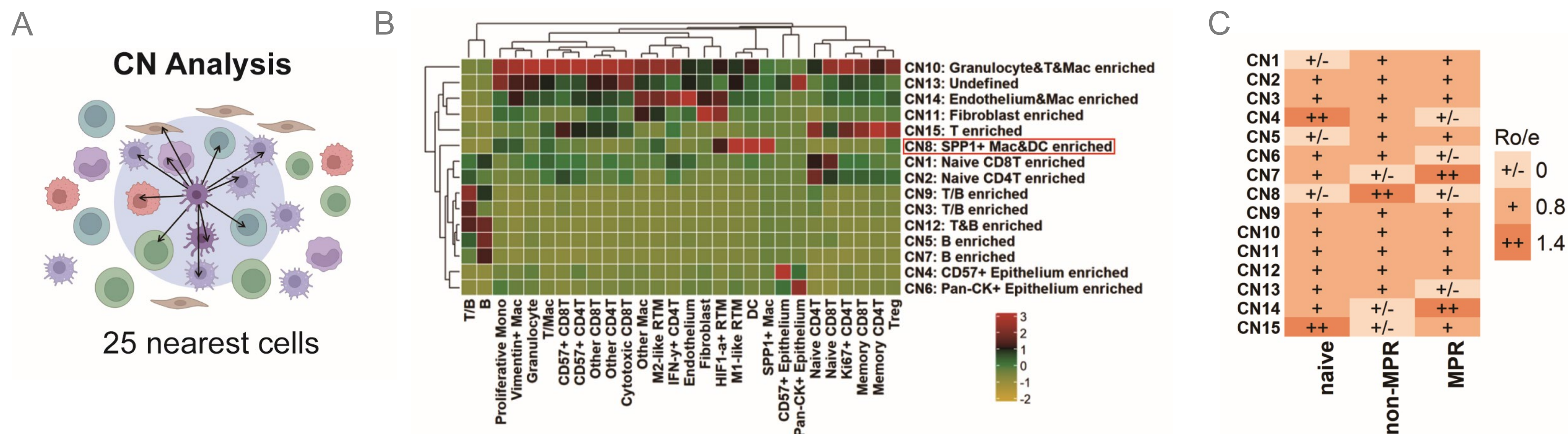


Figure 1: Spatial neighborhood analysis reveals immunosuppressive interactions between SPP1⁺ macrophages and DCs in non-MPR EGFR-mutant NSCLC after immunotherapy. (A) Schematic demonstrating the identification of CNs. The CN was defined based on the center cell and its nearest 25 cells. (B) Identification of 15 distinct CNs from the 28 cell clusters and their corresponding abundances in each CN. (C) Ro/e analysis indicating CN enrichment across different treatment response groups.

SPP1⁺ macrophage-CD1C⁺ cDC crosstalk drives an immunosuppressive microenvironment

- Non-MPR tumors harbor enriched SPP1⁺ macrophages with enhanced M2-like features.
- Spatially interacting CD1C⁺ cDCs show reduced activation, antigen presentation, and pro-inflammatory signaling.

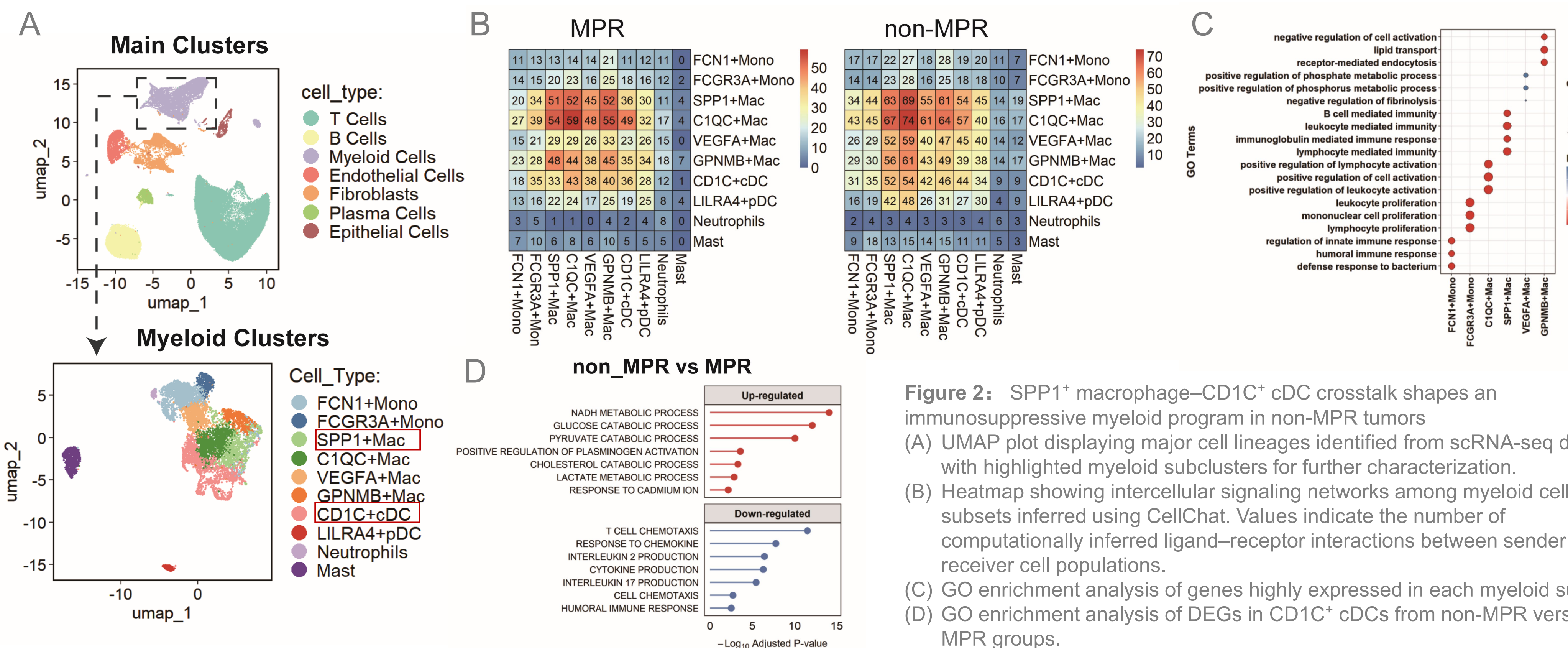


Figure 2: SPP1⁺ macrophage-CD1C⁺ cDC crosstalk shapes an immunosuppressive myeloid program in non-MPR tumors (A) UMAP plot displaying major cell lineages identified from scRNA-seq data, with highlighted myeloid subclusters for further characterization. (B) Heatmap showing intercellular signaling networks among myeloid cell subsets inferred using CellChat. Values indicate the number of computationally inferred ligand-receptor interactions between sender and receiver cell populations. (C) GO enrichment analysis of genes highly expressed in each myeloid subtype. (D) GO enrichment analysis of DEGs in CD1C⁺ cDCs from non-MPR versus MPR groups.