

INTRODUCTION

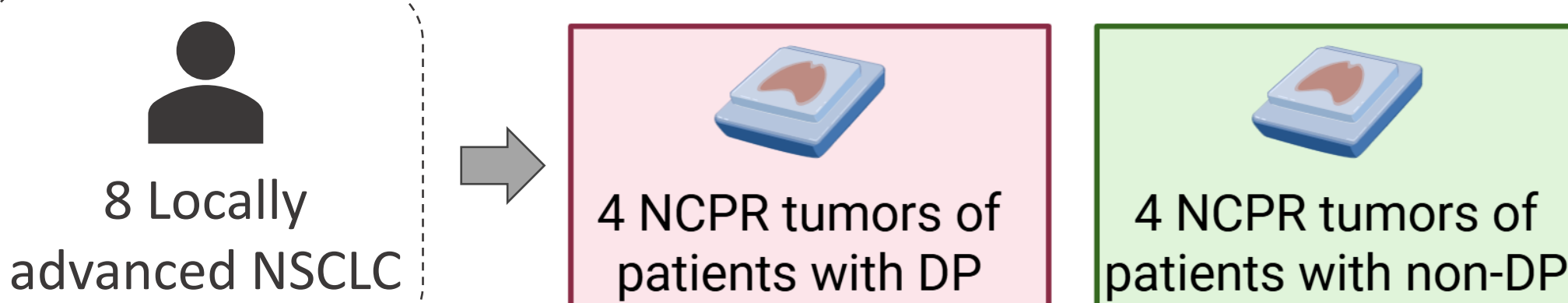
Perioperative chemoimmunotherapy (ChIO) has improved outcomes in **locally advanced NSCLC**, but some tumors exhibit **non-complete pathological responses (NCPR)**. However, this group is heterogeneous, and approximately 40% of patients with NCPR tumors experience **disease progression (DP)**, highlighting the need for better **biomarkers to refine risk stratification** and guide postoperative management.

This study aimed to **spatially analyze** the tumor microenvironment of **NCPR tumors** to identify **signatures of disease relapse** after perioperative ChIO.

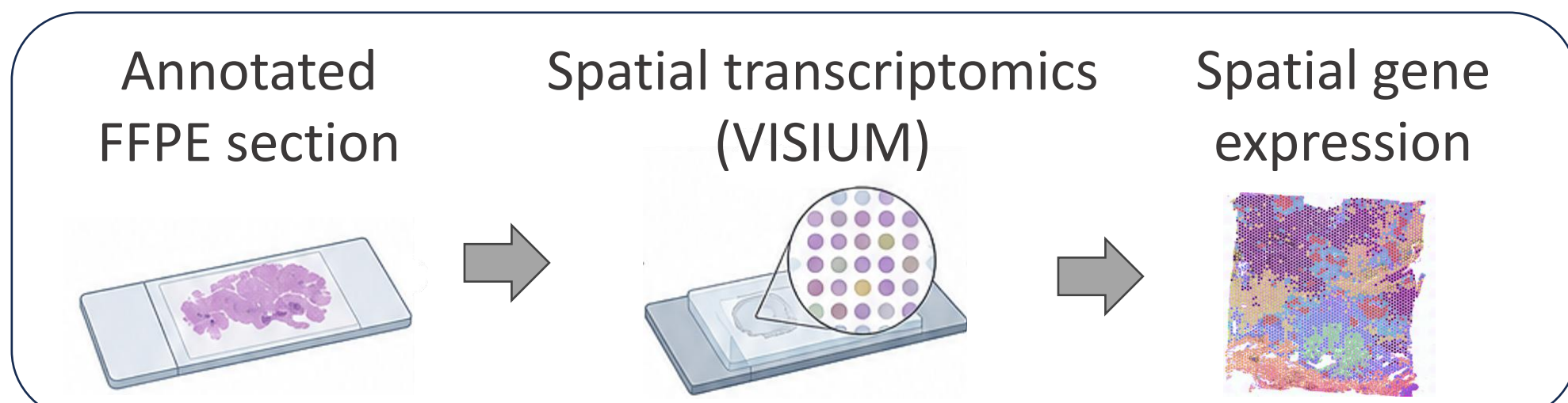
METHODS

NADIM trial

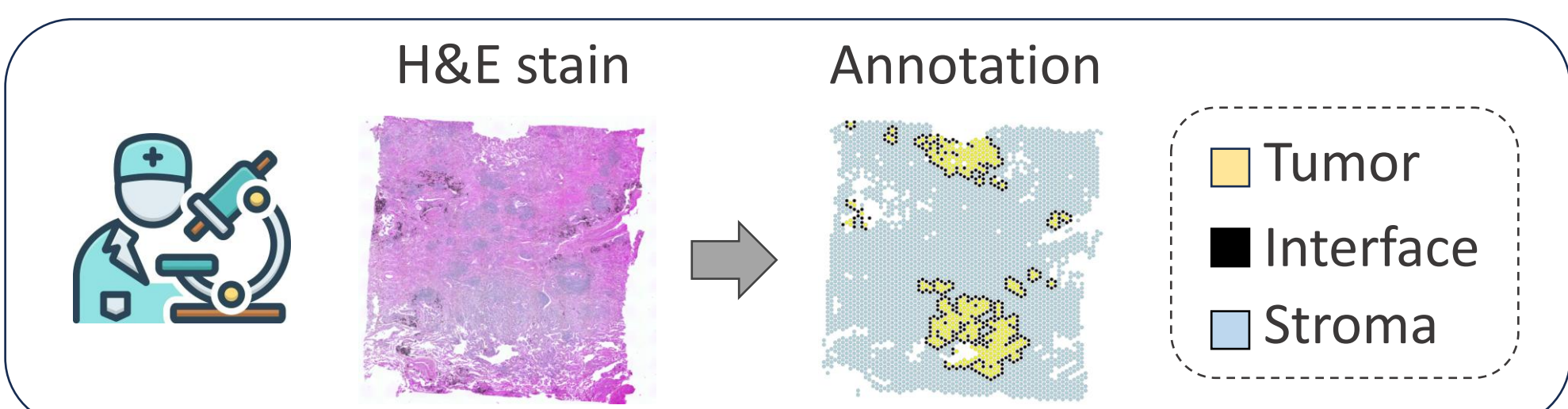
Surgery samples after ChIO treatment



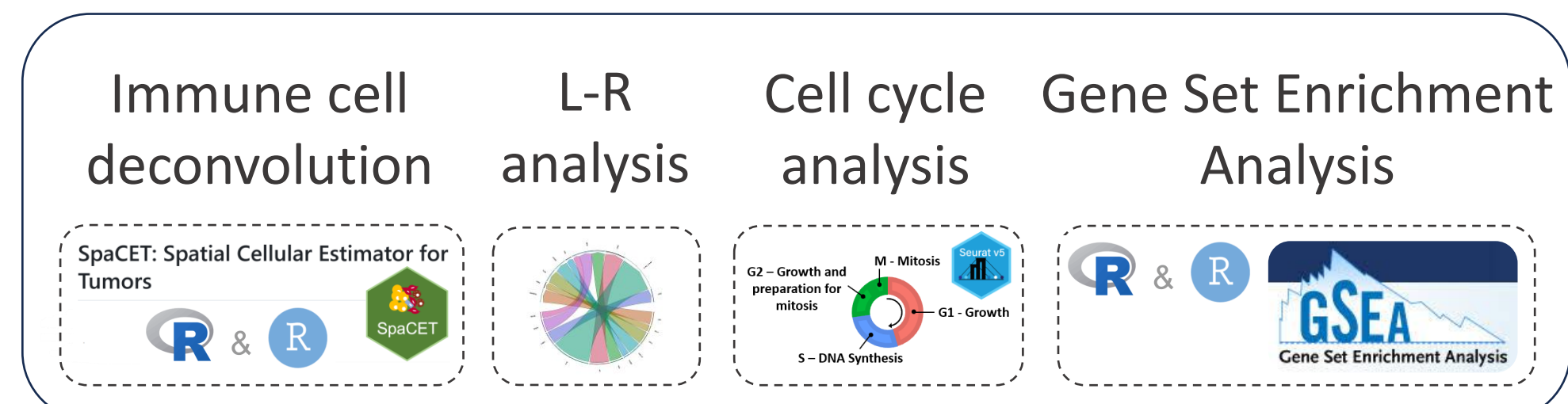
1 SPATIAL TRANSCRIPTOMICS



2 REGION ANNOTATION BY PATHOLOGIST



3 COMPARATIVE ANALYSIS



DISCUSSION AND CONCLUSION

NCPR tumors from patients with disease progression displayed a spatially distinct tumor microenvironment characterized by altered immune organization, reduced ligand-receptor interaction complexity, increased tumor metabolic activity, and enhanced proliferation, particularly at the tumor interface and within tumor regions.

These features may help identify patients at higher risk of relapse after perioperative ChIO.

REFERENCES & ACKNOWLEDGEMENTS

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- Deutsch JS *et al.* Association between pathologic response and survival after neoadjuvant therapy in lung cancer. *Nat Med* (2024).
- Sierra-Rodero B *et al.* Decoding B-cell Signatures of Complete Pathologic Response to Perioperative Chemoimmunotherapy in Non-Small Cell Lung Cancer. *Clin Cancer Res* (2026).

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RESULTS

In NCPR tumors, DP was associated with lower stromal antitumor infiltrate and higher intratumoral infiltrate.

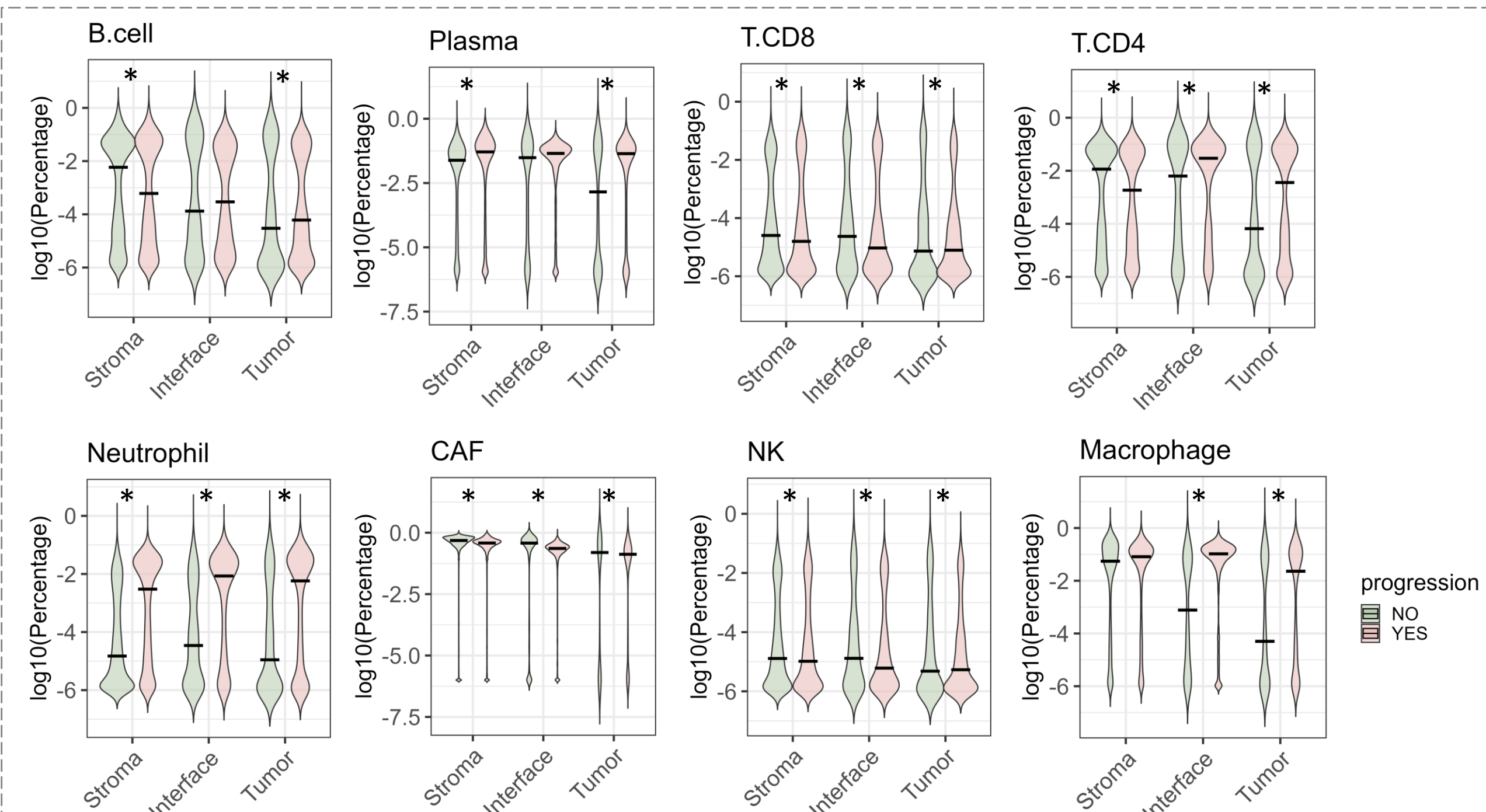


Figure 1. Deconvoluted immune cell populations in stroma, interface and tumor. Dunn's test for multiple comparisons was used to compare immune cells between areas. An adjusted *P* value of <0.05 (*) was considered statistically significant.

Tumor metabolism were higher in patients with PD in interface and tumor regions.

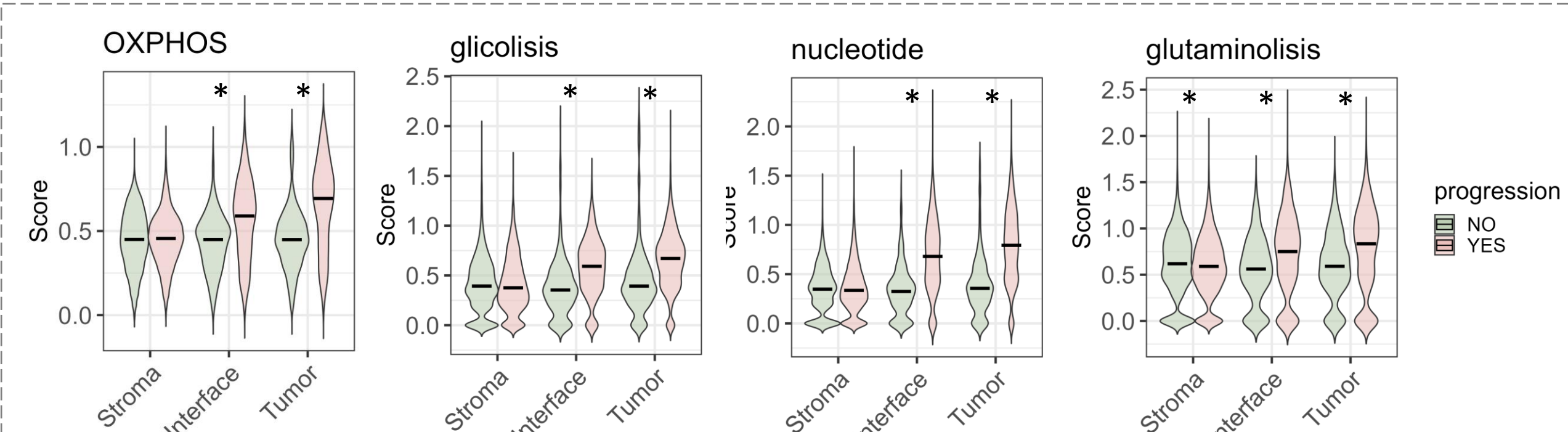


Figure 4. Tumor metabolic pathway activity in the interface and tumor regions. Metabolic pathway scores were estimated using MCP-counter and custom gene signatures for OXPHOS, aerobic glycolysis, glutaminolysis, and nucleotide synthesis. Scores were compared using the Mann-Whitney U test. A *P* value <0.05 (*) was considered statistically significant.

Cell cycle analysis indicated a higher proliferative fraction (G2/M) in interface and tumor areas of tumors of patients with DP.

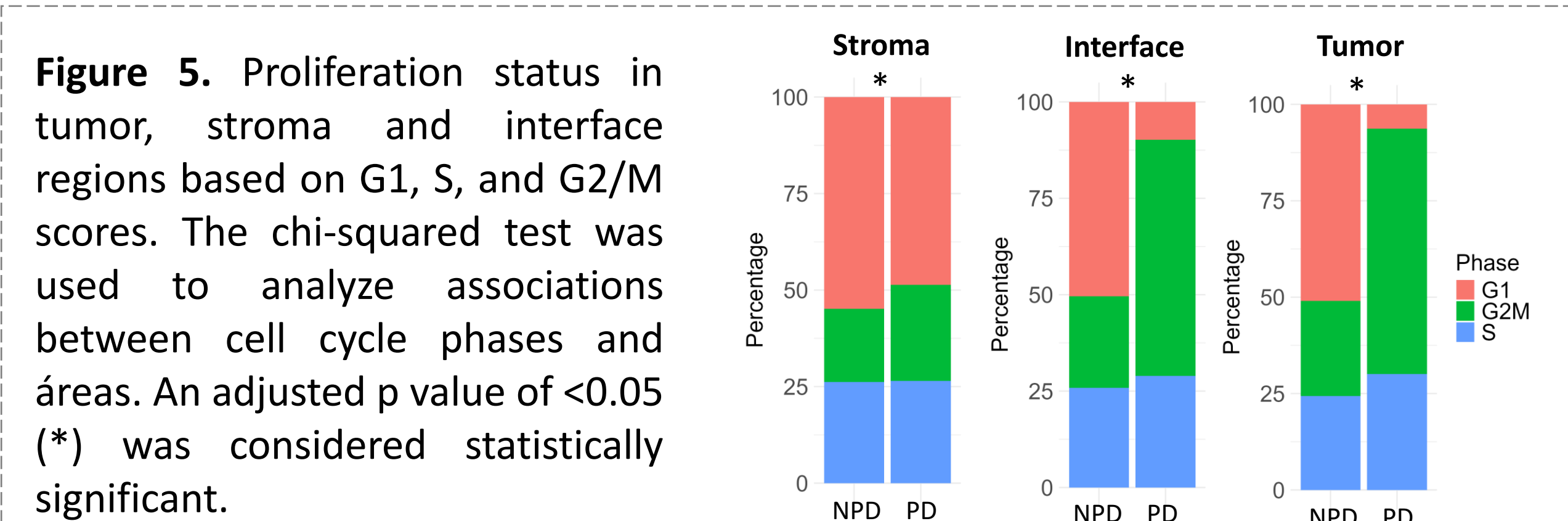


Figure 5. Proliferation status in tumor, stroma and interface regions based on G1, S, and G2/M scores. The chi-squared test was used to analyze associations between cell cycle phases and areas. An adjusted *p* value of <0.05 (*) was considered statistically significant.

In tumor, DP showed lower L-R interaction richness/diversity but higher evenness.

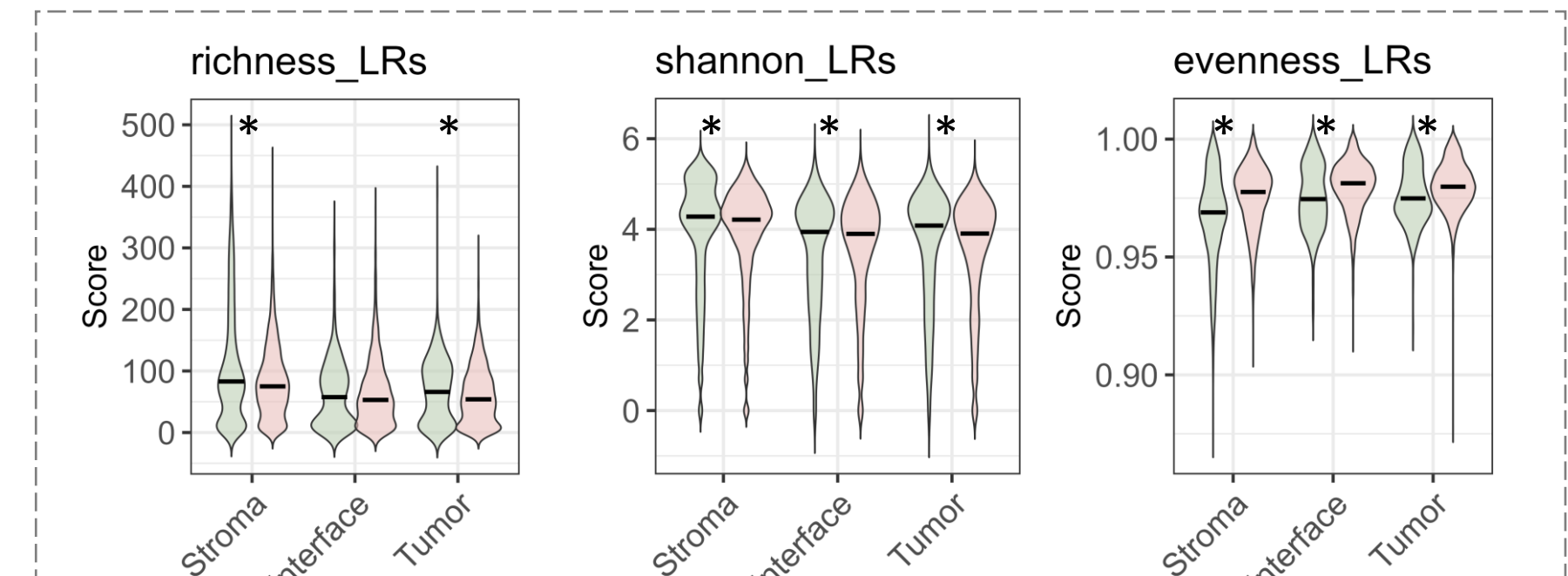


Figure 2. Immune cell-cell communication analysis. Ligand-receptor (L-R) interaction metrics (richness, diversity, and evenness) were compared between groups using the Mann-Whitney U test. An adjusted *P* value <0.05 (*) was considered statistically significant.

In tumor region, PD was associated with increased mitochondrial bioenergetics and decreased B cell-mediated immunity.

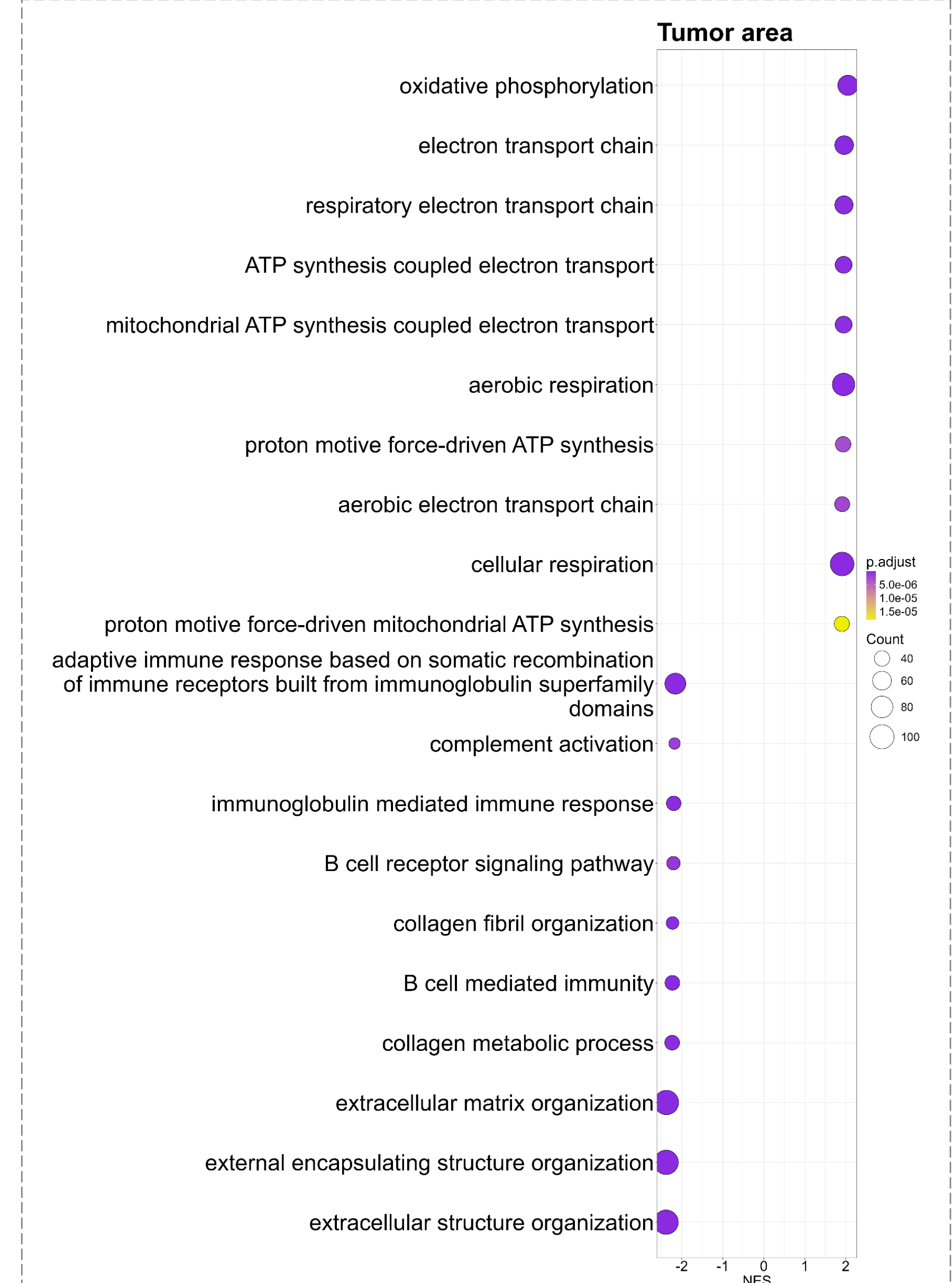


Figure 3. Gene Set Enrichment Analysis (GSEA) tumor regions of patients with DP. Pathways with *p* adjusted <0.01 and core enrichment >15 genes were considered statistically significant.