

SINGLE-CELL ANALYSIS OF HUMAN GLIOMA AND IMMUNE CELLS IDENTIFIES S100A6 AS A NOVEL IMMUNOTHERAPY TARGET

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01 INTRODUCTION

Challenge: Glioblastoma Despite aggressive treatment, glioblastoma (GBM) remains fatal. Its immunosuppressive environment ("cold" tumor) shields the cancer and renders immunotherapies ineffective.

Our Focus: The S100 Family We investigated the S100 protein family to identify a key driver of this immunosuppression.

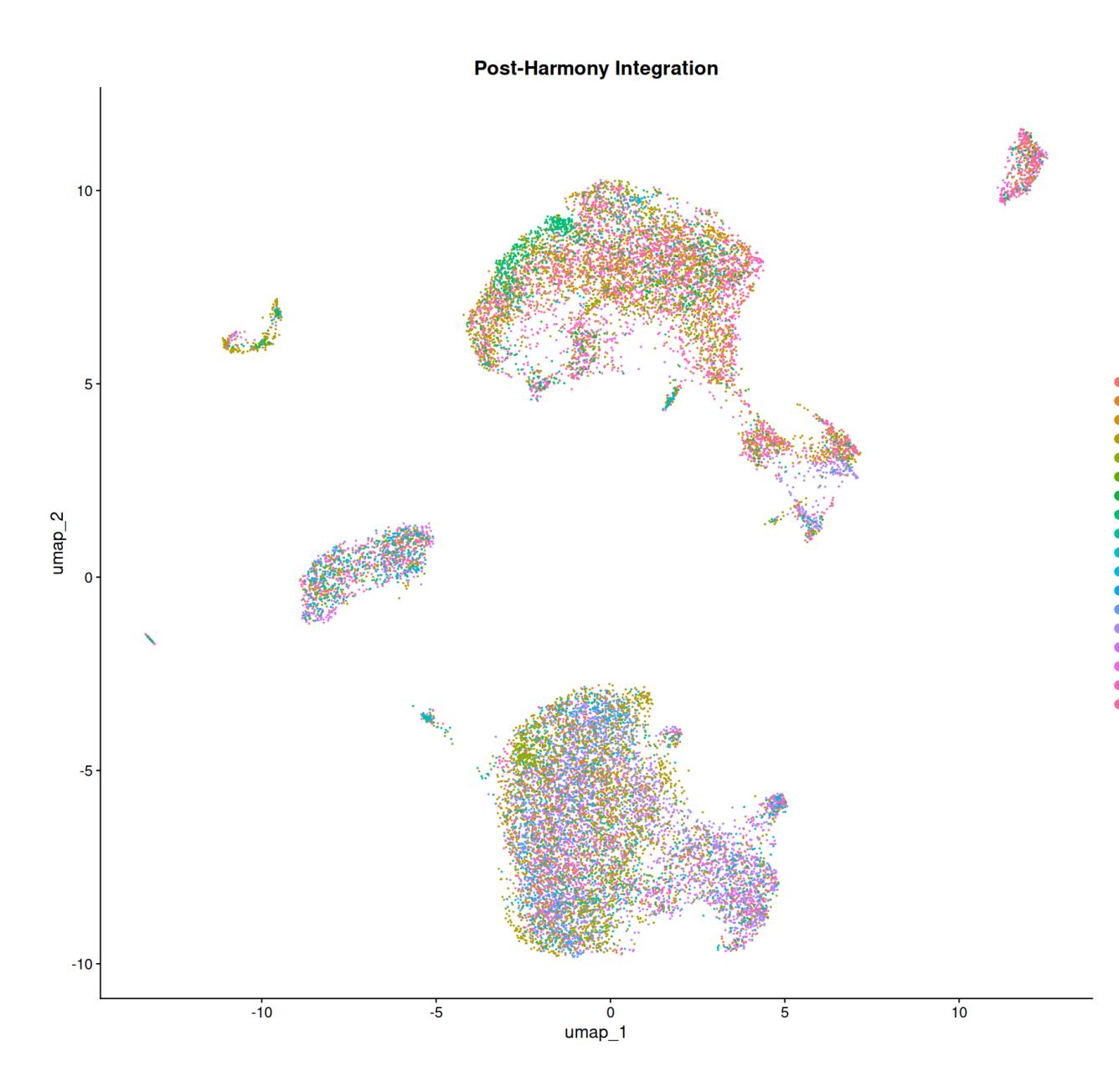
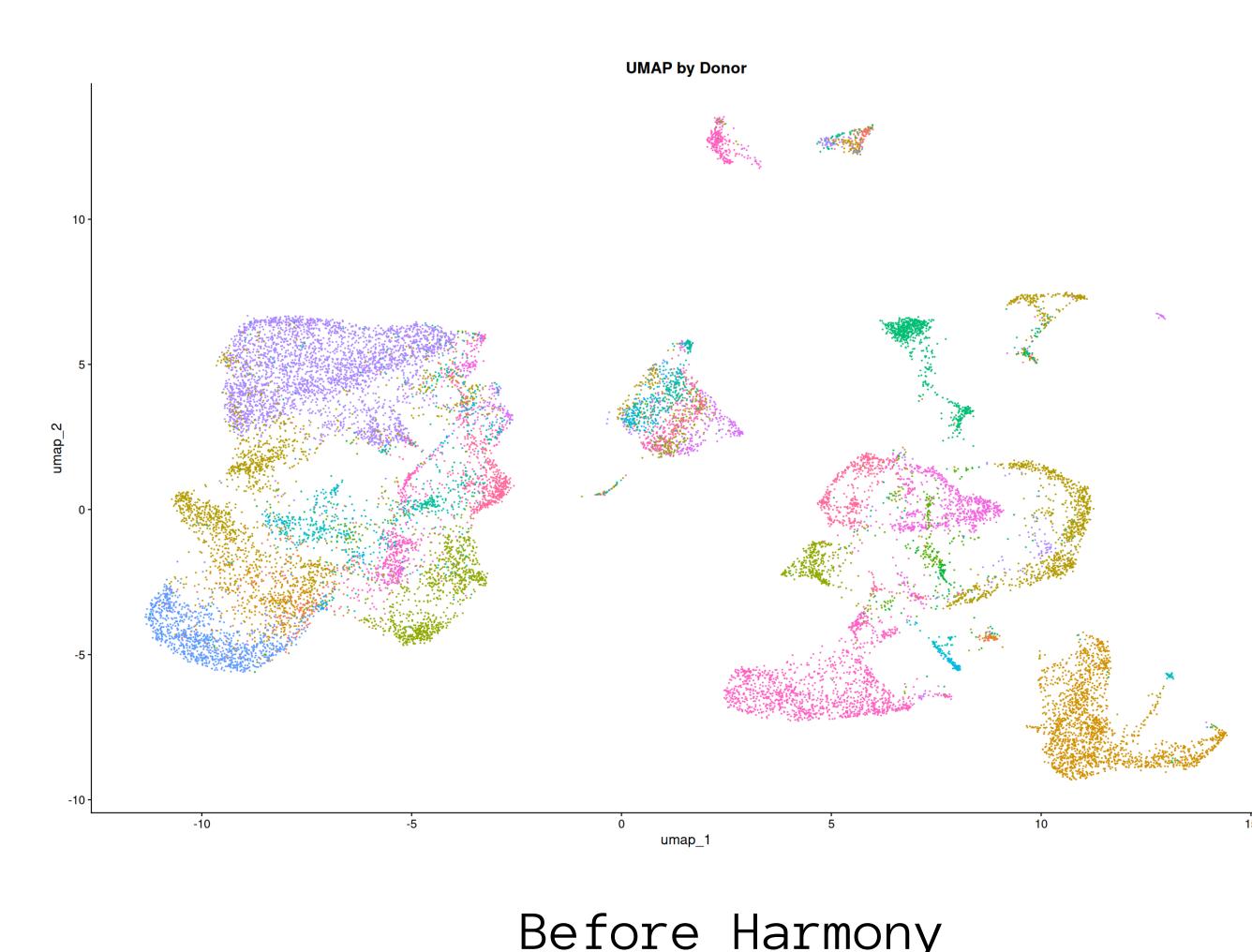
Our Goal: Find a Master Regulator Using single-cell RNA sequencing, we mapped the glioma ecosystem to pinpoint a novel targetable S100 protein that controls tumor aggression and immune evasion.



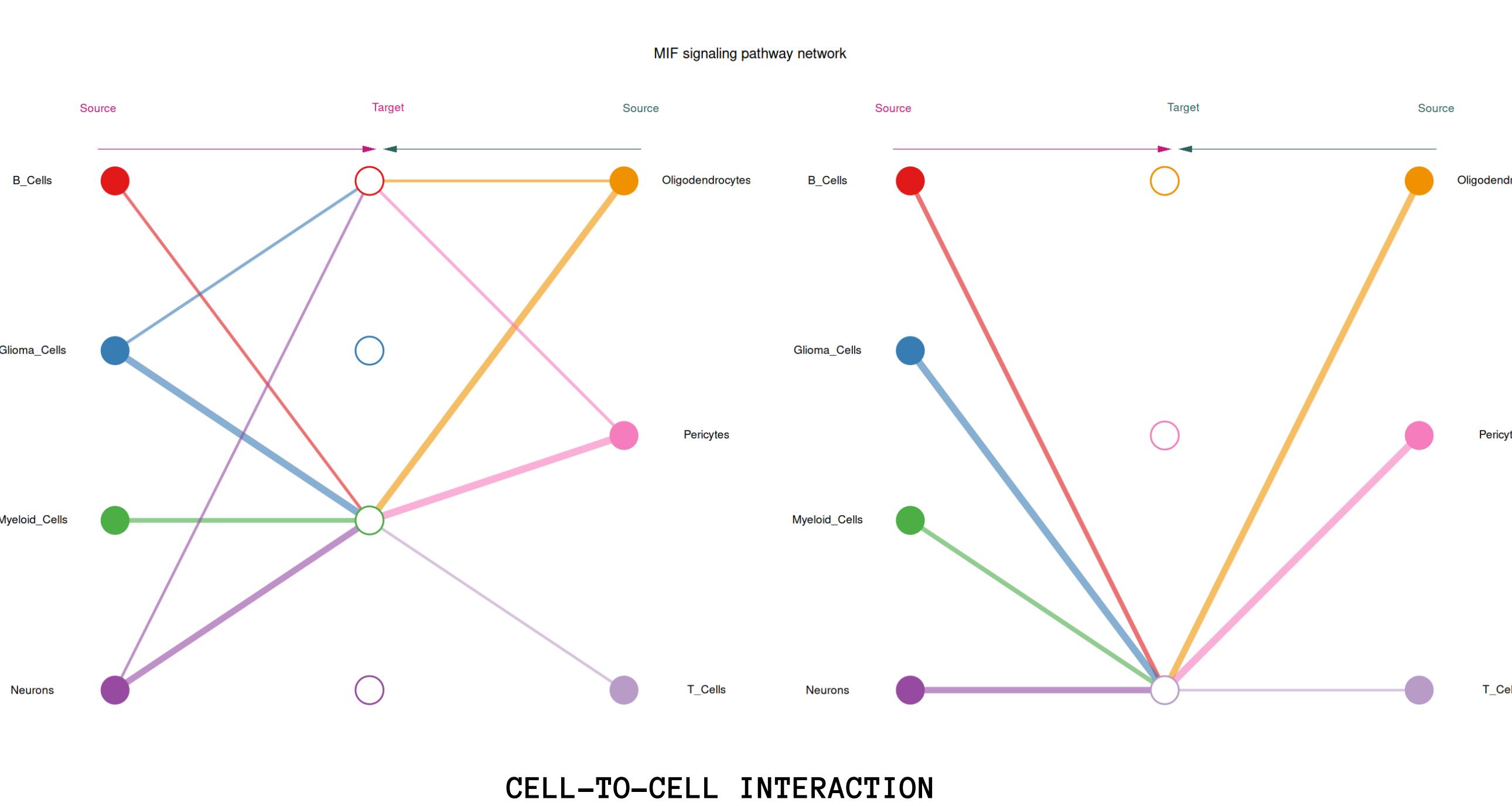
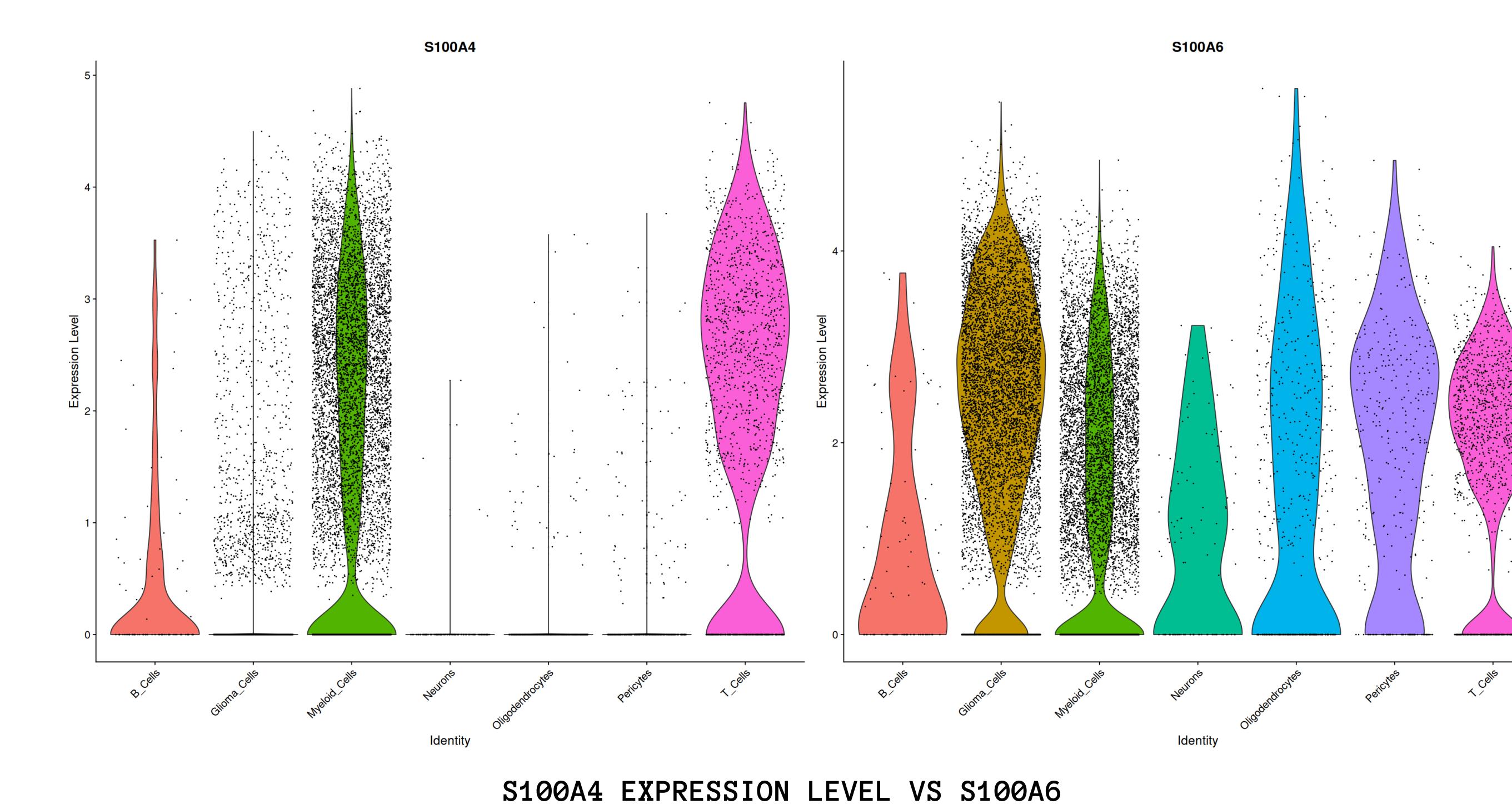
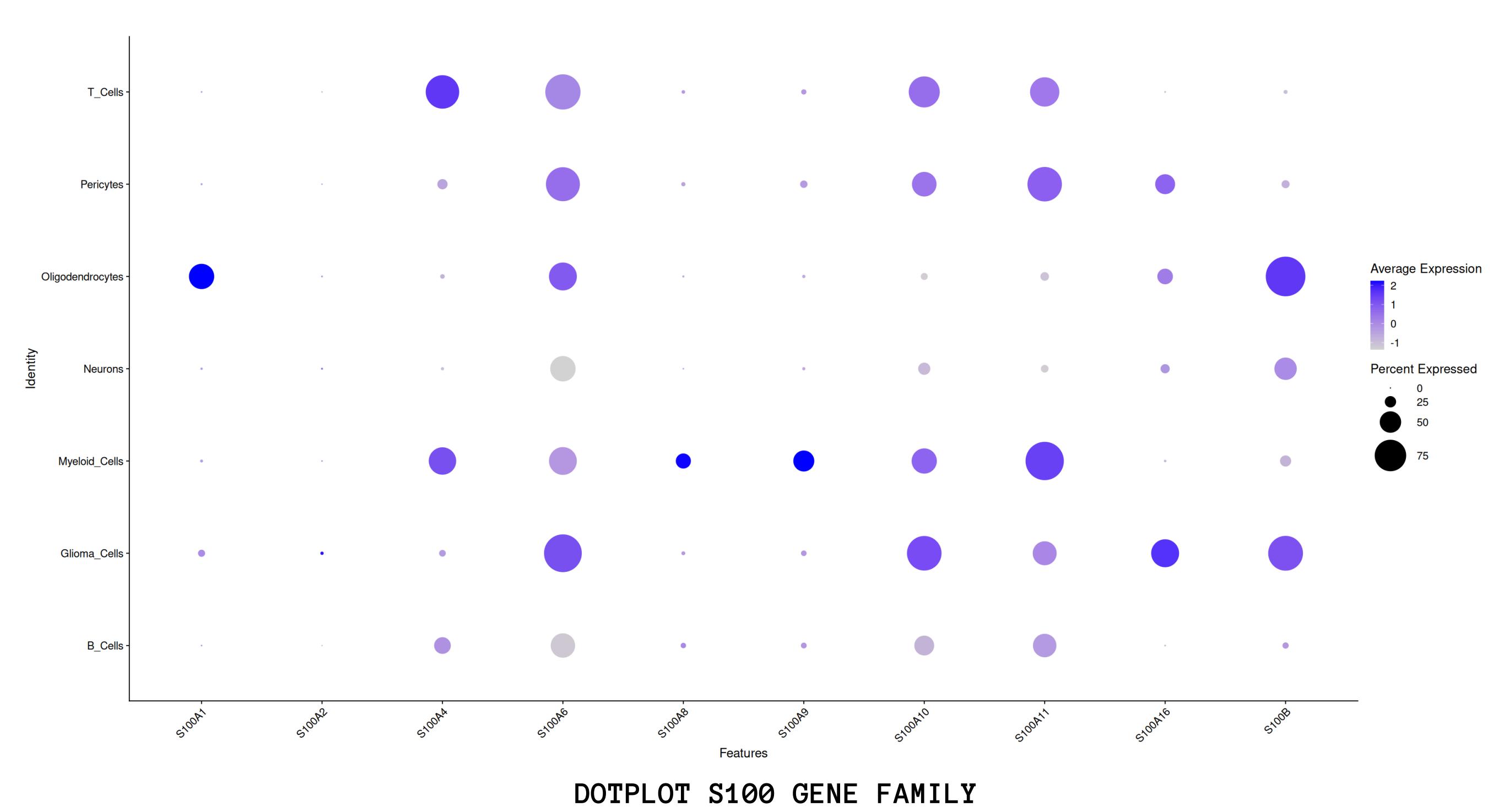
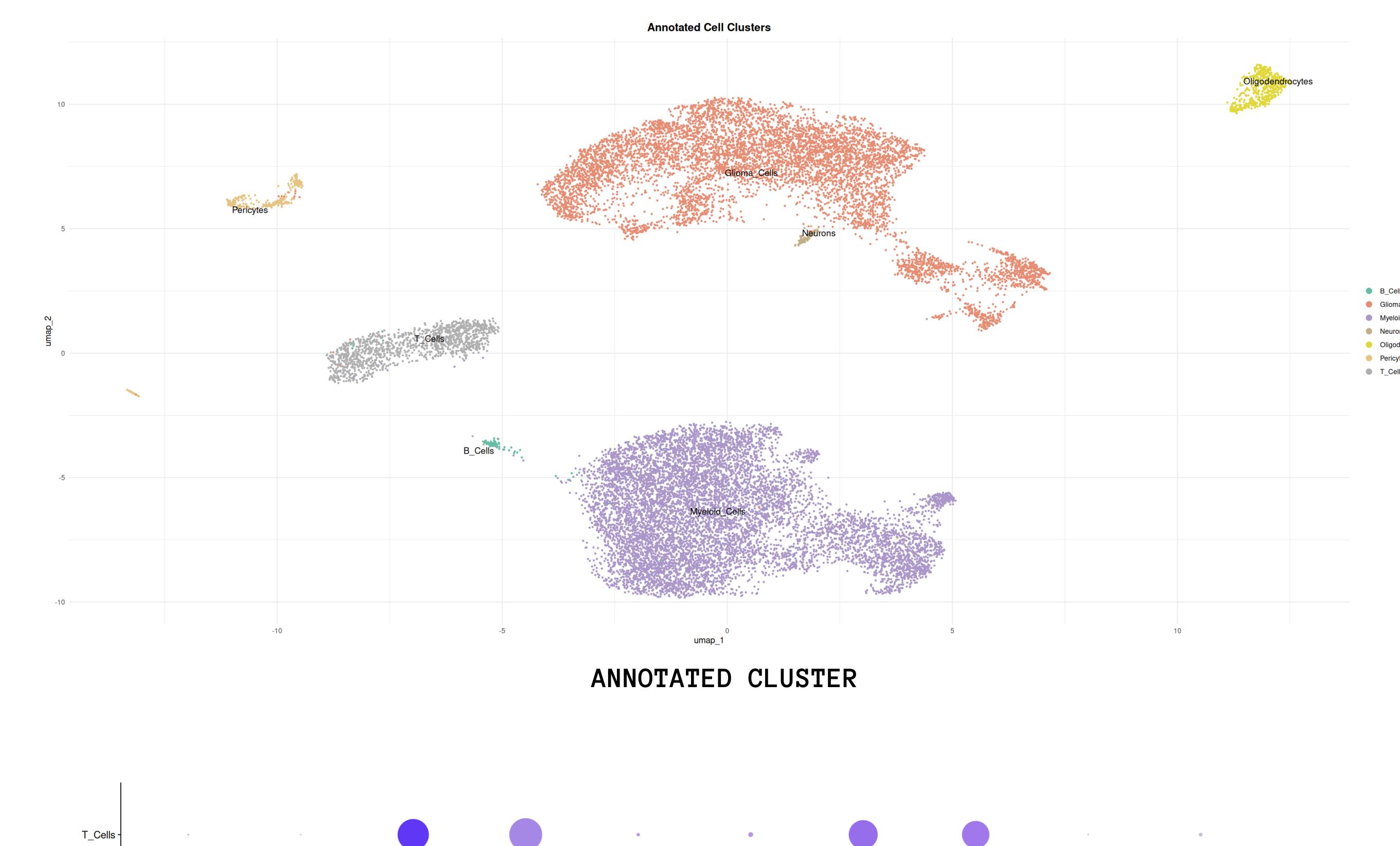
02 METHODS

We analyzed >19,000 single cells from 42 samples with low-grade glioma (LGG) and glioblastoma (GBM).

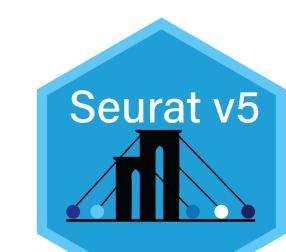
- Technology:** Single-Cell RNA Sequencing (scRNA-seq)
- Bioinformatic Analysis:**
 - Data Integration:** Used Harmony to successfully merge data from different patients and remove batch effects, revealing true biological signals.
 - Cell Type Identification:** Clustered cells and annotated them using known marker genes for 7 targeted cell types.
 - Differential Expression:** Compared gene activity across cell types to find key targets.



03 RESULTS



999 TOOLS



04 DISCUSSION

- Key Finding:** S100A6 is specifically elevated in glioma and myeloid cells, not just a passenger mutation.
- Novel Mechanism:** CellChat analysis suggests these cells use MIF signaling to create an immunosuppressive environment, providing a mechanistic link to T cell exhaustion.
- Broader Context:** This aligns with known roles of S100A6 in invasion and MIF in immune suppression, but uniquely positions S100A6 as an upstream regulator of this pathological crosstalk in glioma.

05 CONCLUSION

- What I found:** Our analysis identifies S100A6, not other S100 family members, as a gene specifically and highly active in human glioma cells and their protumor myeloid supporters.
- Why it matters:** This precise expression pattern suggests that targeting S100A6 could disrupt the core glioma ecosystem while minimizing damage to healthy tissue.
- Future Direction:** We propose S100A6 as a novel immunotherapy target. Inhibiting S100A6 could potentially block tumor growth and disable immunosuppressive myeloid cells, making the tumor vulnerable to the immune system.

06 REFERENCES

