Characterization of the anchor cell in preclinical models of metastatic osteosarcoma

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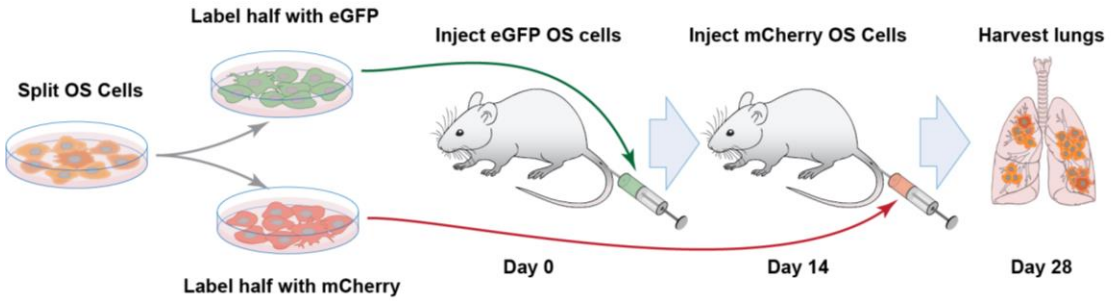
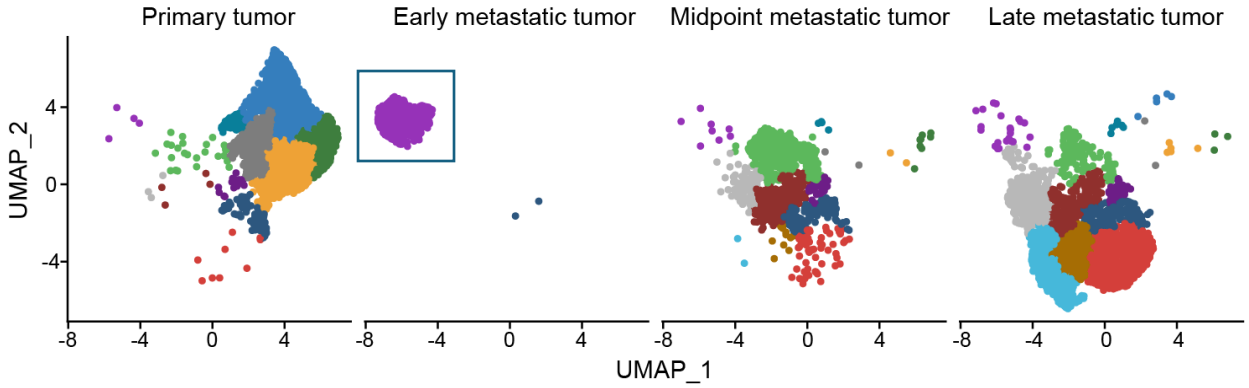
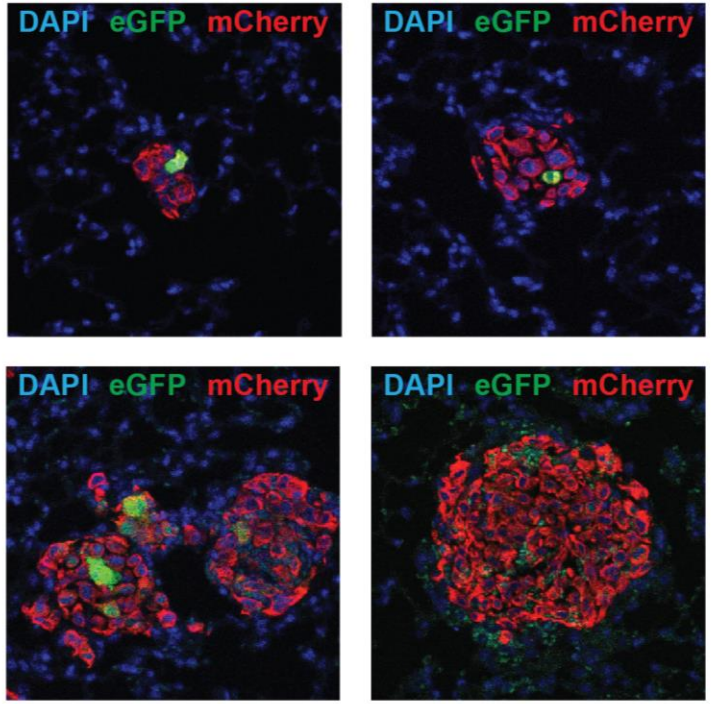
Background: Paracrine interactions between the lung epithelium and early tumor cells establish the metastatic niche

- Many tumor cells enter circulation daily; few colonize the lung
- Hypersecretory, hypo-proliferative cells establish a paracrine loop with the hostile lung environment to help recruit proliferative cells
- These “anchor cells” respond to the lung microenvironment and produce key cytokines including IL-6 and CXCL8







McAloney et al. *Cell Oncol*. 2024

Reinecke et al. 2024 (preprint)

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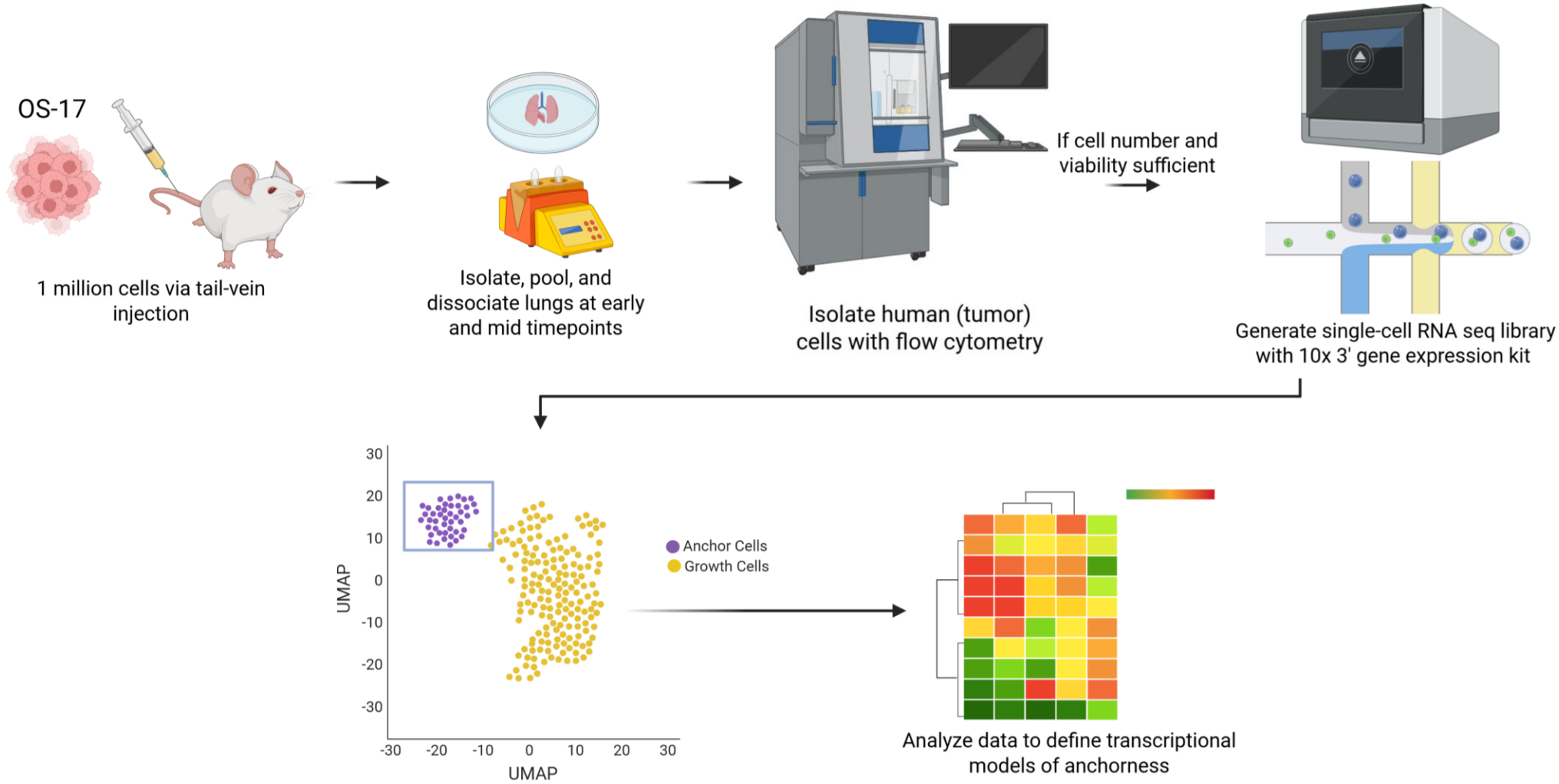
Hypothesis

By understanding the biology of anchor cells through single cell sequencing, we can harness this knowledge to better target them therapeutically

Isolation of early and midpoint OS-17 tumors and generation of scRNA sequence libraries



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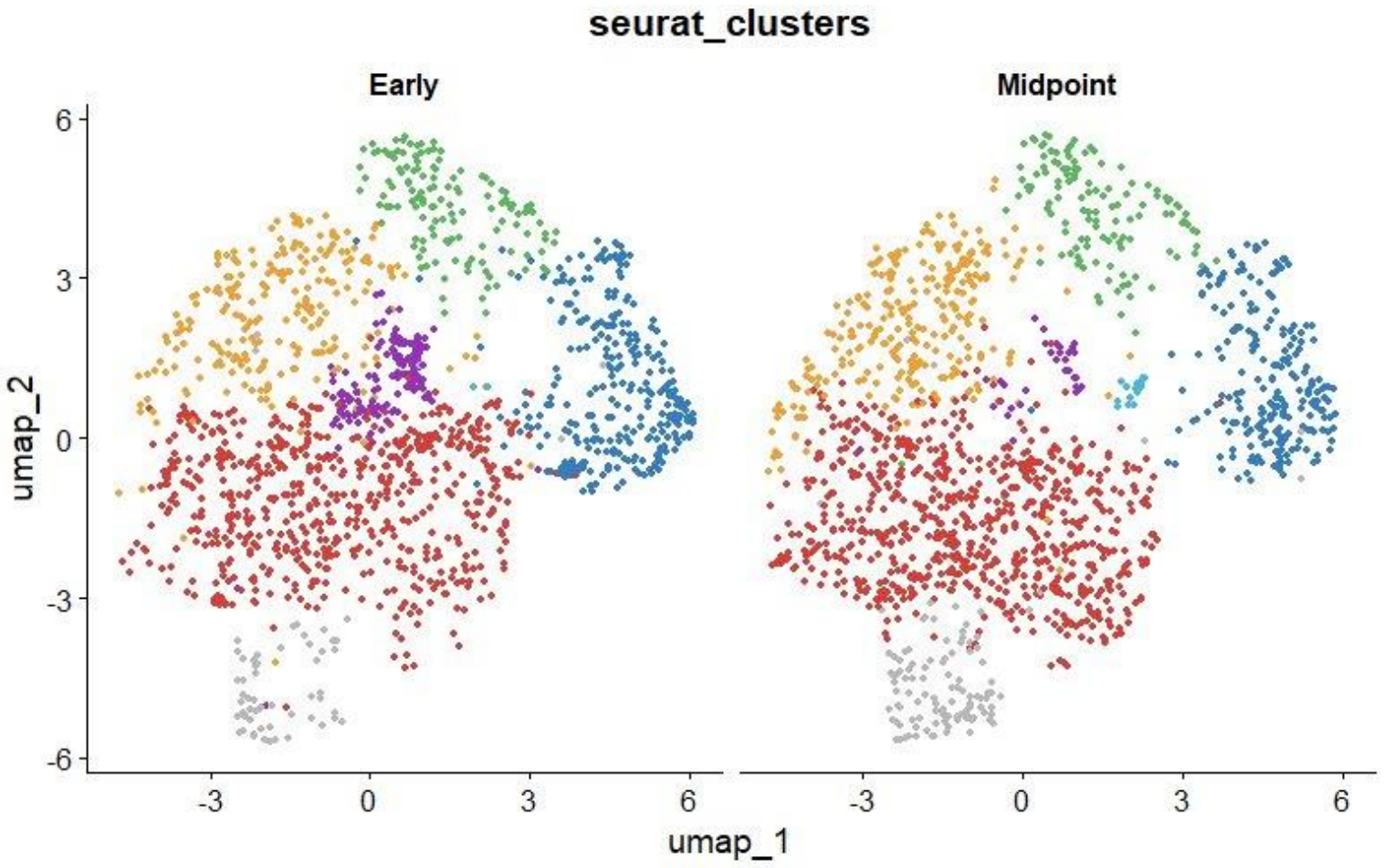
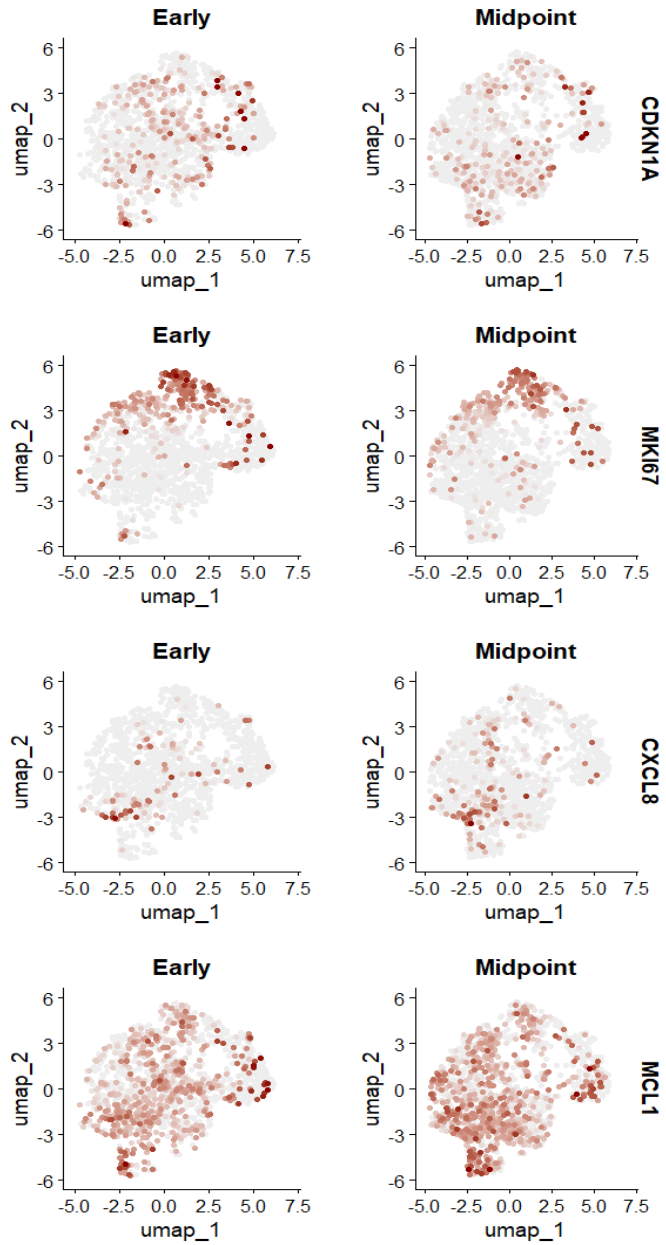
Tumor cells that populate the lung at the early timepoint are transcriptionally diverse and lack the same signature demonstrated in previous functional studies





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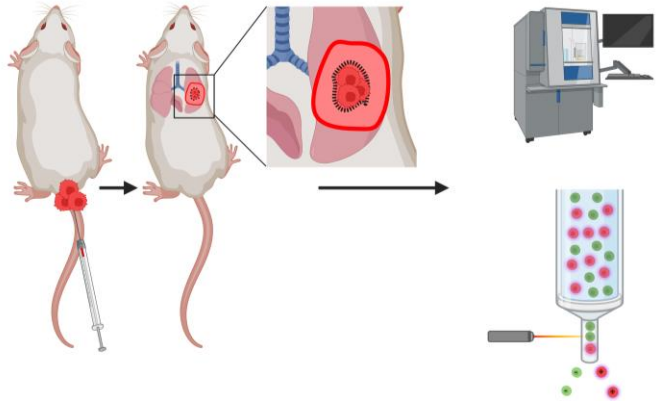
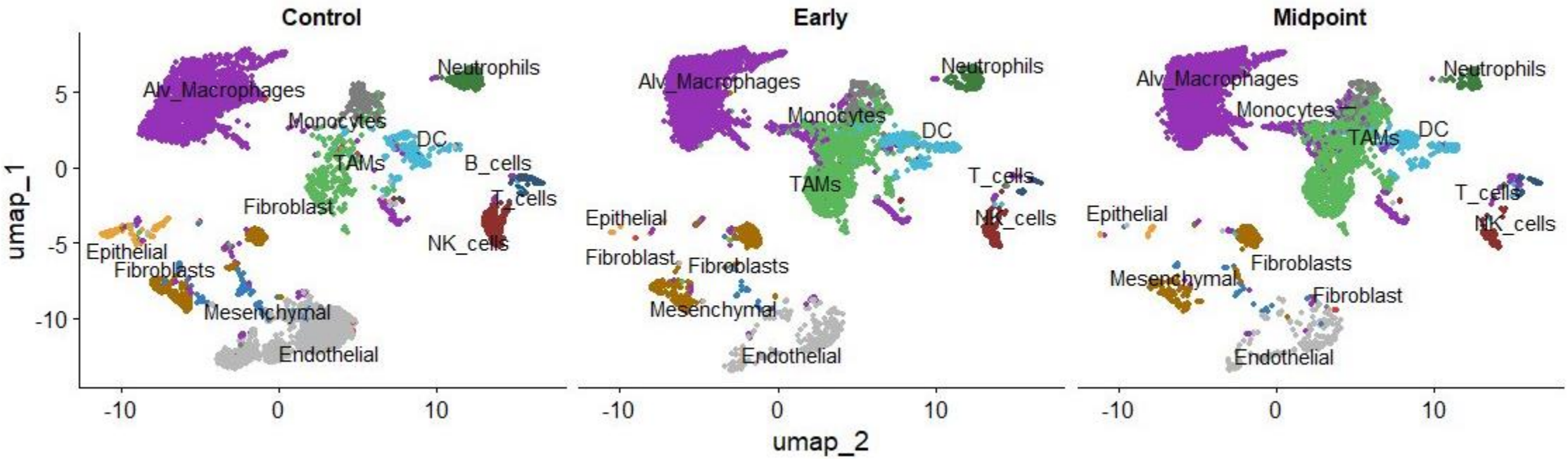
Results: Tumor-lung interactions induce changes in the stroma composition at the early timepoint, and these changes persist through tumor evolution





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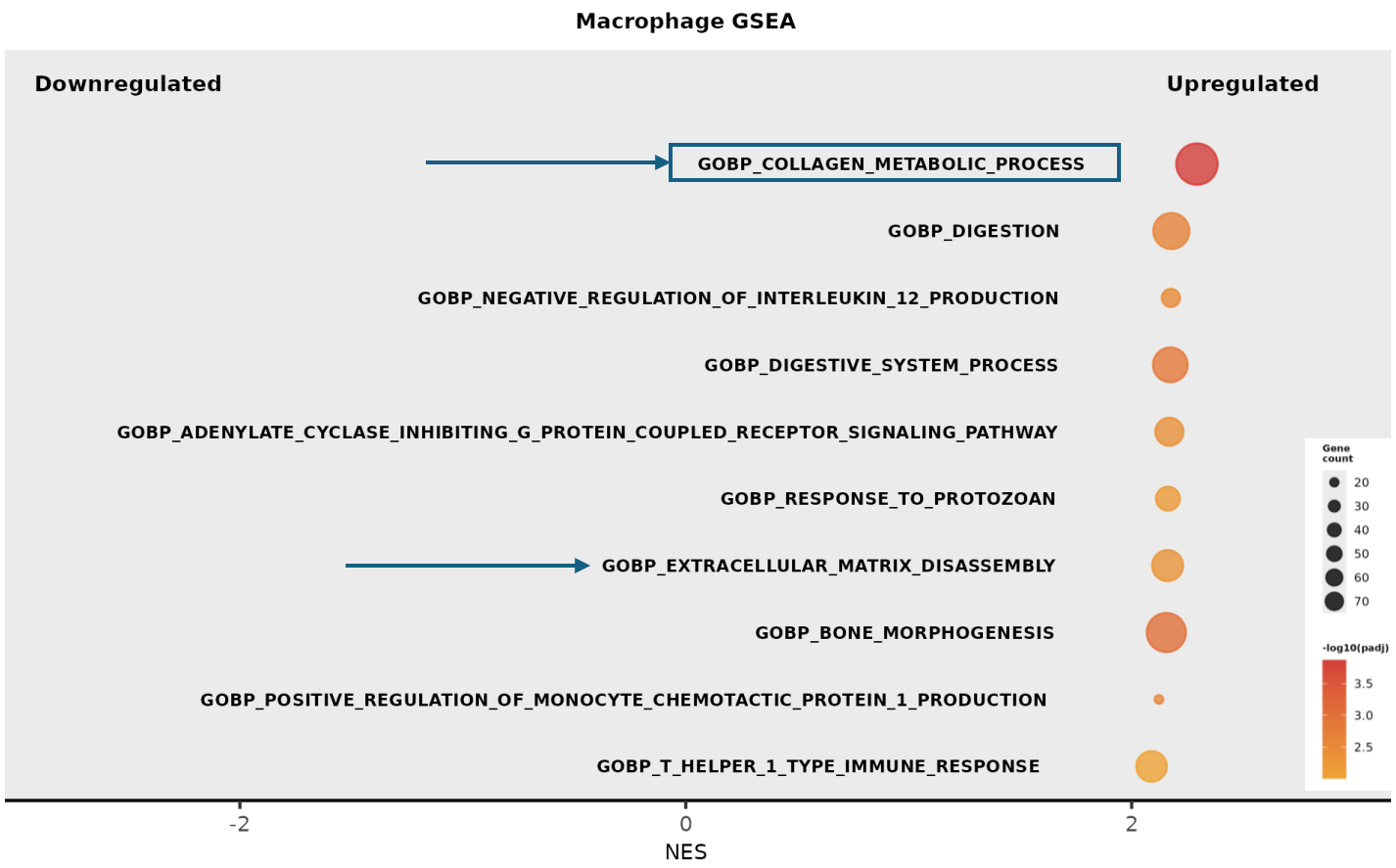
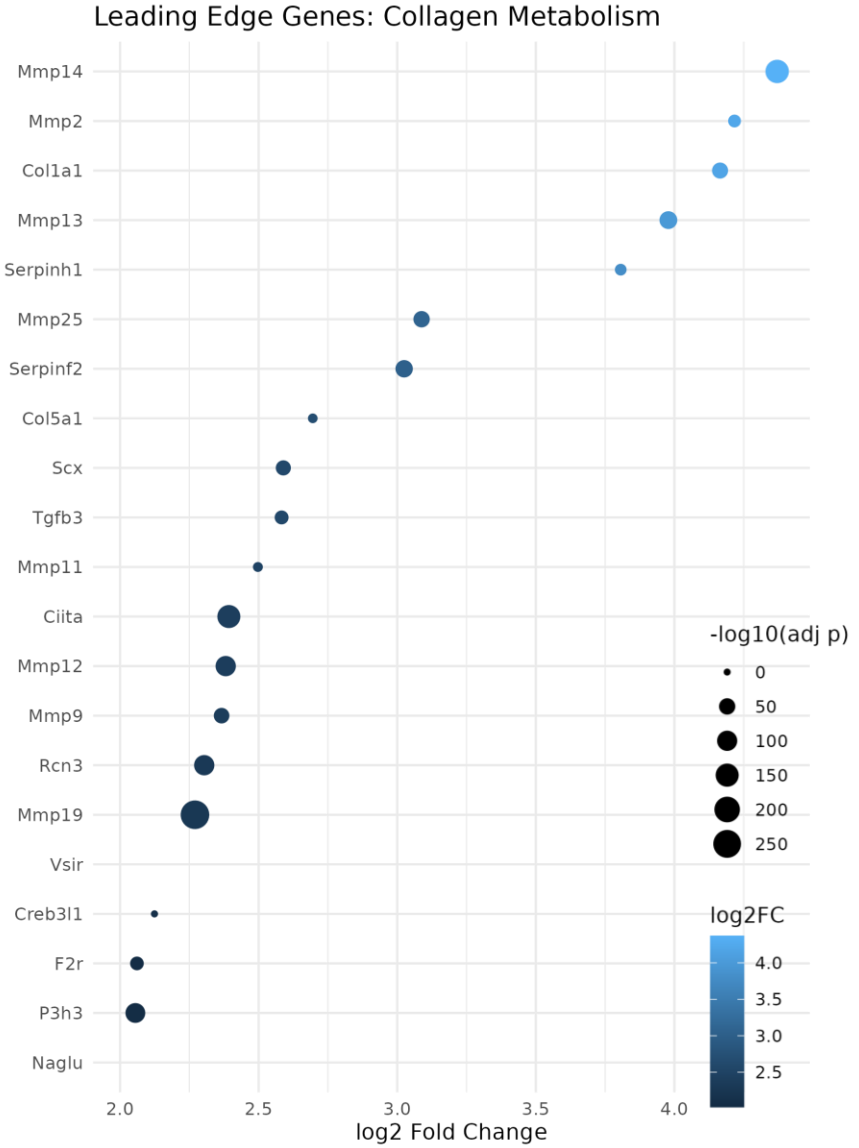
Fibrogenic pathways are upregulated in macrophages at day 14





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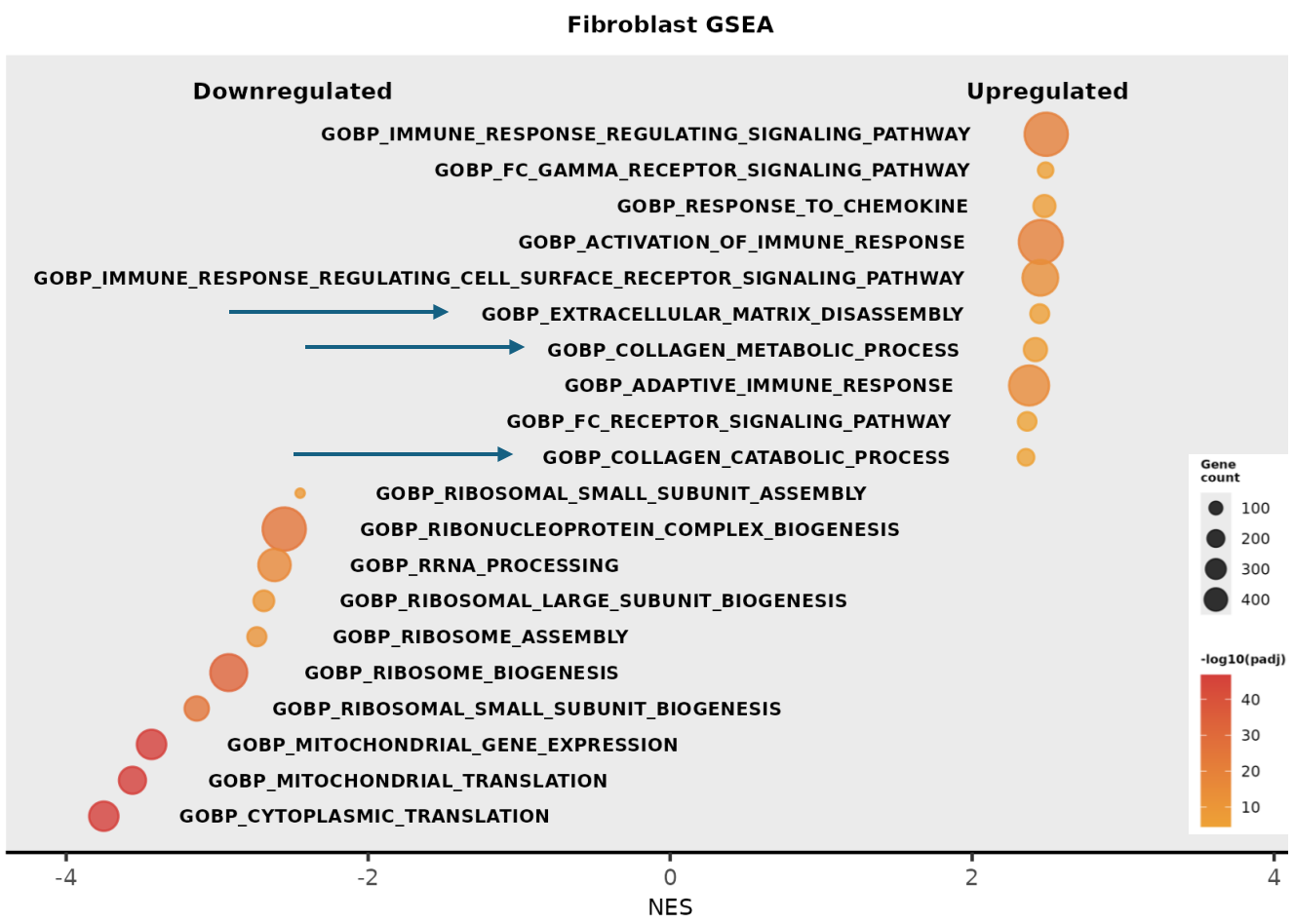
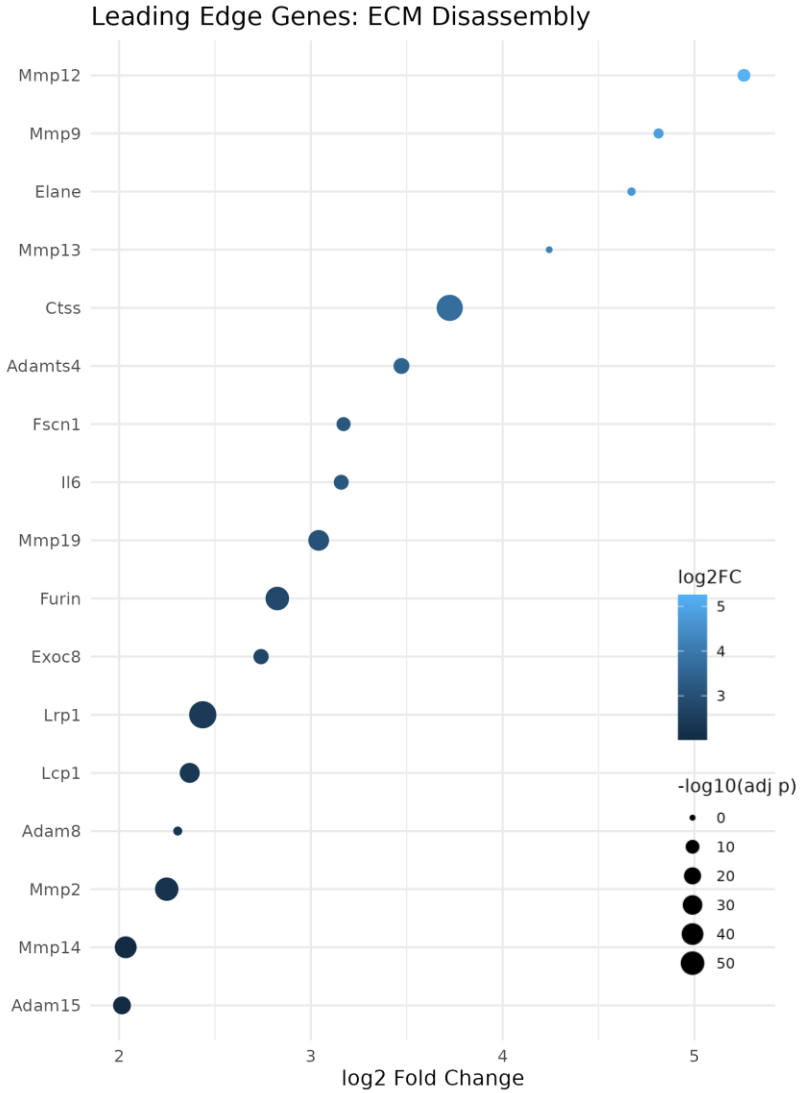
Fibrogenic pathways are upregulated in fibroblasts at day 14





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Summary

- Heterogeneity is preserved even at the bottleneck
- Datasets are only as good as the way in which they were generated
- Fibrogenic changes are resulting from the activity of this tumor heterogeneity, even at early time points

Future Directions

- Shift our focus from the tumor phenotype to the anchor-conditioned niche
- What signals come from the scar-like matrix that allow growth cells to proliferate?
- Future work will aim to identify a list of candidates for further study to determine the tumor-matrix interactions that occur at the metastatic bottleneck and drive tumor cells to adopt a proliferative state

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