ASTRO 2026

Data to Dialogue: Communicating Radiotherapy's Value to Advance Care

SEPTEMBER 26-30, 2026 | THOMAS M. MENINO CONVENTION & EXHIBITION CENTER | BOSTON

Lineage Tracing to Characterize Response to Radiation and Immunotherapy in Breast Cancer

Abigail Marshall

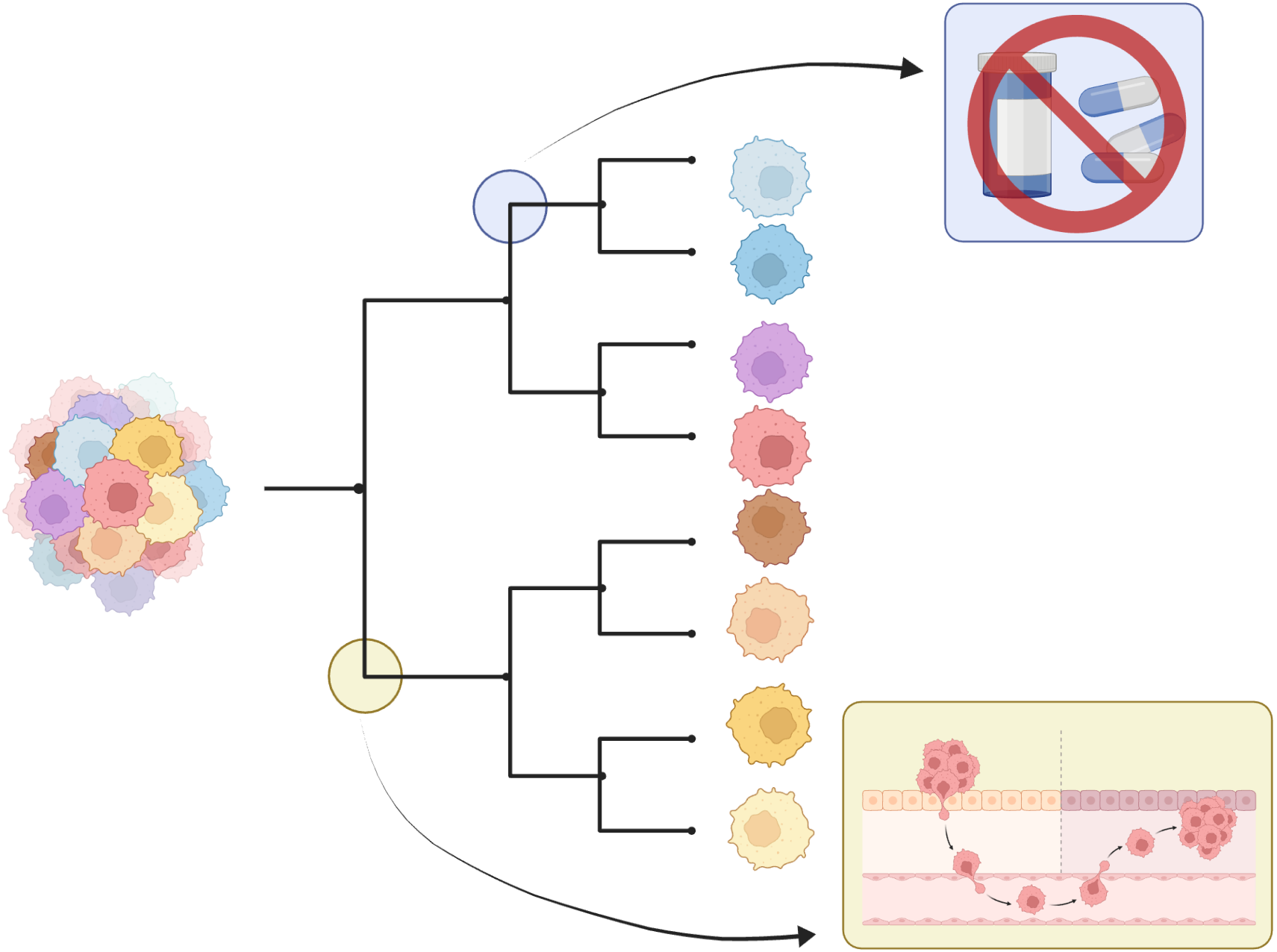
McKenna Lab at Dartmouth Cancer Center

Disclosure

- None

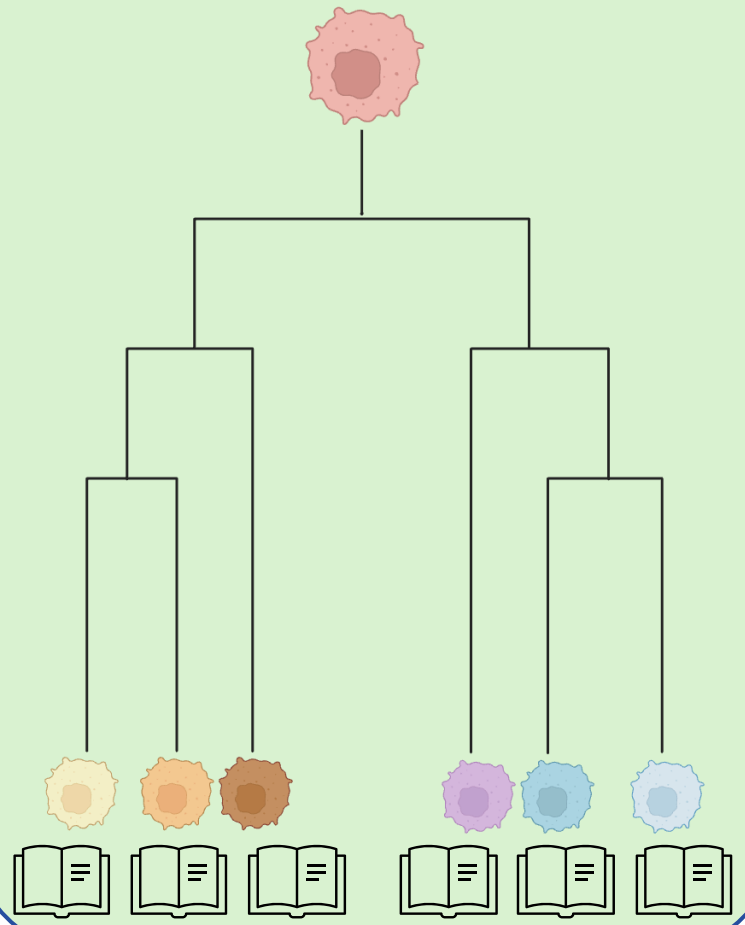
Lineage tracing

Utilizing genomic markers to record cell relationships

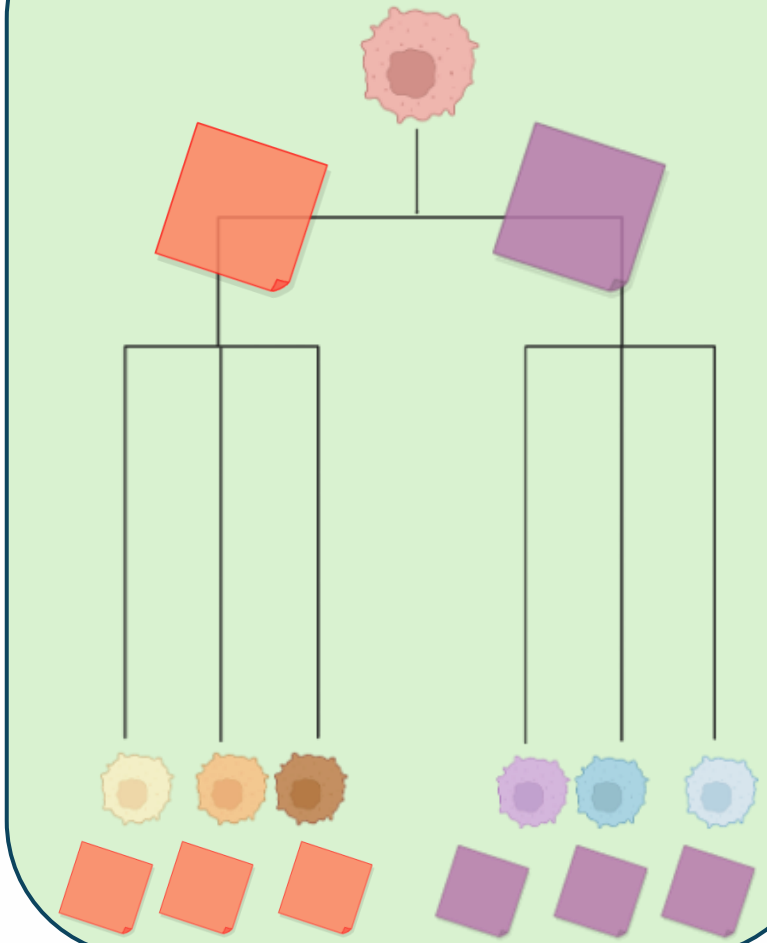


Lineage tracing methods

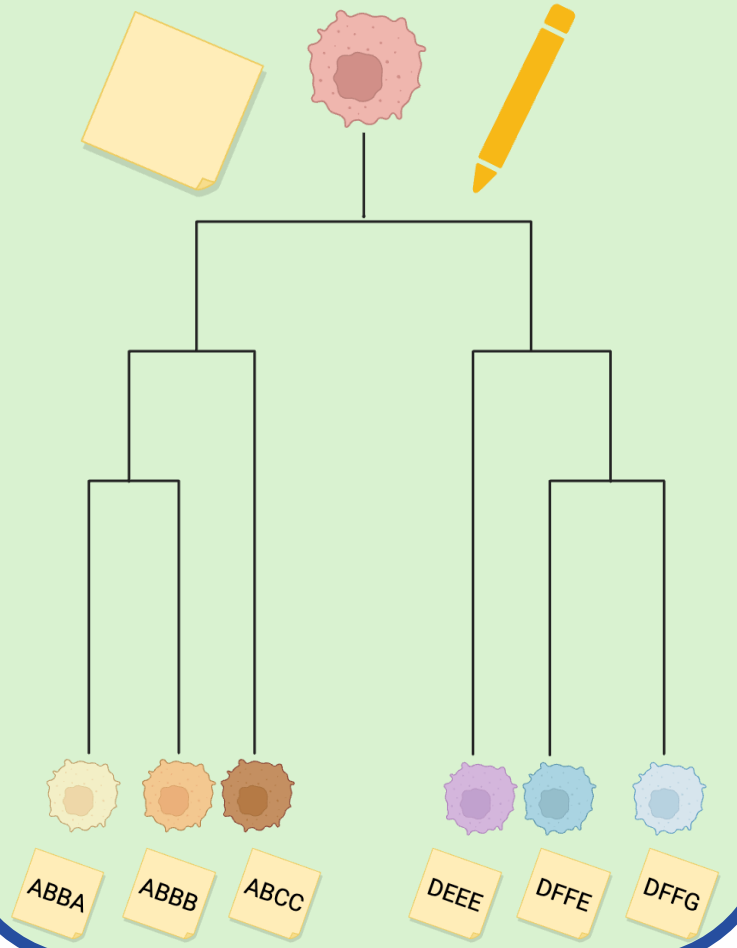
Retrospective approaches:



Static approaches:

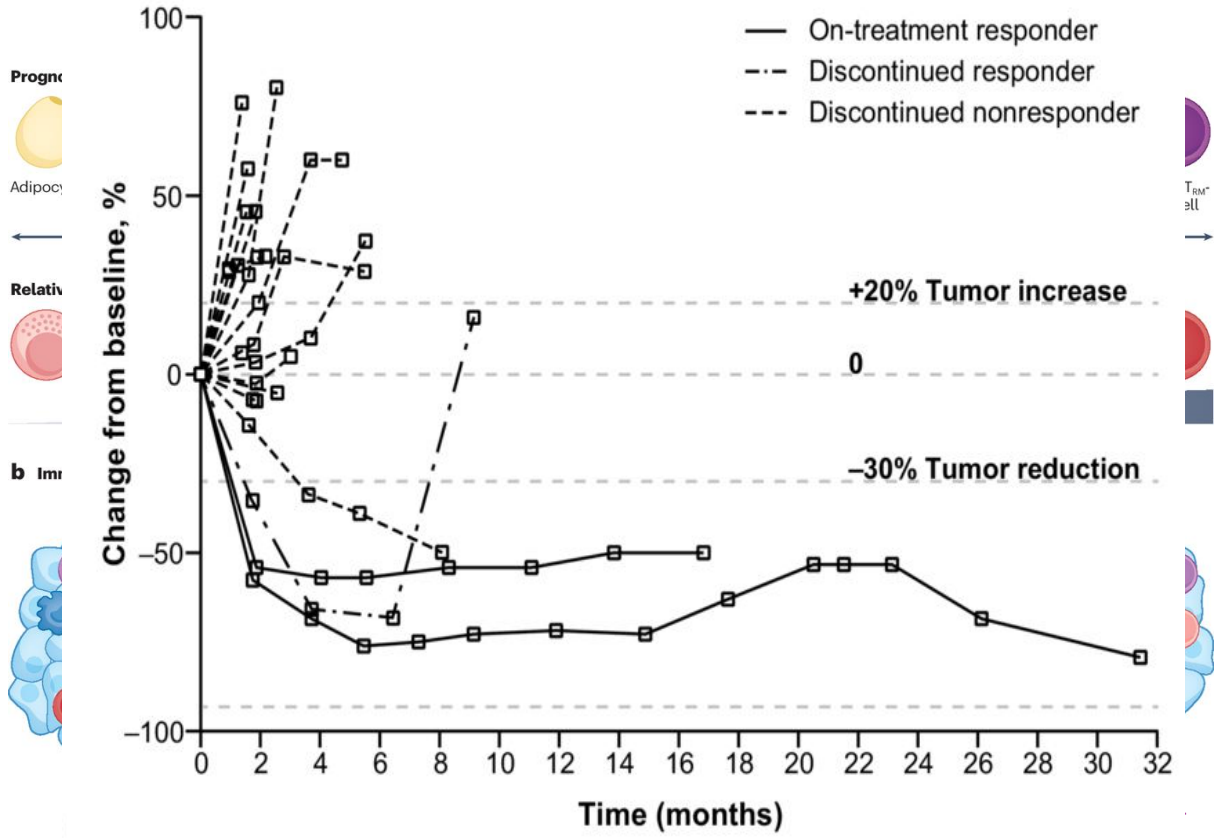


Dynamic approaches:



Breast cancer and tumor microenvironment (TME)

- Most common cancer in women and leading cause of cancer mortality in women worldwide
- ~70% of breast cancer is estrogen receptor positive (ER+)
- Different subtypes= different TMEs
- TME & immune cell populations impact immunotherapy

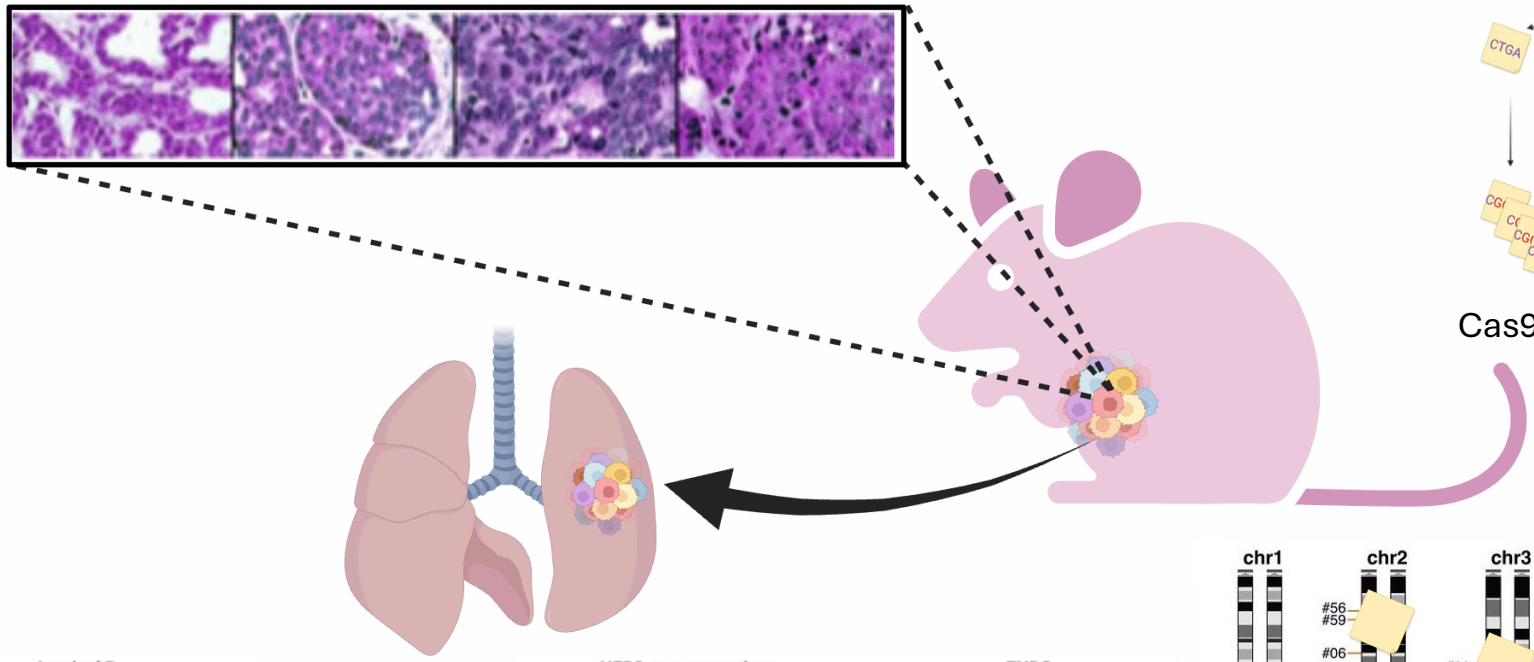


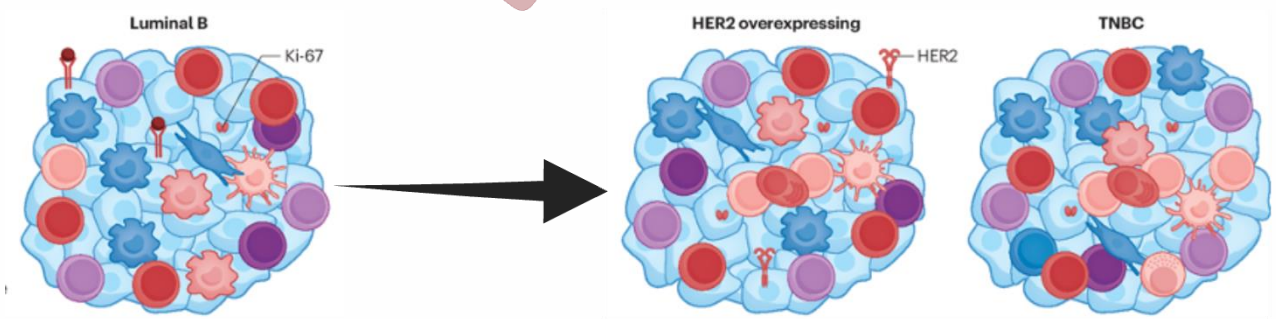
From Rugo et al. 2018

Can neo-adjuvant radiation shift cell populations in TME to improve the efficacy of immunotherapy in ER+ breast cancer?

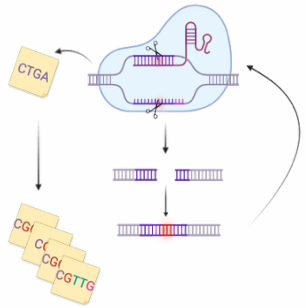
Mouse model of breast cancer

MMTV-PyMT Model

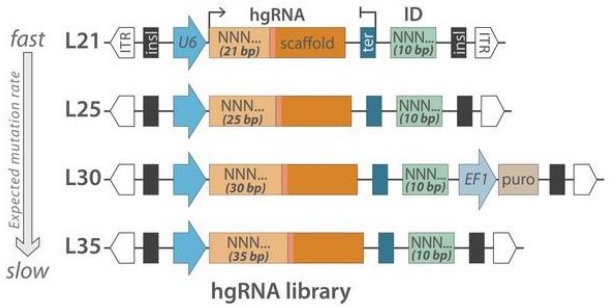




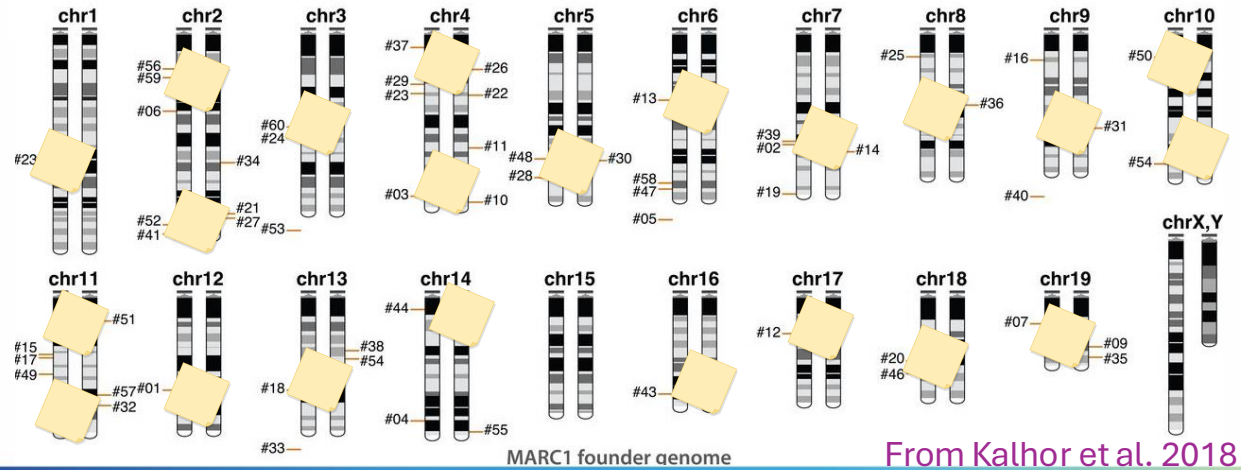
Mouse for Actively Recording Cells 1 (MARC1)



Cas9 + homing guides

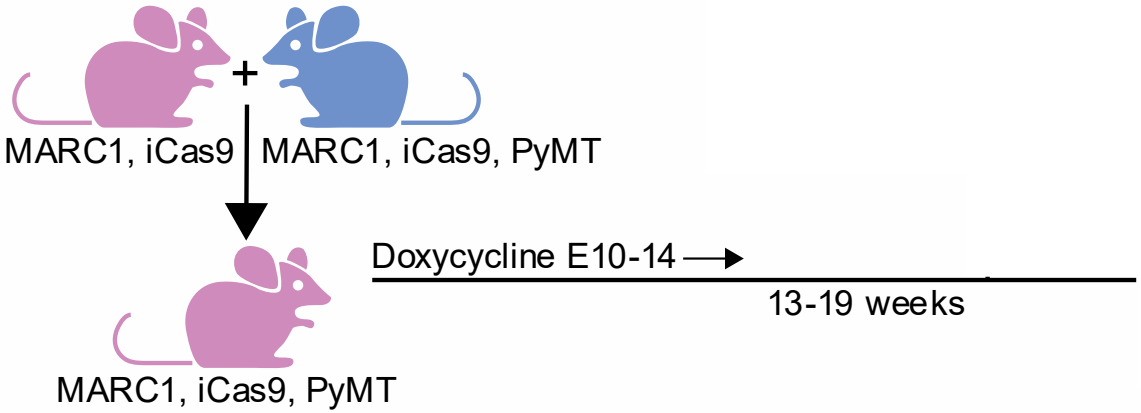


From Leeper et al. 2021

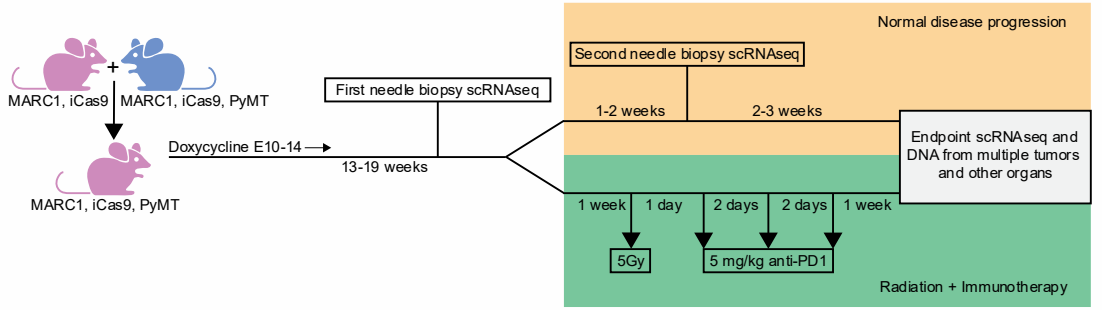


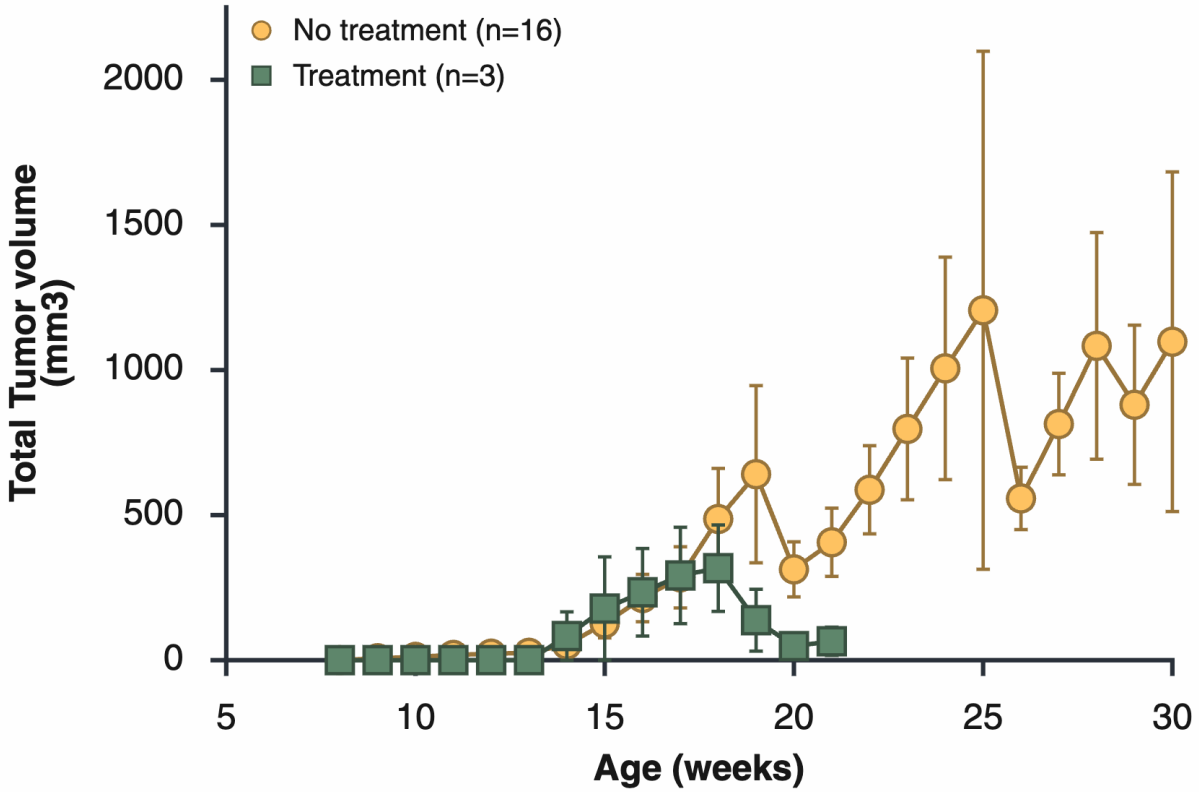
From Kalhor et al. 2018

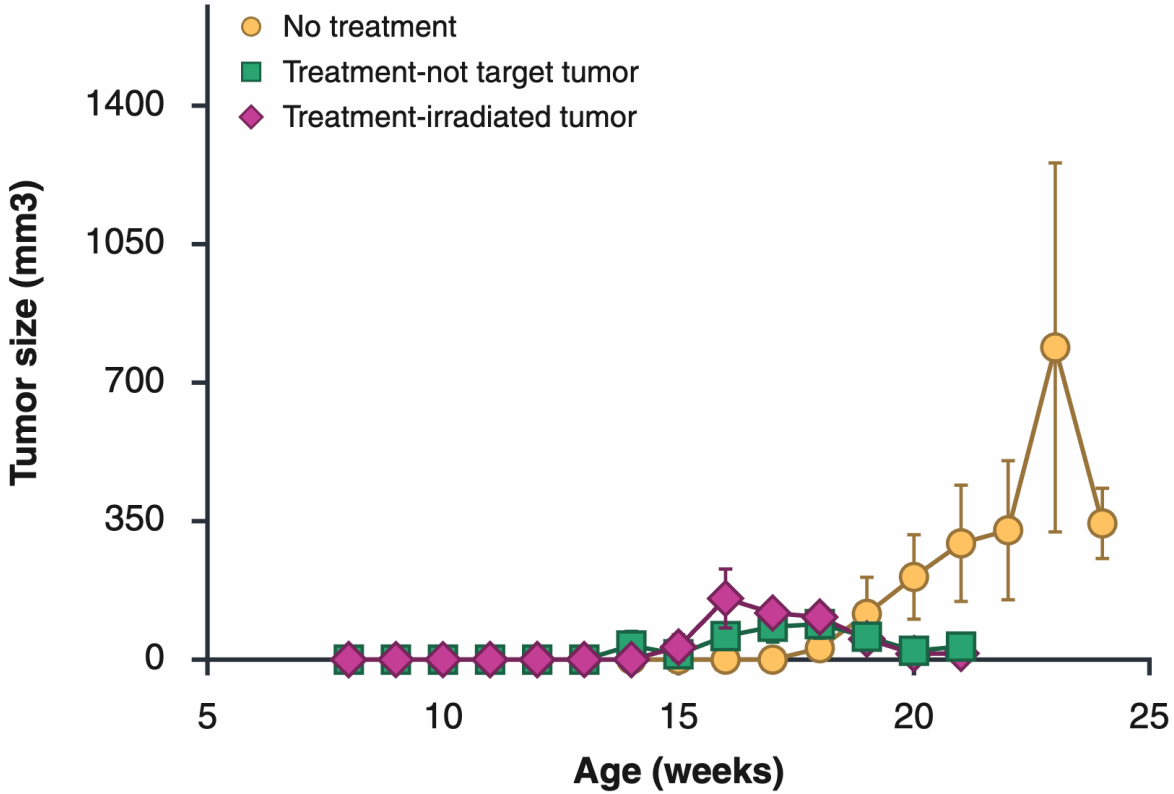
Experimental outline



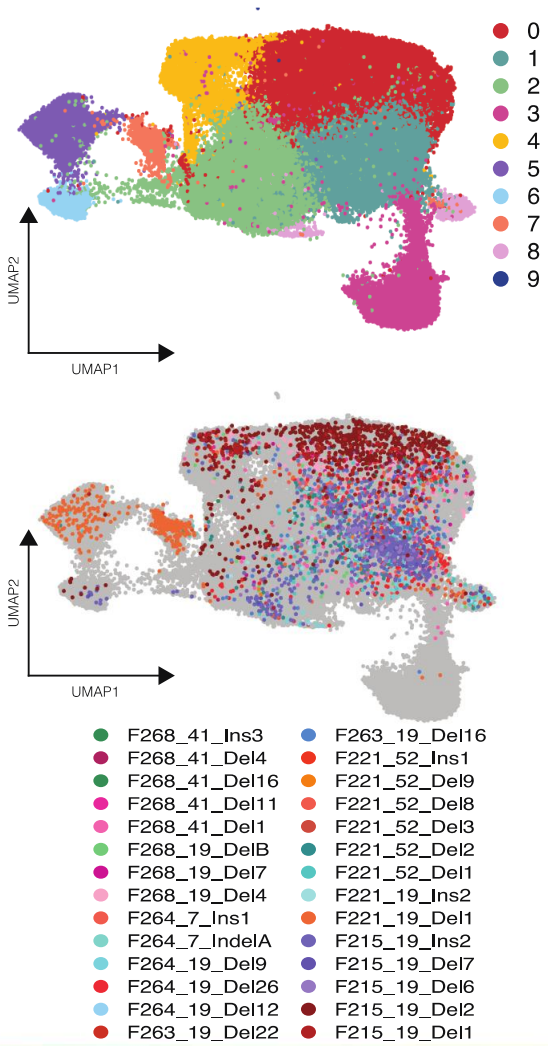
Treatment effect on tumors

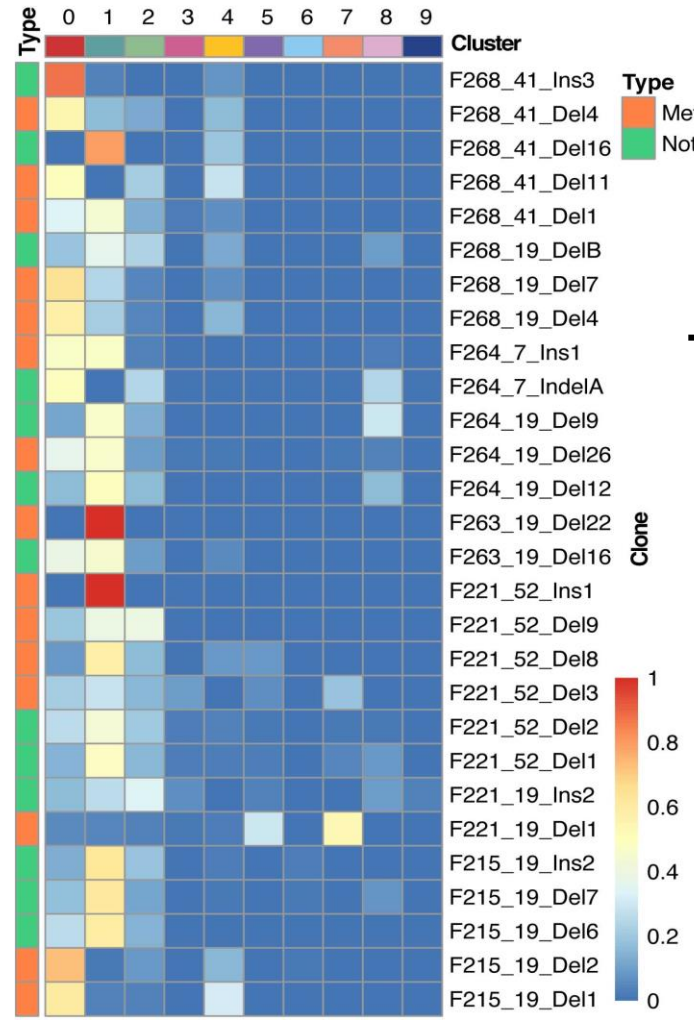


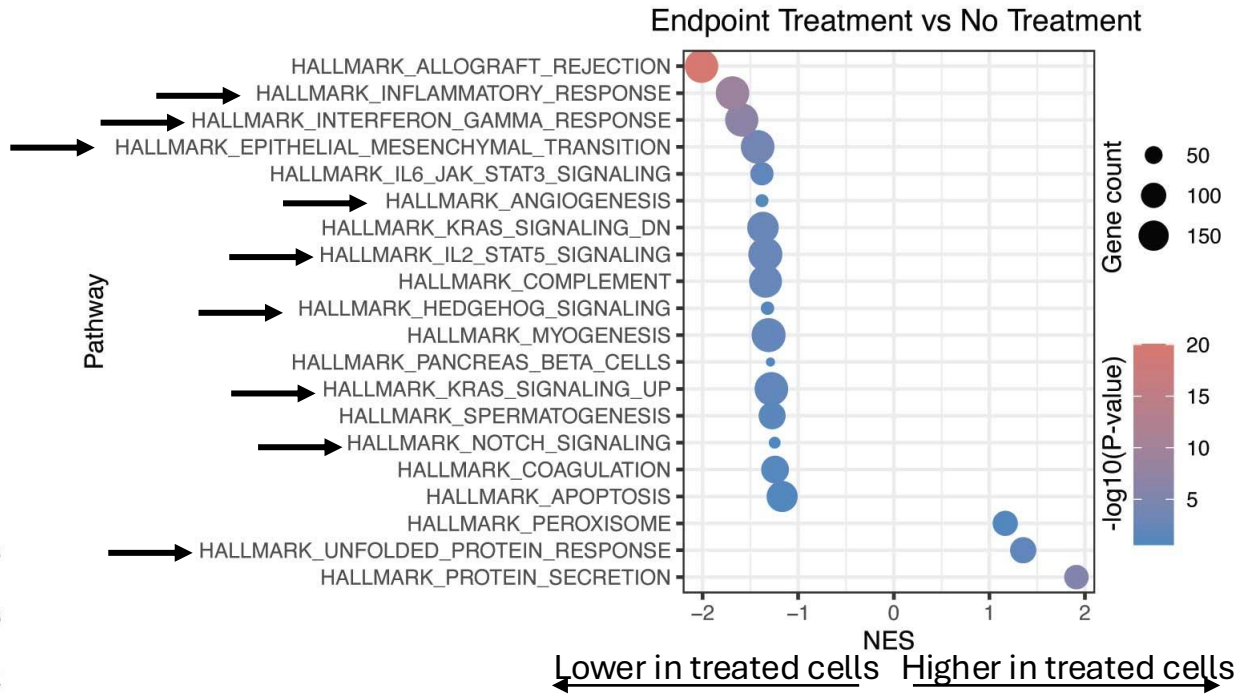




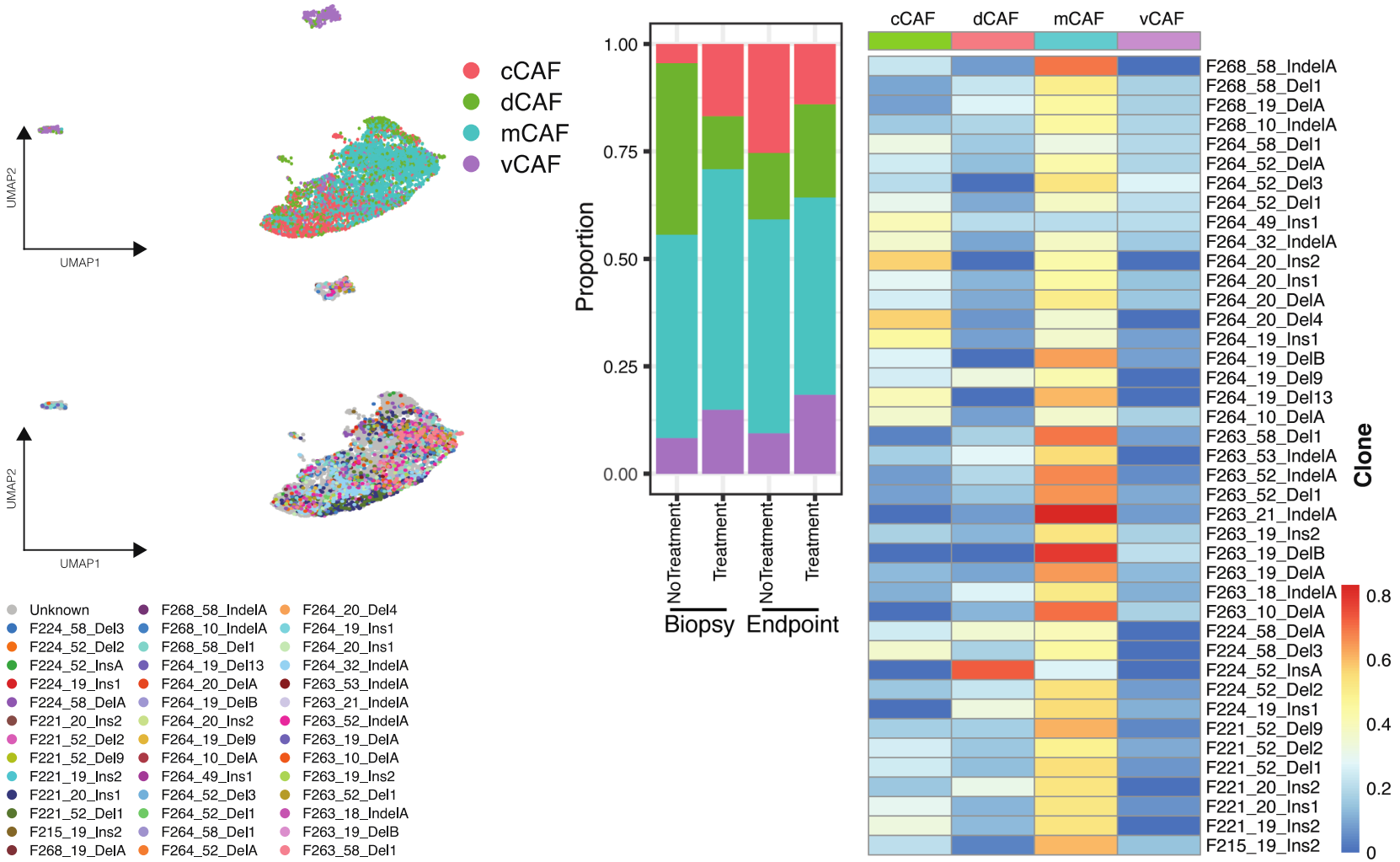
Single Cell Results: Tumor Clones





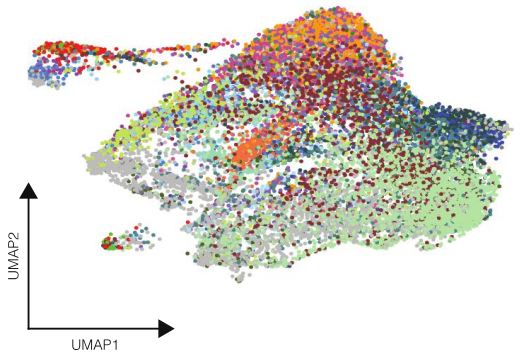


Single Cell Results: Cancer Associated Fibroblasts

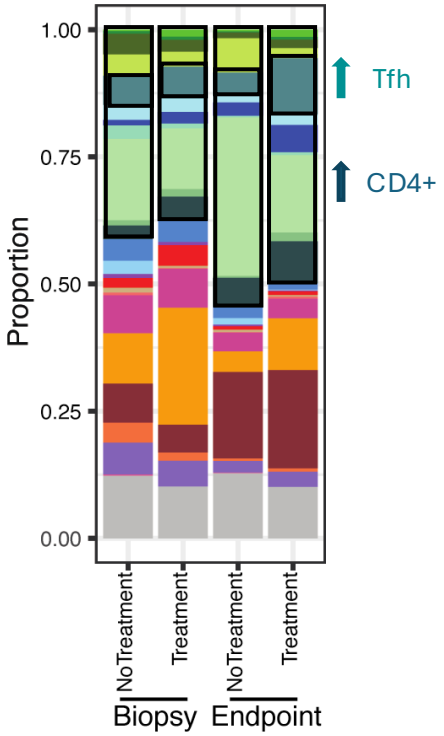


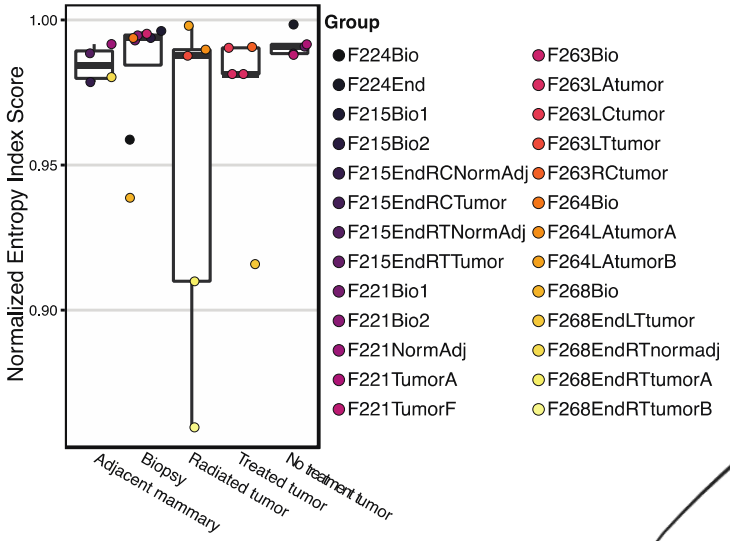
- No clear change in states with time or treatment
- mCAFs dominant in this model
- Different states within same clone suggest phenotypic flexibility of CAFs

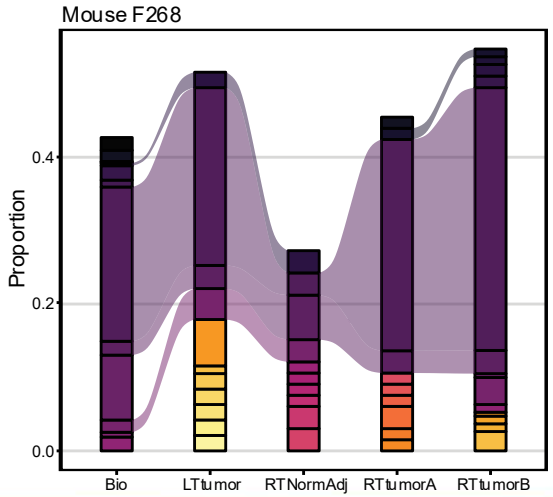
Single Cell Results: T cells

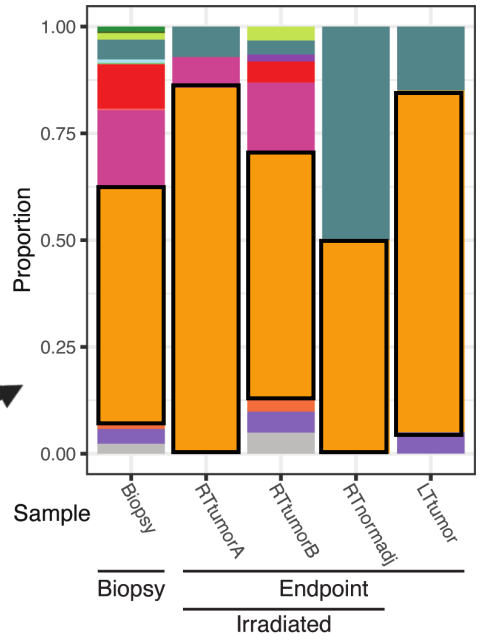


- CD4 proliferation
- CD4 Tc
- CD4 Tem
- CD4 Temra
- CD4 Tfh
- CD4 Th1
- CD4 Th17
- CD4 Tisg
- CD4 Tn
- CD4 Tn regulating
- CD4 Treg
- CD4 Trm
- CD4 Trm cytotoxicity
- CD8 NKT–like
- CD8 proliferation
- CD8 quiescence
- CD8 Tcm IFN–response
- CD8 Tem
- CD8 Tex
- CD8 Tn
- CD8 Tn IFN–response
- CD8 Trm
- CD8 Trm anergy
- Inconclusive









- CD4 Tc
- CD4 Tem
- CD4 Temra
- CD4 Tfh
- CD4 Th1
- CD4 Tn regulating
- CD8 NKT–like
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- CD8 Tem
- CD8 Tex
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- CD8 Trm
- Inconclusive

Key findings:

- MARC1 lineage system can be combined with immunocompetent, spontaneous cancer model
- Radiation + anti-PD1 is effective in MMTV-PyMT model
  - Next step: larger cohorts with single-agent controls
- High transcriptional heterogeneity within tumor clones
  - Radiation + anti-PD1 decreases pro-oncogenic pathways
- CAFs exhibit state plasticity, no clear treatment effect
- T cell response:
  - More CD4+ Tfh cells following radiation + anti-PD1
  - Expanding clones predominantly exhausted CD8+ clones

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- BioRender used to make some figures

Thank you!

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Financial Support:

Dartmouth Cancer Center Travel Fund

Geisel School of Medicine Medical Student Research Fund

ASTRO Annual Meeting Abstract Award