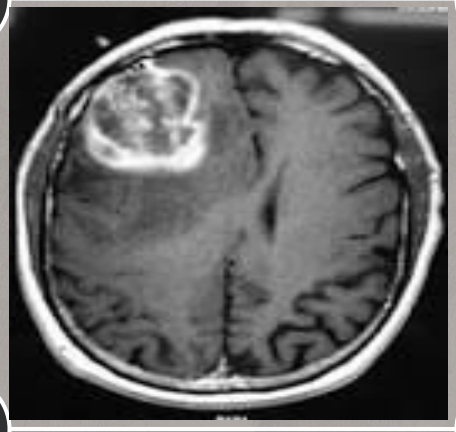
Glioblastoma Multiforme

Andrew Wilk and Angela Bai

Overview

5% five-year survival rate

Most common malignant brain tumor



Resistant to common treatments

Genetics extensively characterized

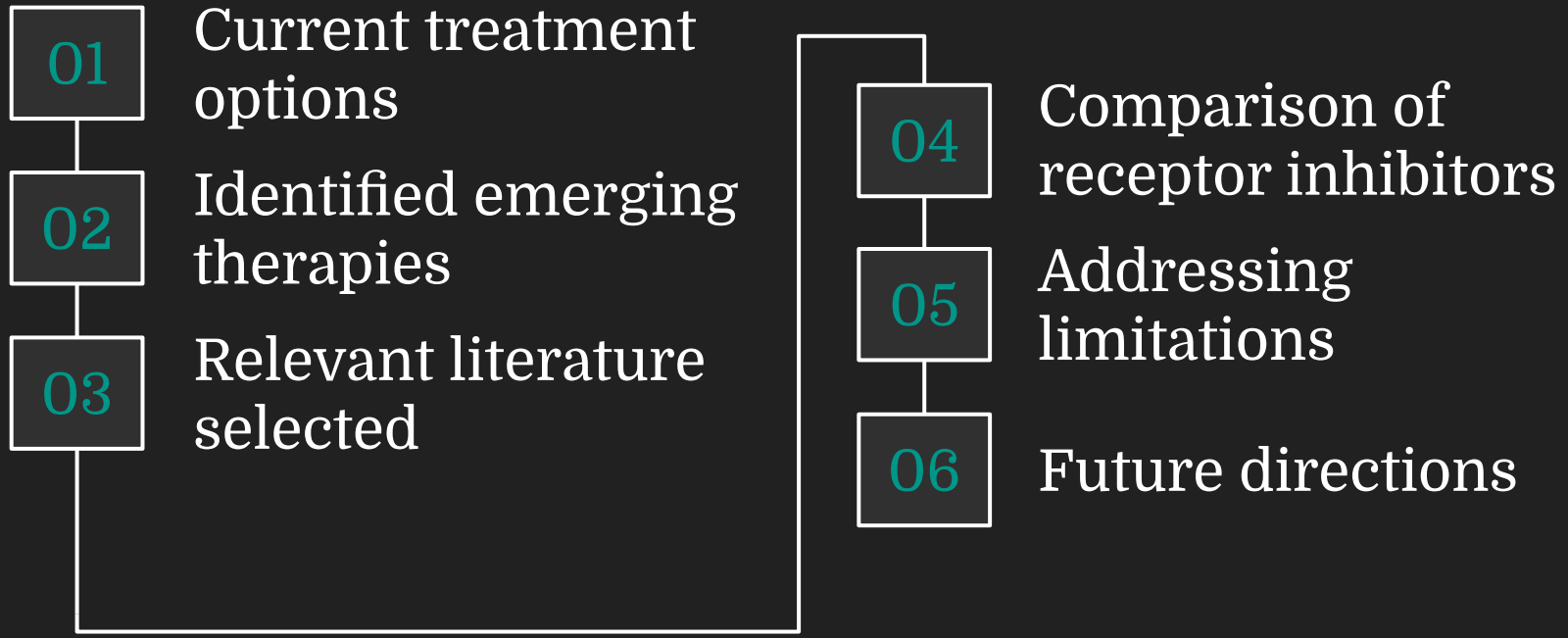
Review Paper:

Glioblastoma Multiforme: An Overview of Emerging Therapeutic Targets (2019)
Olivia G. Taylor, Joshua S. Brzozowski, Kathryn A. Skelding
Frontiers in Oncology

Goals:

- ★ Outline current treatment options for glioblastoma multiforme (GBM)
- ★ Discuss recent advances in targeted therapies for GBM

Review Paper: Methodology



Review Paper: Conclusions

- ★ A personalized therapeutic approach that stratifies GBM patients is necessary for patient survival rates to improve

- ★ There are several potential therapeutic targets:
  - Examples: EphA3, EGFR, VEGF, PDGFR, and MET
- ★ But inhibitors of these targets have only exhibited limited clinical success

- ★ To improve clinical outcomes, we need :
  - More basic research into GBM
  - Development of therapeutics that can maintain concentration across the BBB

Research Paper: Hypothesis

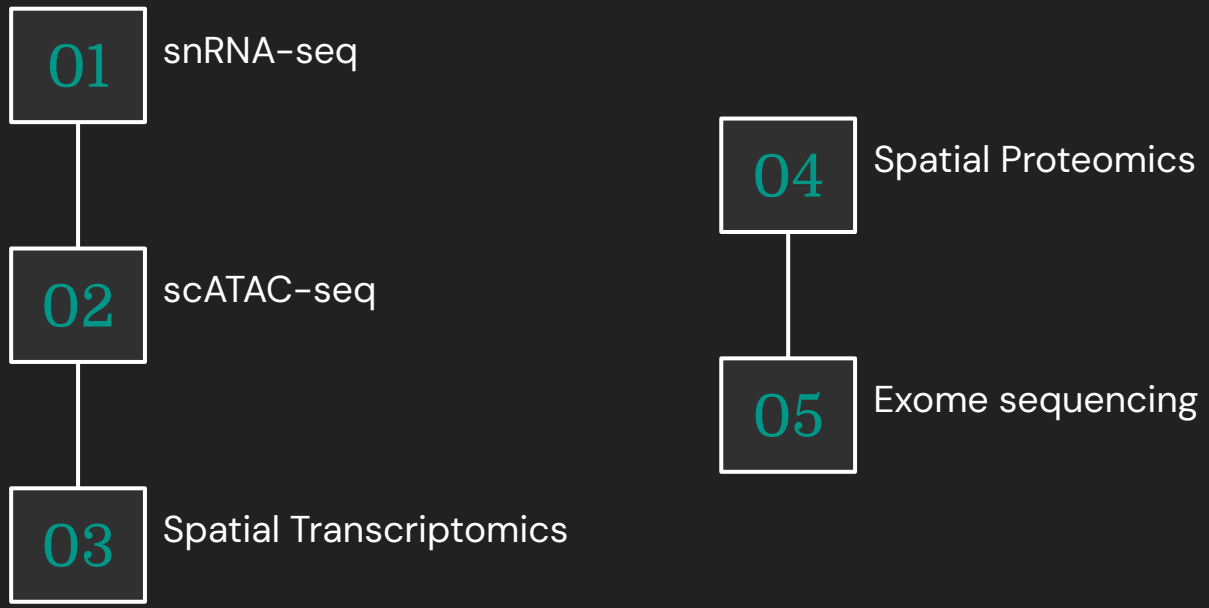
Employed multiple hypothesis testing:

- Selection pressure for specific mutations occurs mostly during initial malignant transformation
- Standard chemotherapy does not apply selective pressure at genetic level
- Glioblastoma cells present high levels of phenotypic plasticity

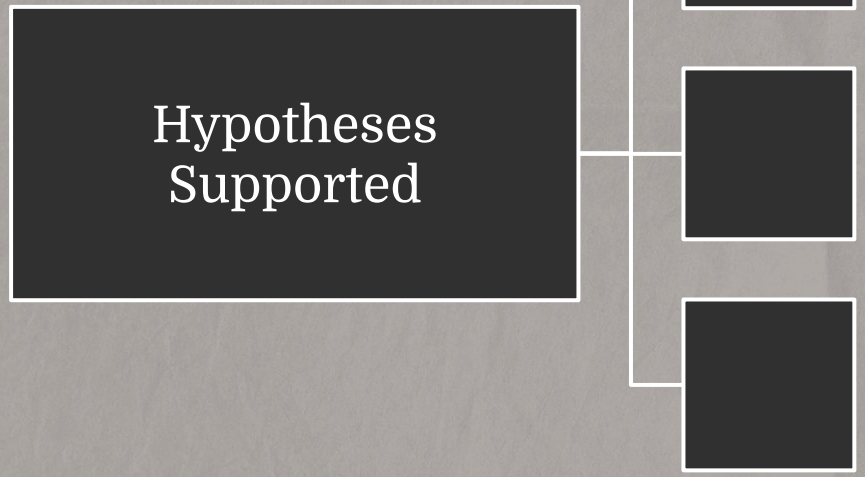
Research Paper: Methodologies

A single-cell multi-omics atlas of GBM evolution under therapy

For 86 patient-matched primary-recurrent paired specimens, they performed:



Research Paper: Findings/Conclusions



Recurrent glioblastoma associated with MES phenotype

MES phenotype is inducible

Cellular targets for therapy

Figure 1

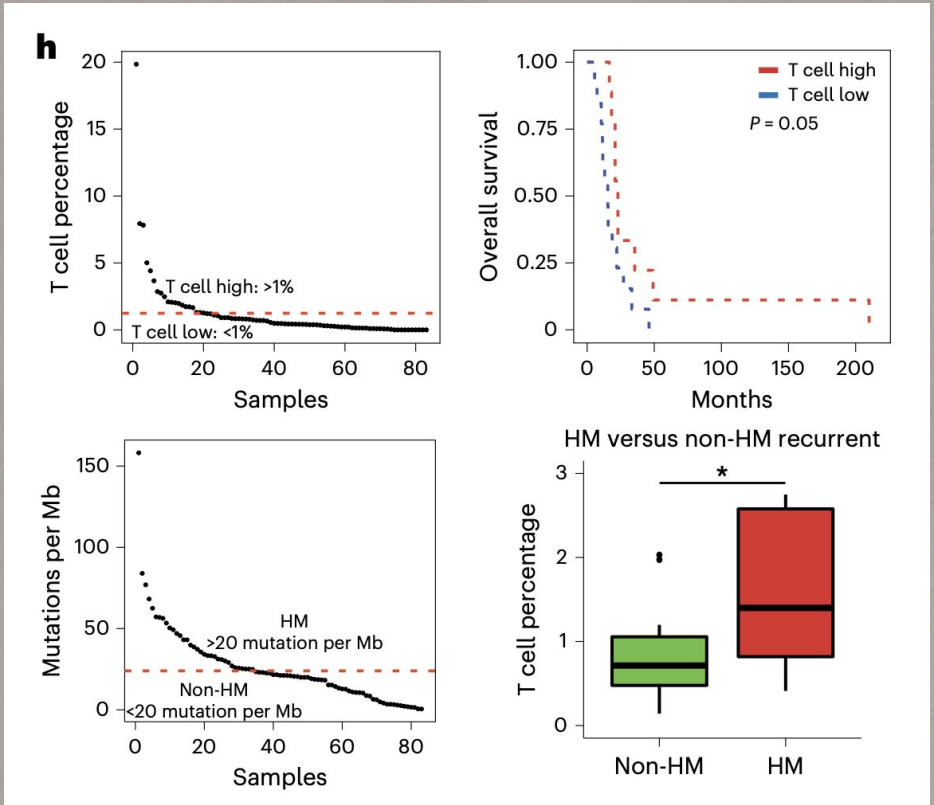
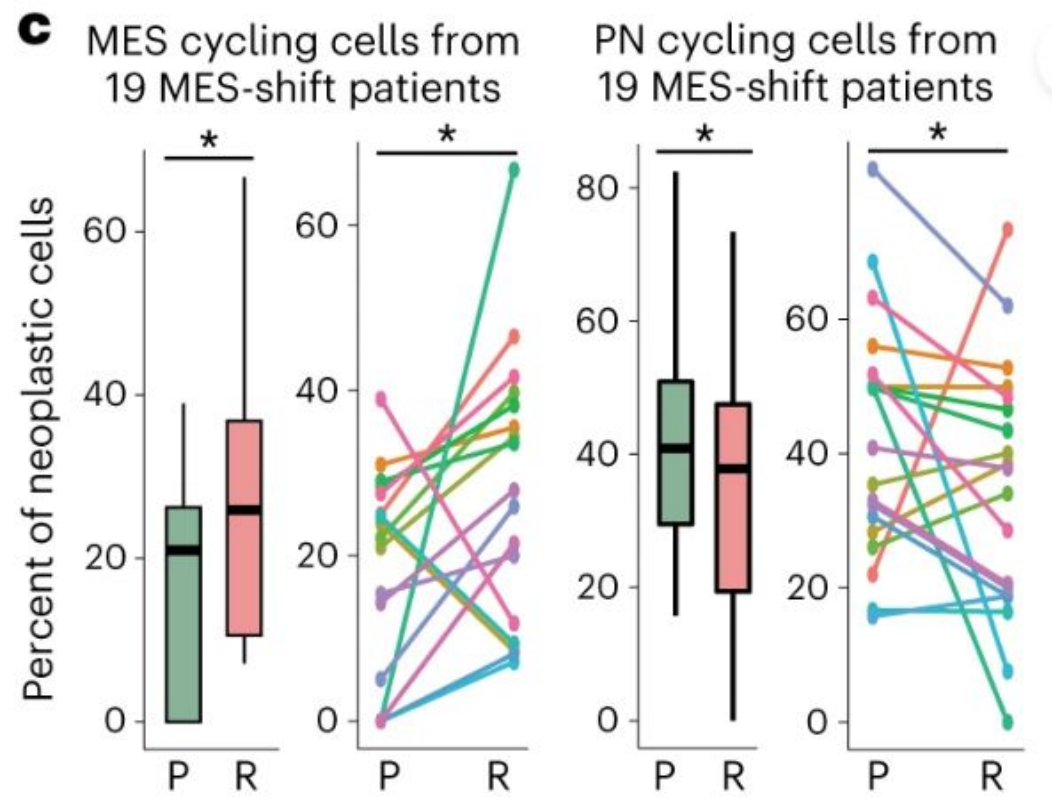

h
T cell percentage
T cell high: >1%
T cell low: <1%
Samples
Overall survival
T cell high
T cell low
P = 0.05
Months
Mutations per Mb
HM
>20 mutation per Mb
Non-HM
<20 mutation per Mb
Samples
HM versus non-HM recurrent
T cell percentage
Non-HM
HM

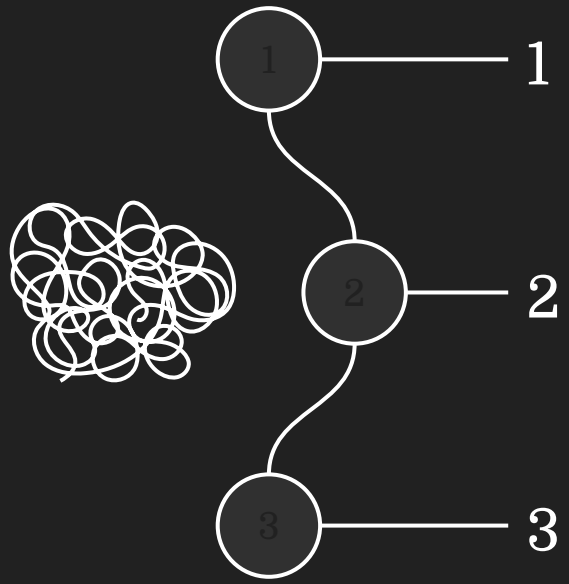
Figure 2



Notes

Distribution of cell phenotypes in GBM patients show association between MES phenotype and disease recurrence.

Questions



How might using a multi hypothesis approach limit or expand the relevance of this study?

How will the knowledge that the mesenchymal phenotype is inducible impact direction for disease treatment?

What challenges remain in designing therapeutics that can act on the targets found in this study?