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Effects of Metabolic Conditions on Gene Expression of Macrophages

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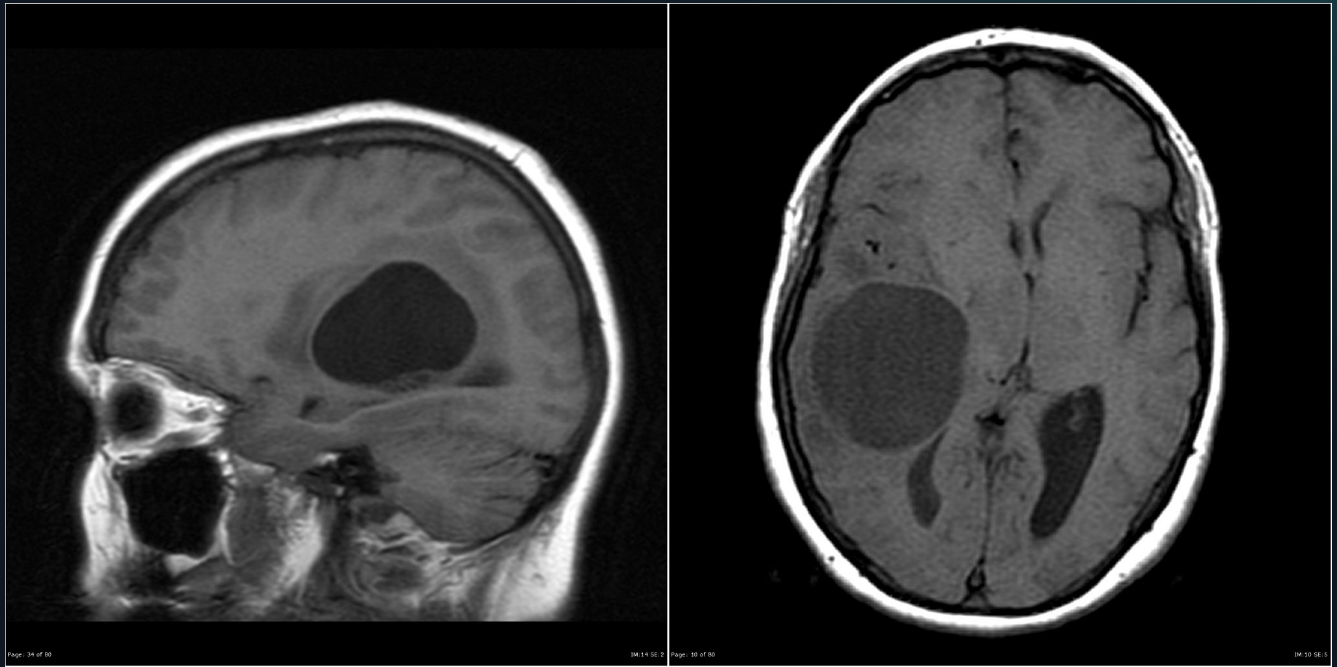
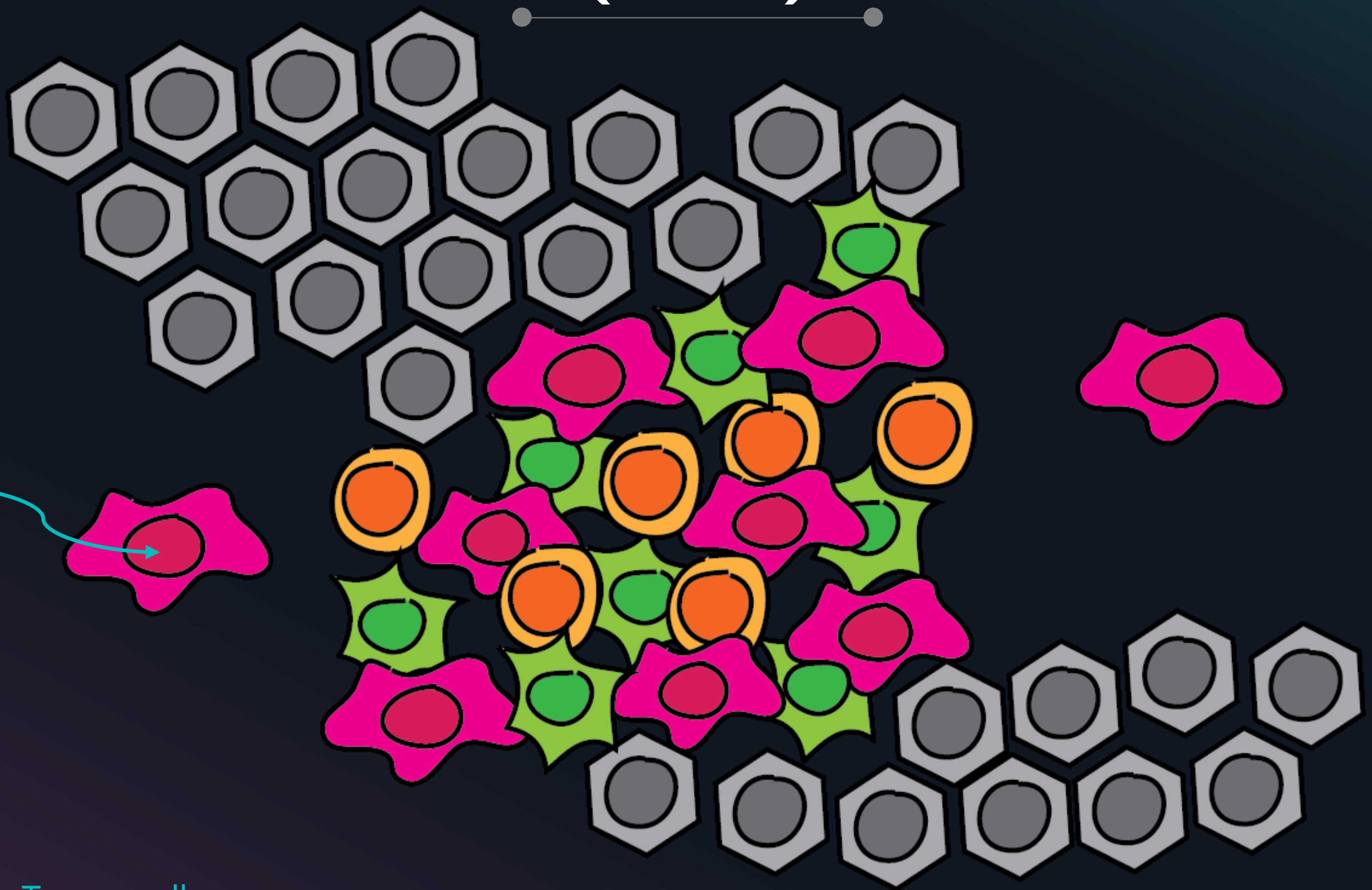
Background

Glioblastoma (GBM) poses a significant hurdle for immunotherapy

- 12,000-13,000 adult diagnoses
- GBM are high-grade gliomas (grade IV WHO)
- 10% survival past 5 years
- Establishment of Tumor Microenvironment



The Tumor Microenvironment (TME)



30% of tumor mass
Immunosuppression
Pro-tumor functions

Tumor cell

Tumor Associated Macrophage (TAM)

Regulatory T cell

Normal Brain Cell

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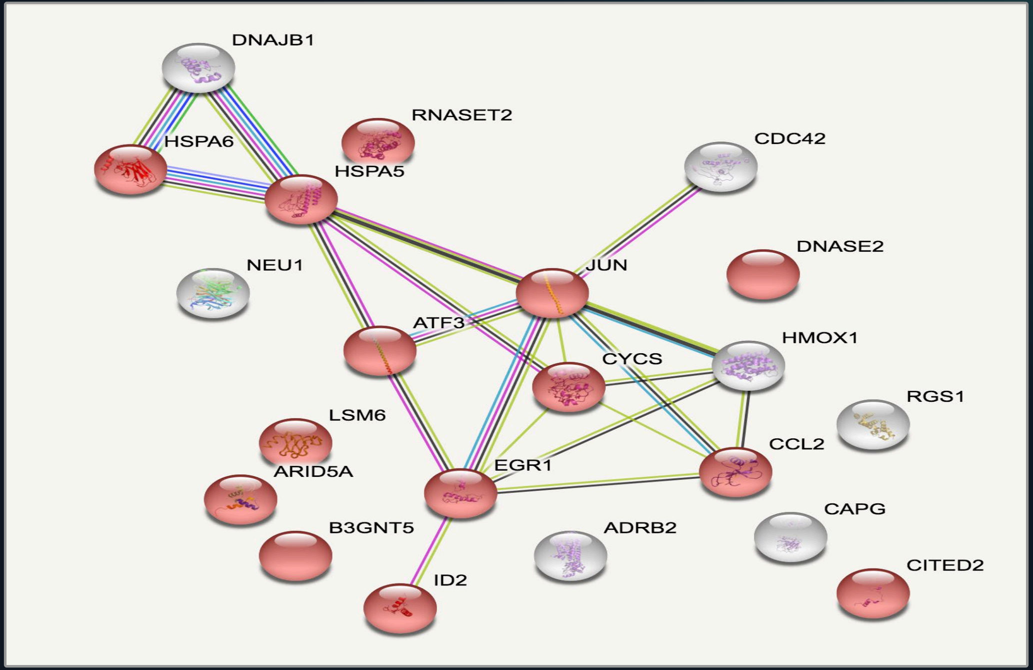
Tumor Associated Macrophages (TAMs) have altered expression of select genes

Single cell RNA Sequencing Reveals 21 genes that are abnormally expressed in TAMs

- Adult Glioblastoma samples taken from surgeries conducted at UW
- Macrophages were isolated from tumor samples and underwent RNA sequencing
- Compared to normal donor macrophages, TAMs displayed abnormal expression of select genes



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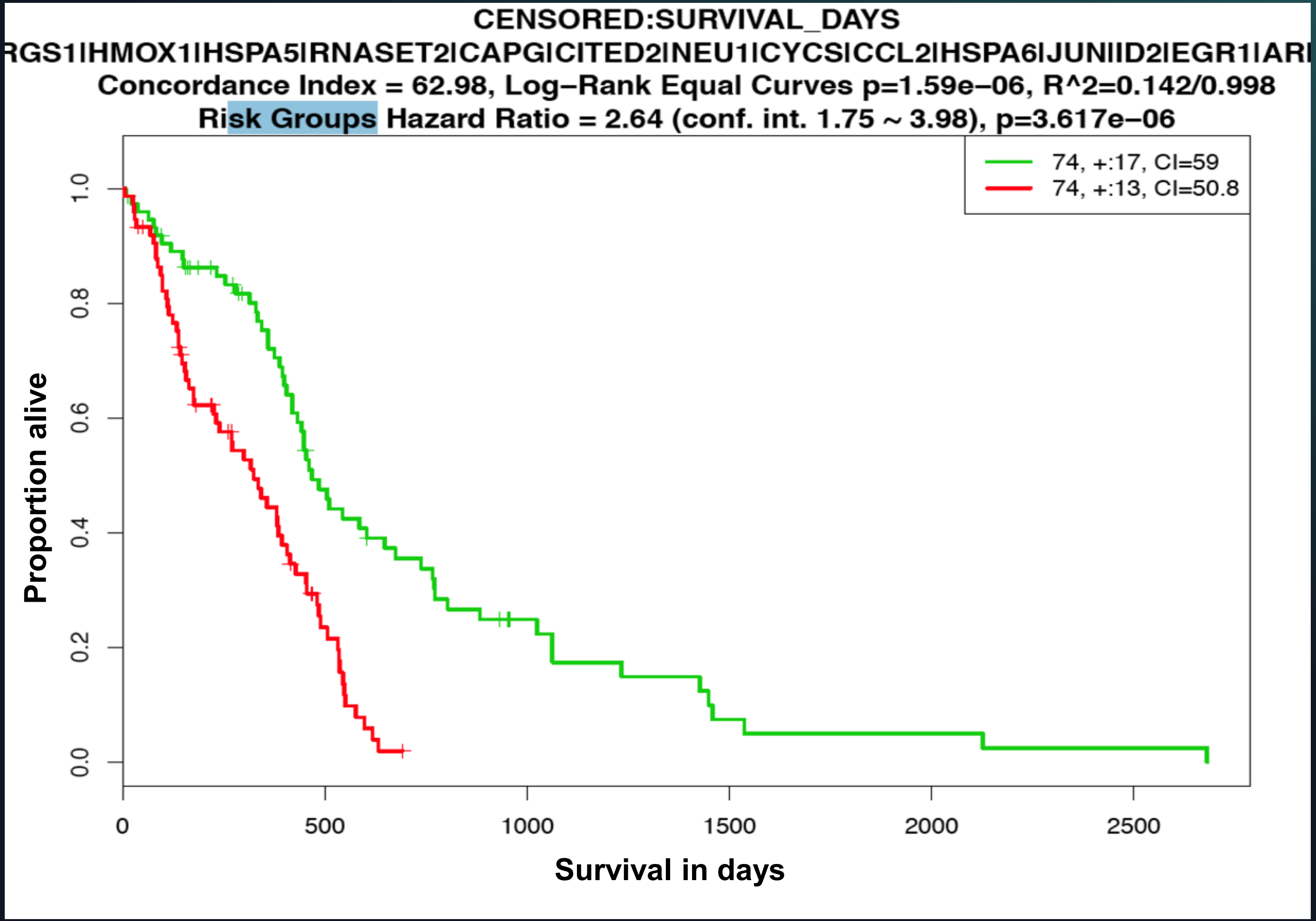
Elevated expression of genes of interest correlates to poor prognosis

- Using public databases, we created a function that correlated expression of target genes to poor tumor prognosis in GBM

Can we influence the expression of these genes, and therefore tumor prognosis?

<u>Hypothesis</u>: Different Metabolic environments will influence the expression of genes of interest.



Higher expression
lower expression

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Methods

Project Overview

Sample Collection and Incubation

Phase 1

- Collection and isolation monocytes from donors, differentiation in vitro into macrophages, and incubate in six different metabolic conditions

RNA Isolation and cDNA Synthesis

Phase 2

- Isolation of RNA after incubation and cDNA synthesis using reverse transcriptase

qPCR Analysis

Phase 3

- Quantitative PCR analysis of gene expression in macrophages under different metabolic conditions

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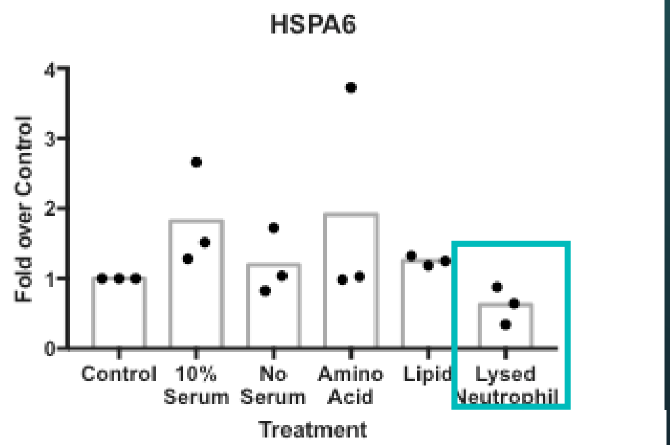
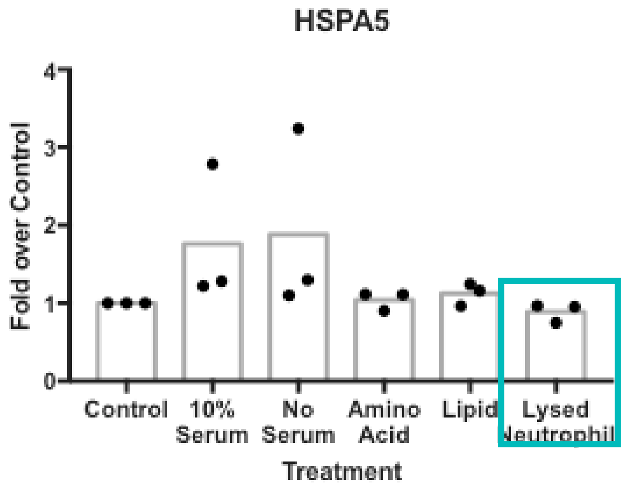
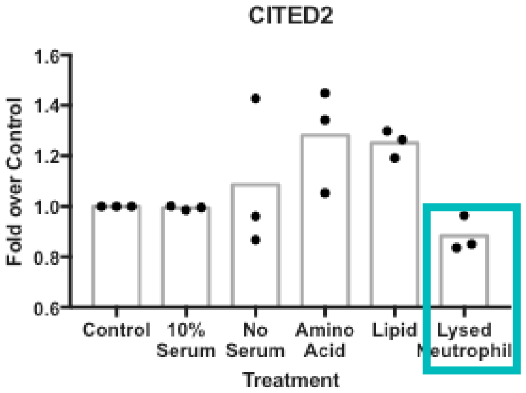
Results and conclusion

- Downregulatory trends seen in certain gene expression
- HSPA5, HSPA6 and CITED2 show downward trends in phagocytotic environments
- Anti CD47 antibody treatments show an increase of macrophage phagocytosis of tumor cells

Conclusion: metabolic environments do show an effect on the expression of target genes in macrophages







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THANK YOU!

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Next Presentation