Role of Glycolytic Metabolism in Glioblastoma Multiforme

Shreya Udawant* and Megan Keniry

Department of Biology, The University of Texas Rio Grande Valley, Edinburg, 78539

***Presenting author: shreya.udawant01@utrgv.edu**

Research Objectives

- To study the differentially regulated genes and biological pathways in glioblastoma (GBM) associated with PI3K inhibition using RNA-seq technology
- Understand the role of molecular regulation of glycolysis related genes in GBM

Project Overview

- GBM cell lines were treated with control vehicle (DSMO) and PI3K inhibitor NVP-*BEZ235*
- Samples were collected with three biological replicates and extracted the RNA for RNA-sequencing (RNA-seq)
- Computational Bioinformatics followed by validation analysis performed for identifying the target genes involved in GBM for drug development to ultimately treat GBM

Experimental design and data analysis strategy

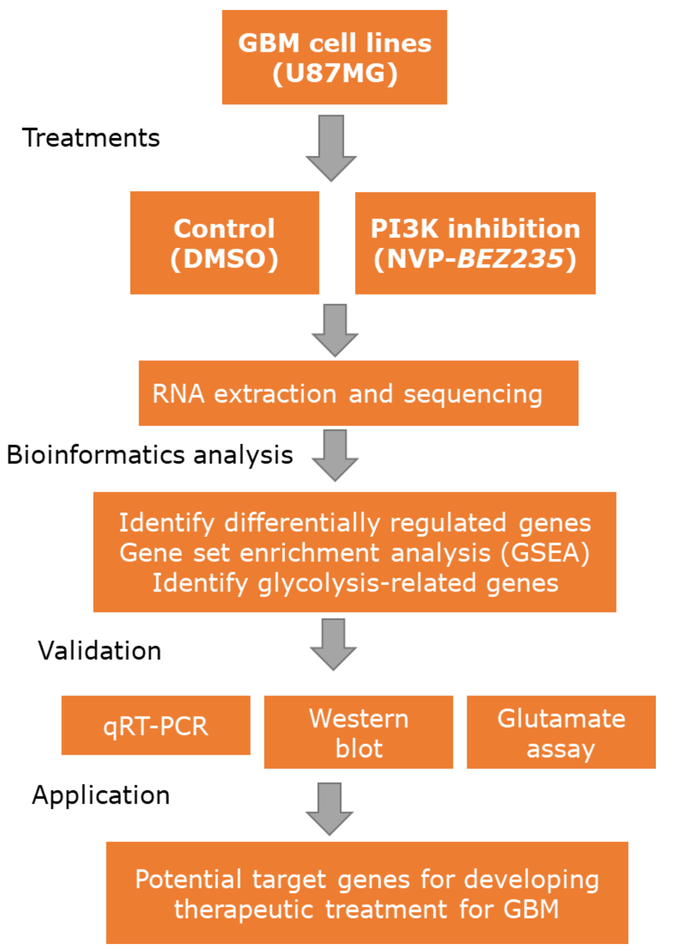

Figure 1. Experimental design

Results

Glycolysis-related genes were highly downregulated in response to PI3K inhibition

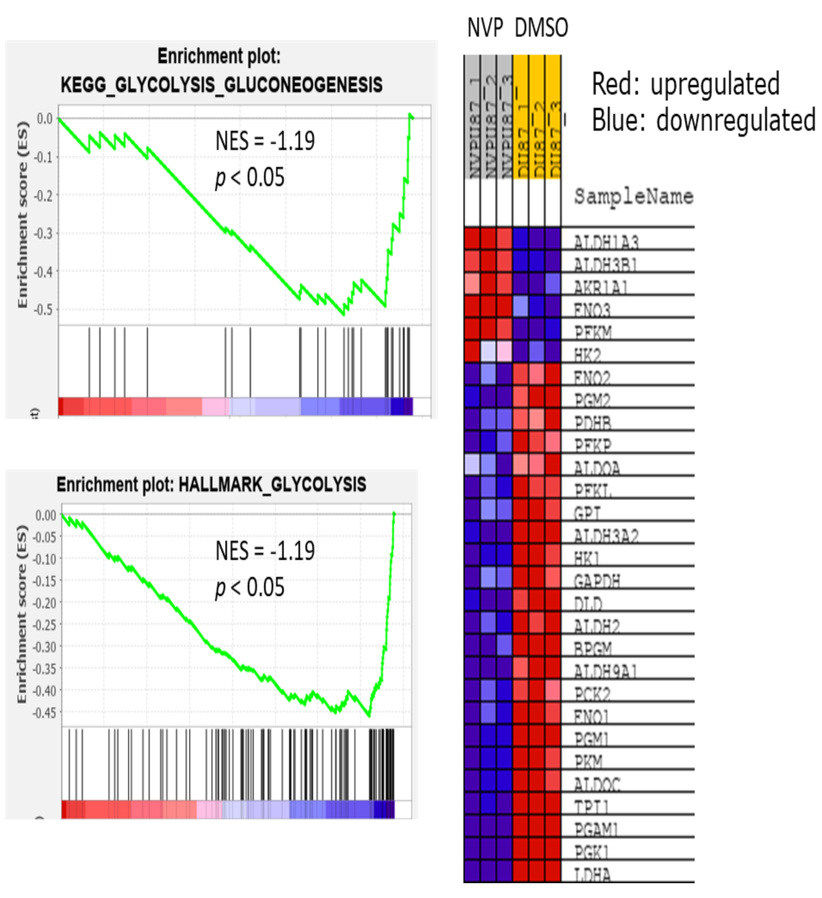

Figure 2. GSEA enrichment and heatmap plot of glycolytic genes in KEGG_GLYCOLYSIS_GLUCONEOGENESIS and HALLMARK_GLYCOLYSIS gene sets

Results

ENO1 and *GAPDH* have shown significant correlations (log rank $p < 0.05$) with the survival

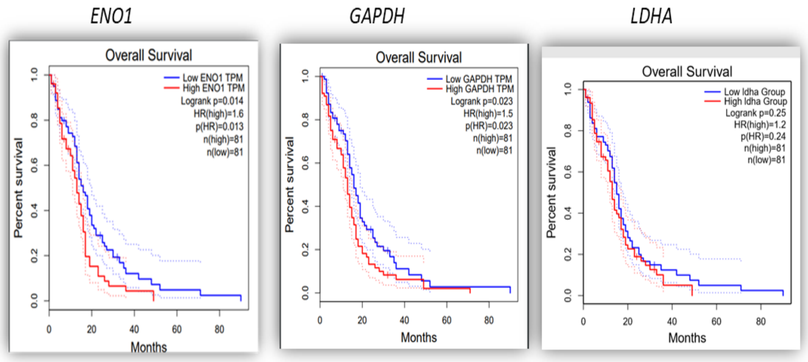

Figure 3. Overall survival analysis of glycolysis-related genes in clinical samples

LDHA, ENO1, and *GAPDH* have shown overall higher expression in clinical tumor samples as compared to the normal controls

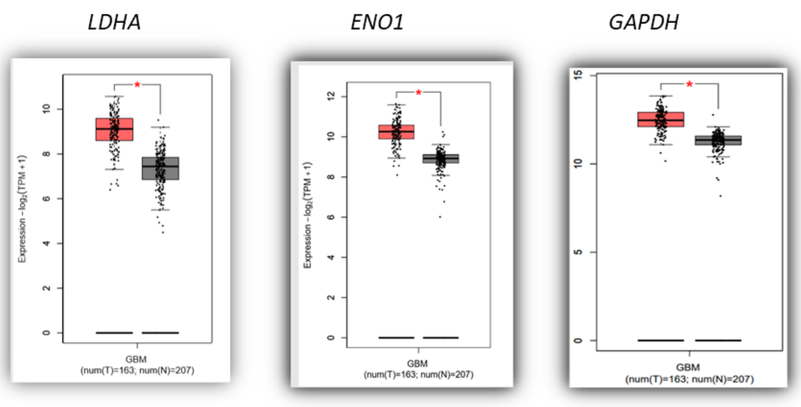

Figure 4. The differential expression boxplot of genes

Validated several genes including, *ENO1*, *GAPDH*, and *LDHA* that were downregulated in response to PI3K inhibition as identified by RNA-seq analysis

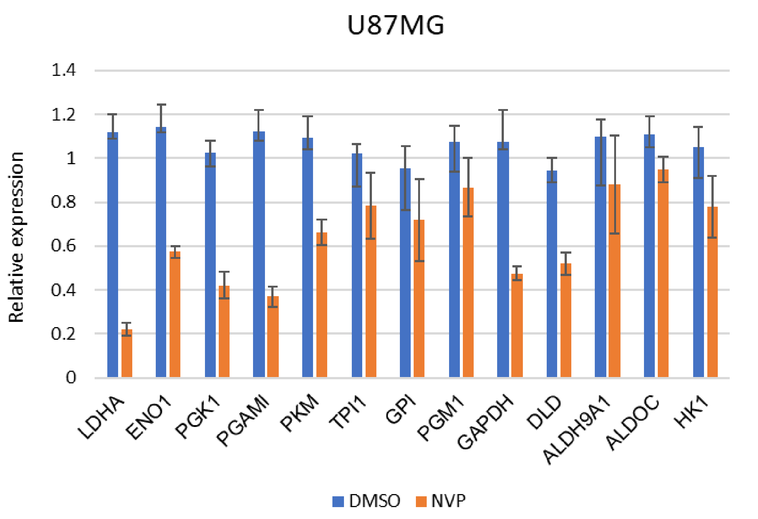

Figure 5. qRT-PCR validation of the glycolysis-related genes

Glutamate concentration was significantly higher in control sample as compared to the NVP-*BEZ235*

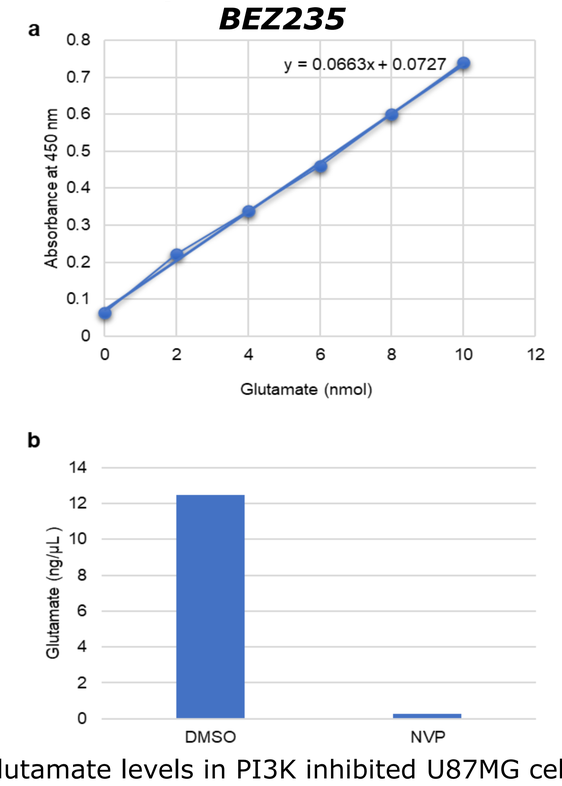

Figure 6. Glutamate levels in PI3K inhibited U87MG cells

Results

Glycolytic genes have shown consistent response across various GBM cell lines

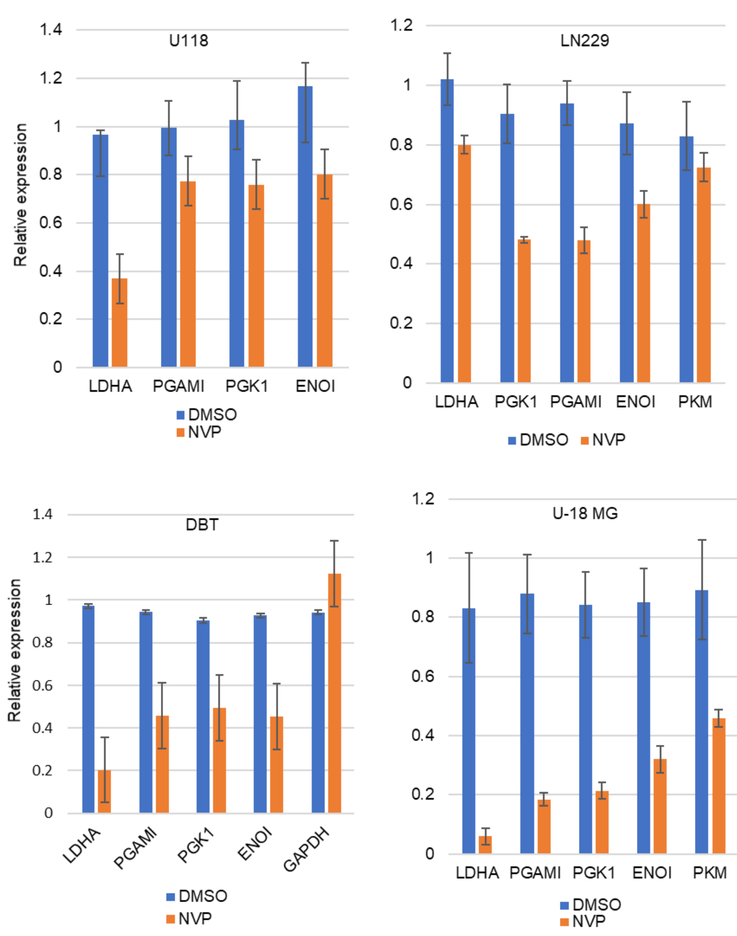

Figure 6. qRT-PCR validation of the glycolysis-related genes in various cell lines

The expression levels of LDHA, PKM2, and GAPDH were higher in DMSO as compared to that of NVP-*BEZ235* treated samples

Figure 7. The expression changes of glycolysis-related genes at protein level (Western blot)

Conclusions

- Glycolysis genes were found downregulated by PI3K inhibition in GBM
- The differentially regulated glycolytic genes were validated using the qRT-PCR and Western blot suggesting their significance in GBM
- Our study provides novel potential therapeutic targets for developing molecular treatment for treating GBM

References

- Batsios, G. et al. *Sci. Rep Sci. Rep.* 2019;9(1):10521.
- Zhao, H. et al. *Mol. Cancer* 2017;16(1):100
- Martinez, E., *et al. J. Cancer Res. Clin. Oncol.* 2020;146(3):593-604.
- Li, H.C., et al. *J. Cell. Biochem.* 2019;120(5):7257-7264.

Acknowledgement

- I would like to thank Dr. Megan Keniry, Mrs. Bonnie Gunn, and Keniry lab members for their time and continuous support