GLIOBLASTOMA MULTIFORME:

CD38 expression implications on glioblastoma progression and survival

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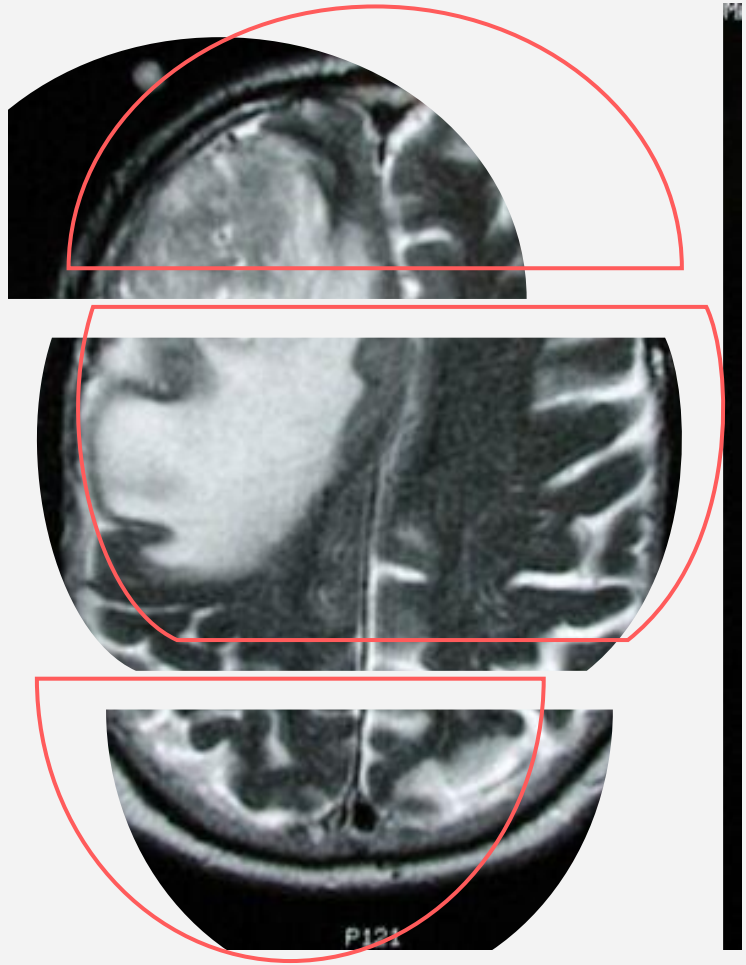

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GLIOBLASTOMA BACKGROUND

304 days

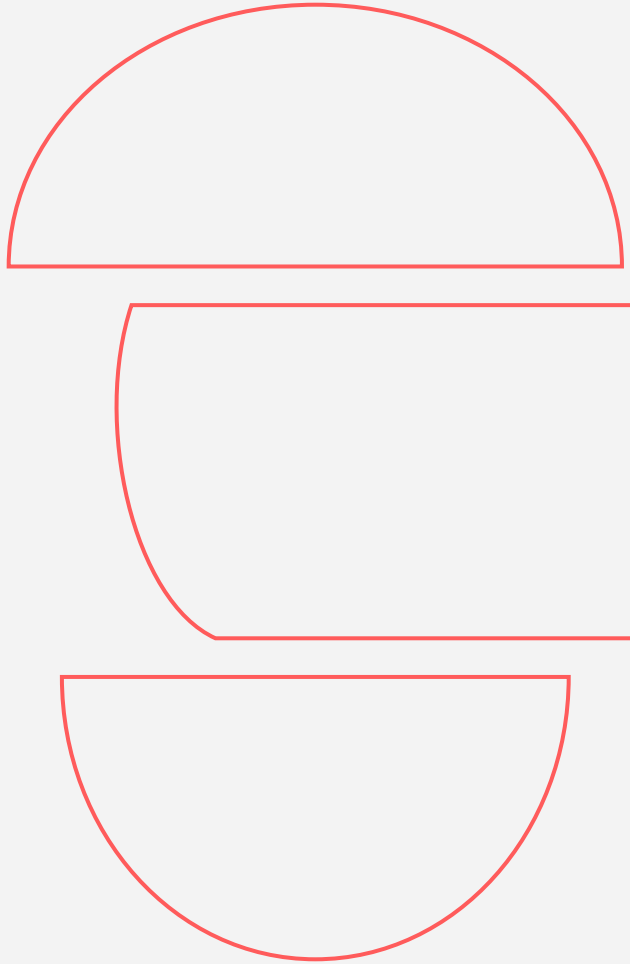
Average survival time of GBM patients after diagnosis

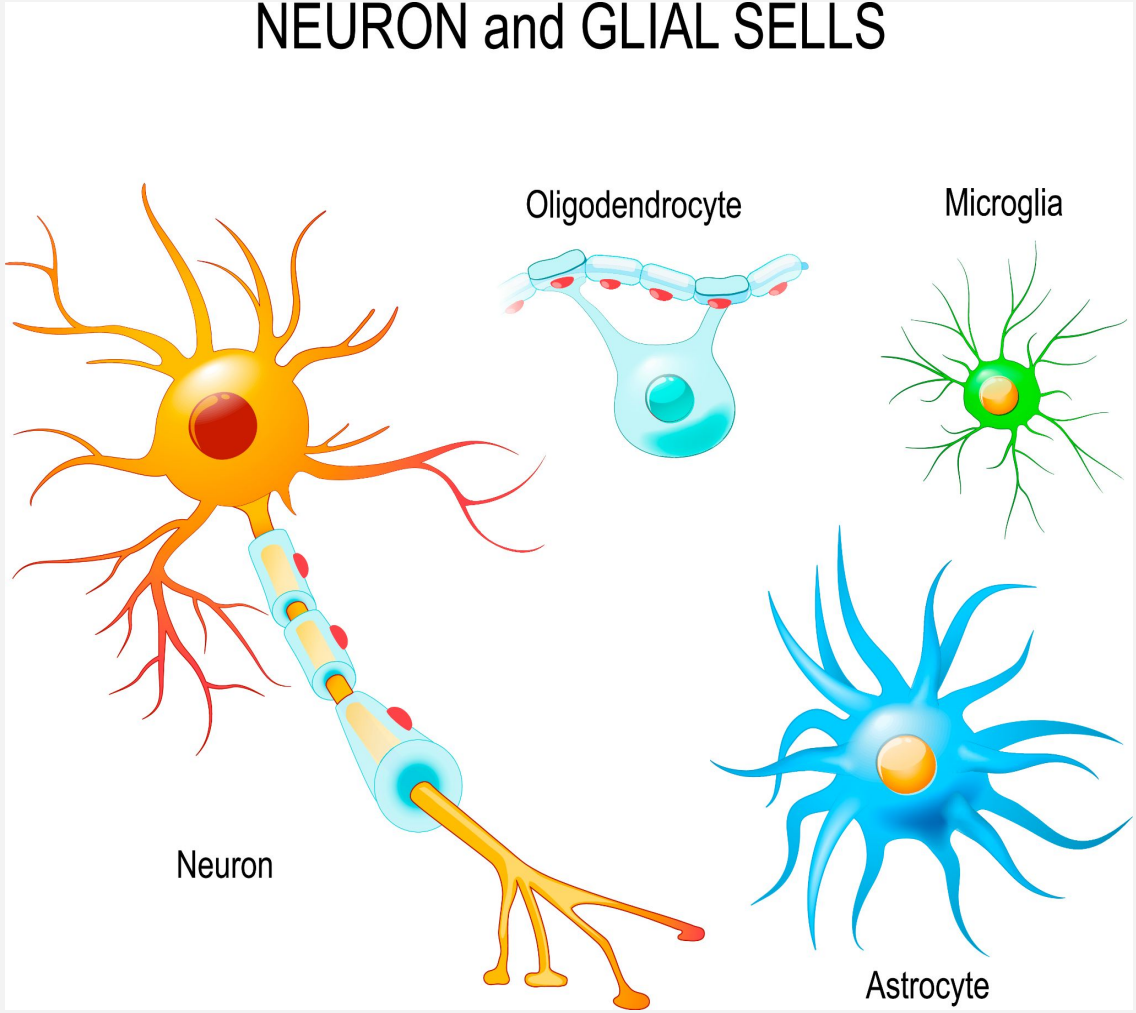
12,000

Cases annually diagnosed within the US alone

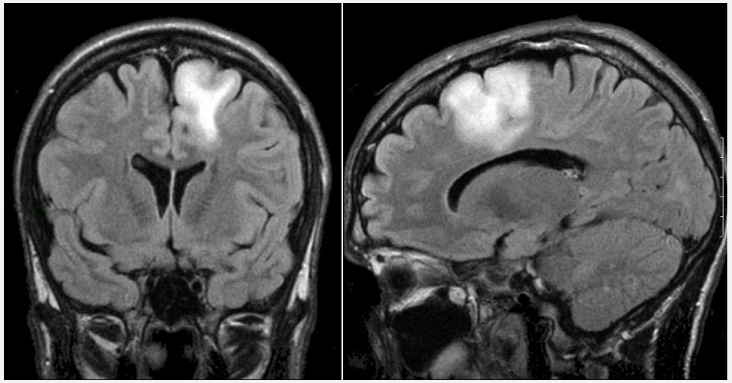
15% of all primary brain tumors

The most complex, deadly, and treatment-resistant brain cancer

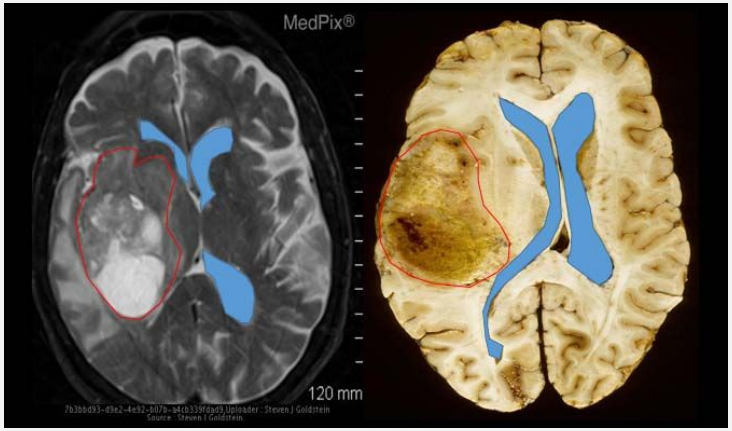




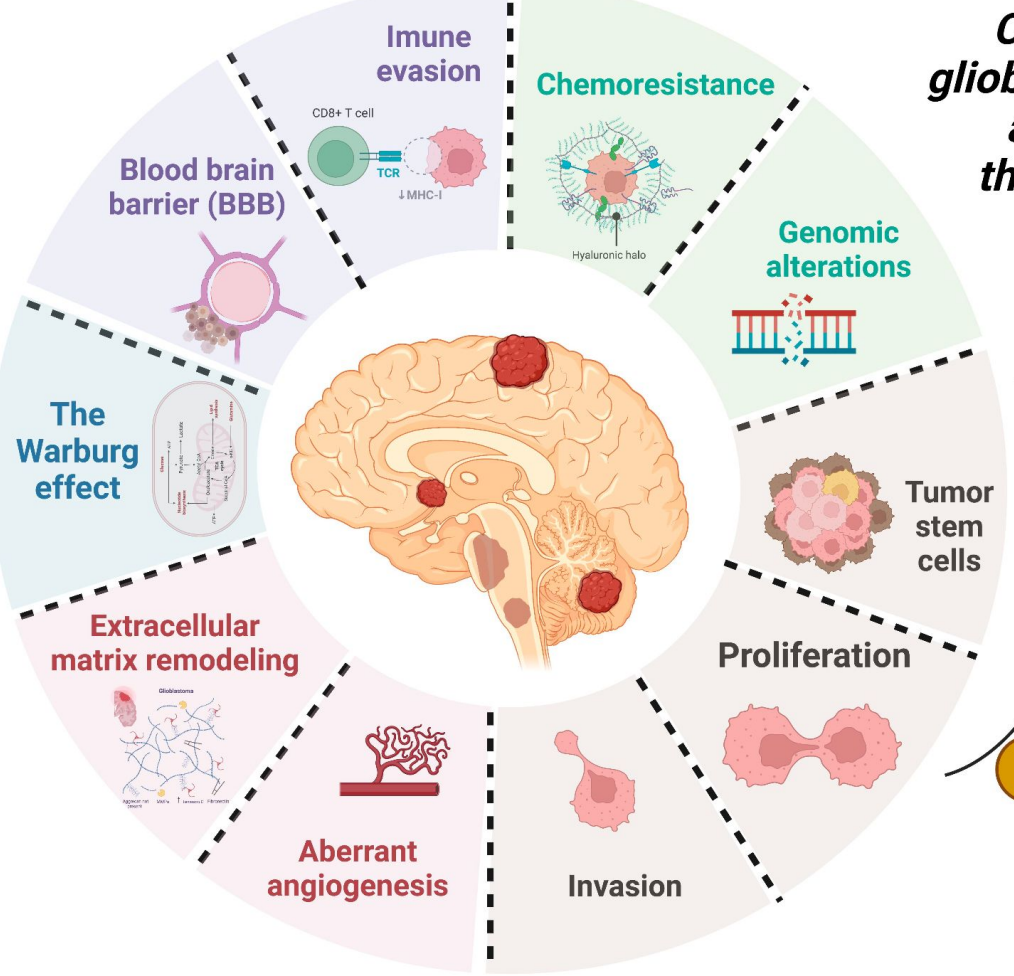
Low-Grade Glioma



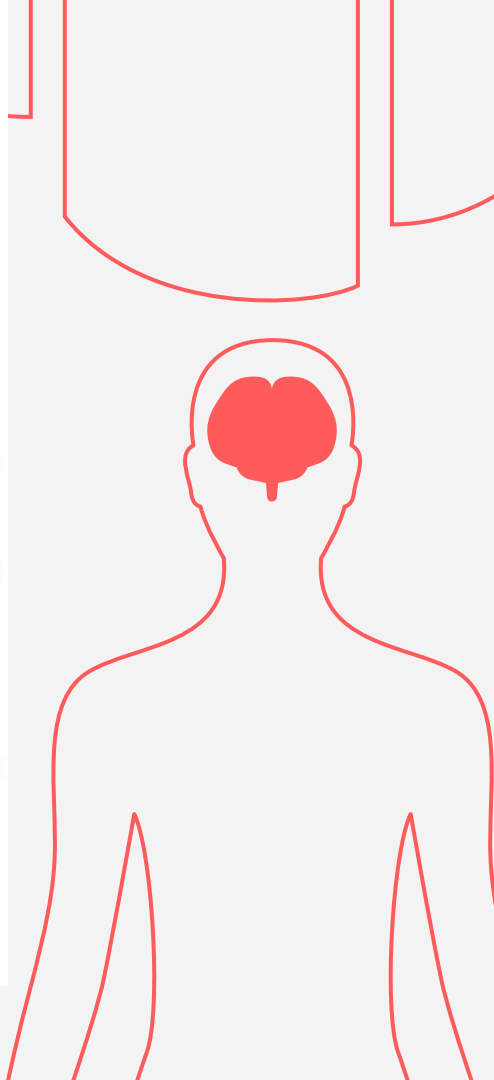
Glioblastoma

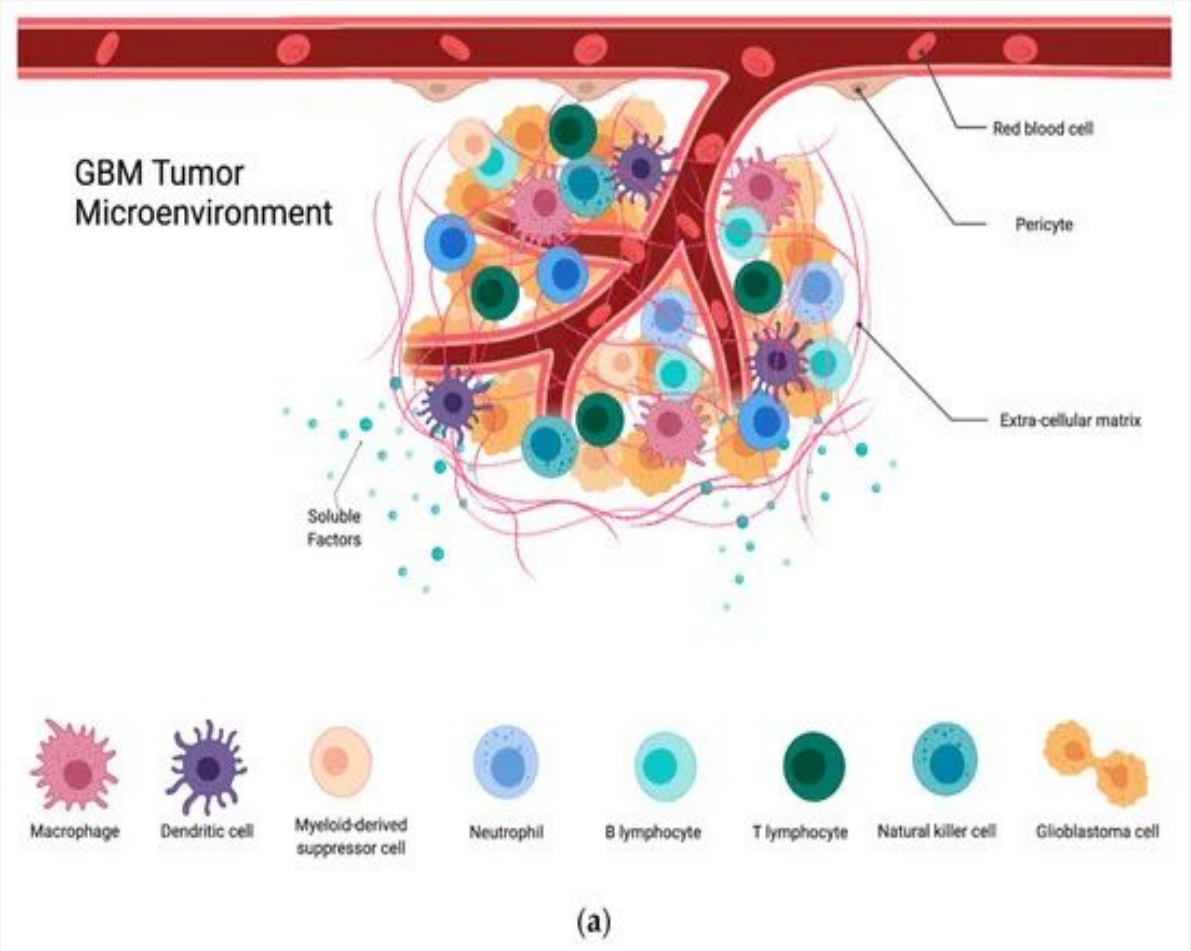


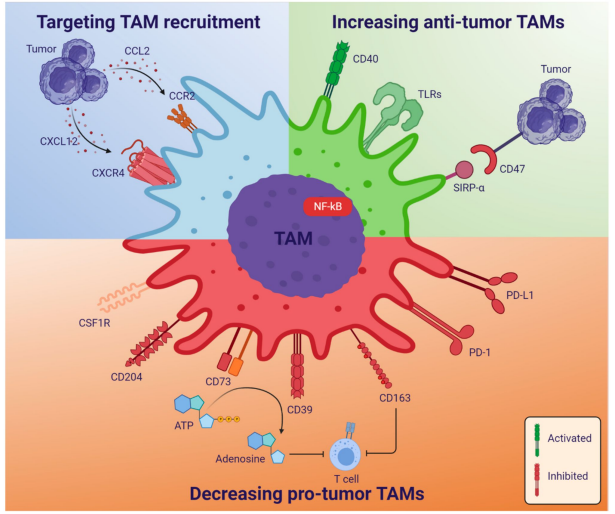
Characteristics of glioblastoma multiforme and the possible therapeutic options



- Immunotherapy
- Chemotherapy
- Radiotherapy
- Precision oncology
- Combination therapy

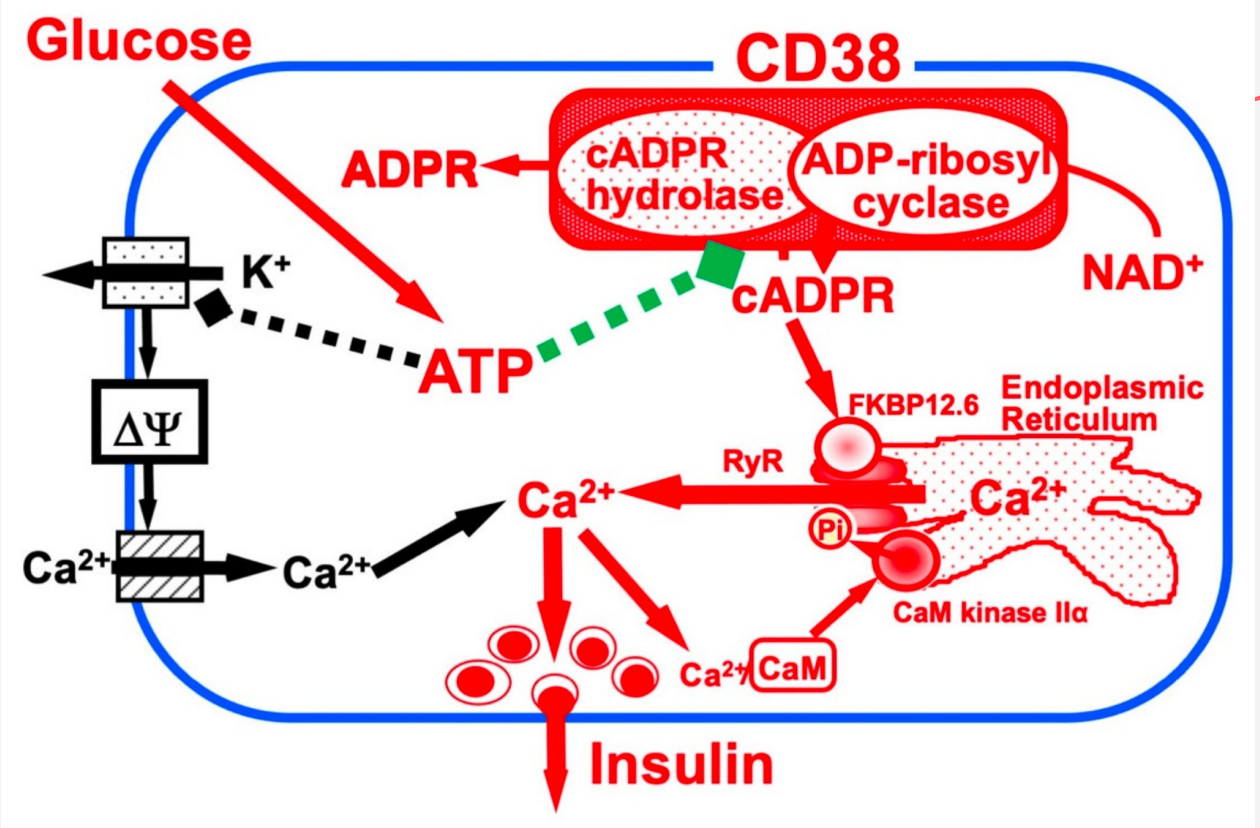



GBM Tumor Microenvironment
Red blood cell
Pericyte
Extra-cellular matrix
Soluble Factors
Macrophage
Dendritic cell
Myeloid-derived suppressor cell
Neutrophil
B lymphocyte
T lymphocyte
Natural killer cell
Glioblastoma cell
(a)


Targeting TAM recruitment
Increasing anti-tumor TAMs
Tumor
CCL2
CCR2
CXCL12
CXCR4
CD40
TLRs
Tumor
CD47
SIRP-α
NF-kB
TAM
PD-L1
CSF1R
PD-1
CD204
CD73
CD39
CD163
ATP
Adenosine
T cell
Activated
Inhibited
Decreasing pro-tumor TAMs

CD38

CD38 or cyclic ADP ribose hydrolase is a robust transmembrane glycoprotein involved in a variety of cellular functions including cell adhesion, differentiation, proliferation, signal transduction in immune responses, and calcium signaling through the synthesis of cyclic-ADP ribose (cADPR).



Hypothesis

High CD38 expression and mutation may exacerbate glioblastoma tumorigenesis and reduce the overall survival time of patients that develop glioblastoma.

02

METHODS

Analyzing expression rates and survival time in R

R Methods

1 High/Low CD38 Expression

- Literature review found cutoff to be at 25% expression
- Segmented patients into 2 categories: high vs low CD38

2 Kaplan Meier Survival

- Compared survival over time

3 Differential Expression Analysis

- Identified upregulated and downregulated genes

4 PANTHER

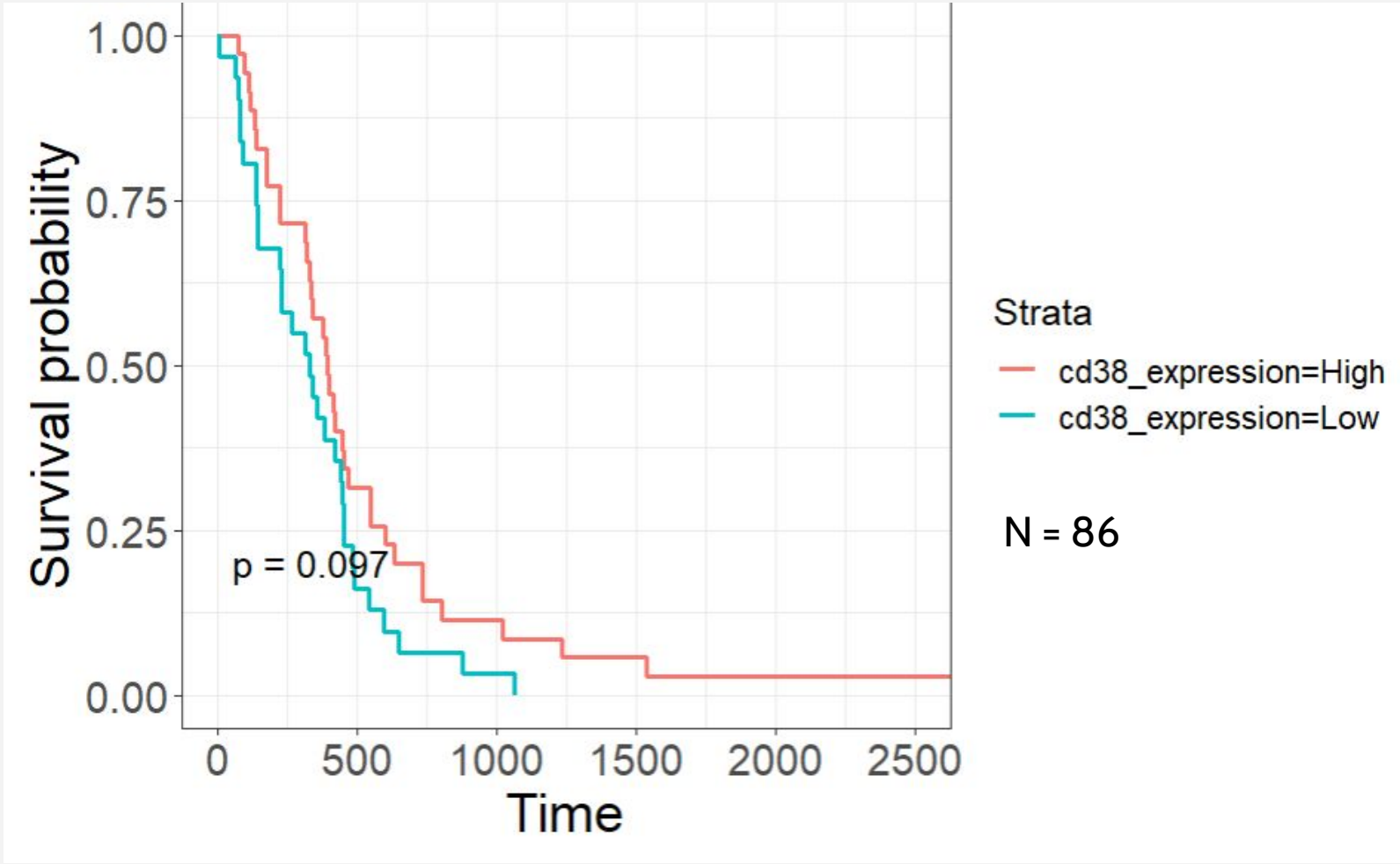
- Biological pathways

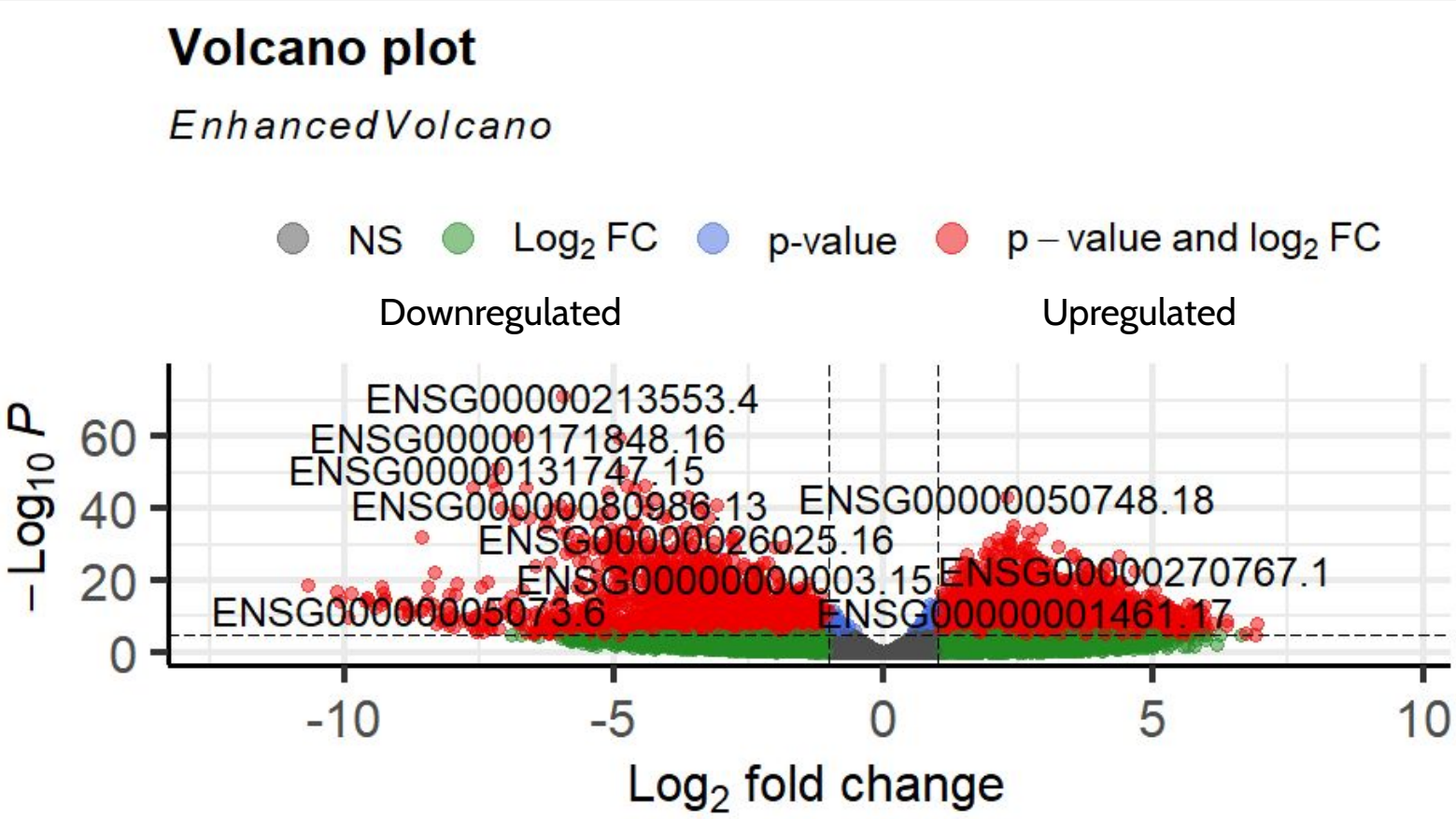
5 Lollipop Plot

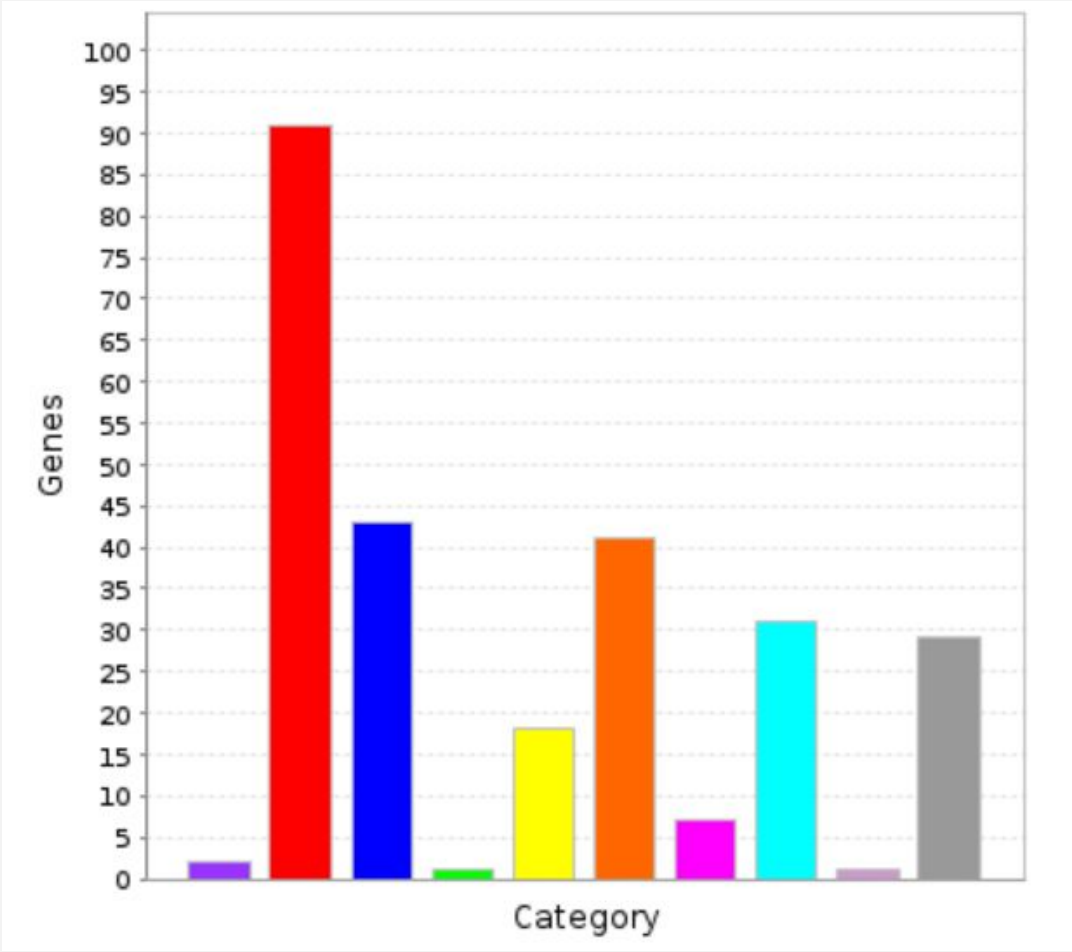
- Mutations on CD38

03

RESULTS


1.00
0.75
0.50
0.25
0.00
Survival probability
p = 0.097
0
500
1000
1500
2000
2500
Time
Strata
cd38_expression=High
cd38_expression=Low
N = 86


Volcano plot
EnhancedVolcano
NS
Log2 FC
p-value
p – value and log2 FC
Downregulated
Upregulated
ENSG00000213553.4
ENSG00000171848.16
ENSG00000131747.15
ENSG00000080986.13
ENSG00000026025.16
ENSG00000000003.15
ENSG00000005073.6
ENSG00000050748.18
ENSG00000270767.1
ENSG00000001461.17
−Log10 P
60
40
20
0
-10
-5
0
5
10
Log2 fold change

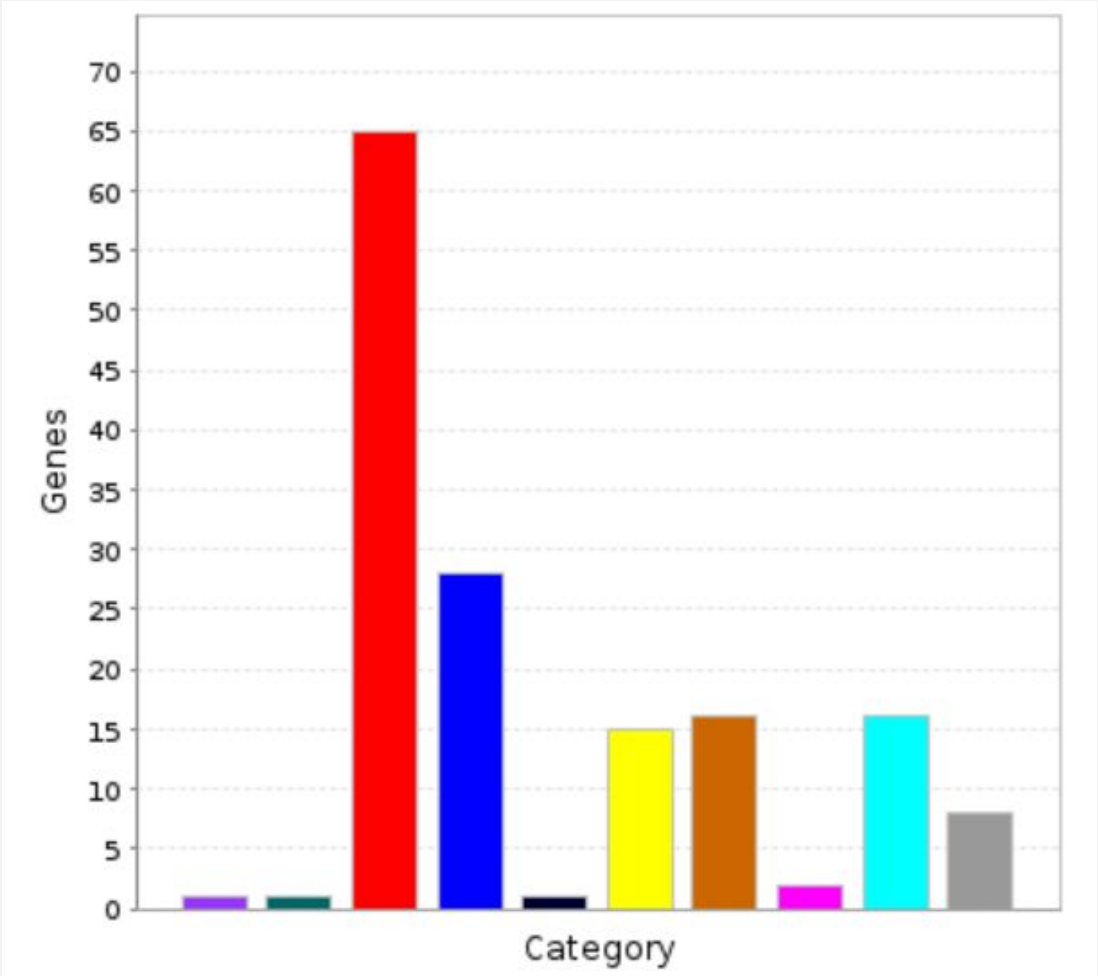


PANTHER Molecular Function- Upregulated Genes

N = 1290

Categorized = 328

- ATP-dependent activity (GO:0140657)
- binding (GO:0005488)
- catalytic activity (GO:0003824)
- molecular adaptor activity (GO:0060090)
- molecular function regulator activity (GO:0098772)
- molecular transducer activity (GO:0060089)
- structural molecule activity (GO:0005198)
- transcription regulator activity (GO:0140110)
- translation regulator activity (GO:0045182)
- transporter activity (GO:0005215)

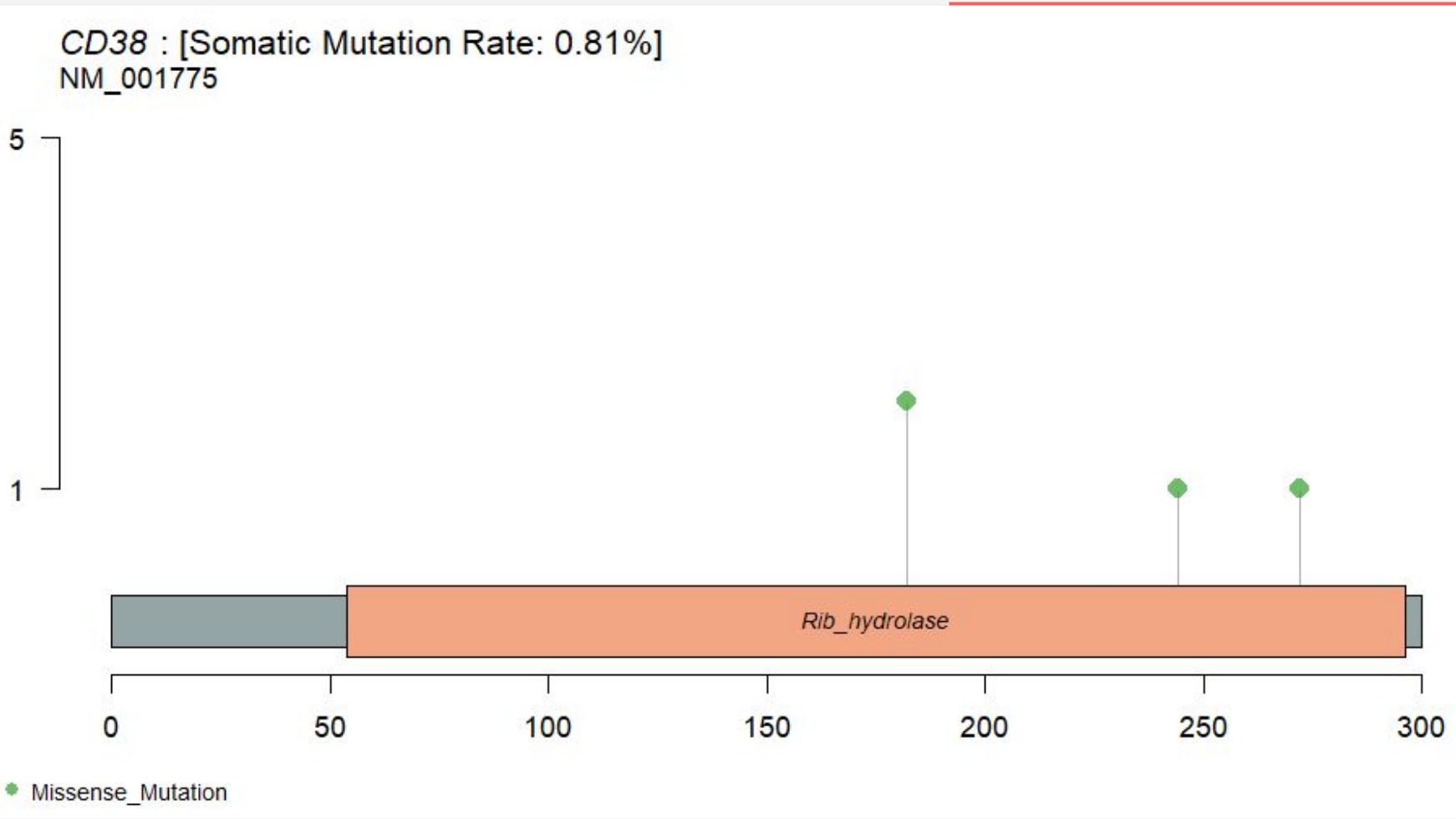


PANTHER Molecular Function- Downregulated Genes

N = 2436

Categorized = 195

- ATP-dependent activity (GO:0140657)
- antioxidant activity (GO:0016209)
- binding (GO:0005488)
- catalytic activity (GO:0003824)
- cytoskeletal motor activity (GO:0003774)
- molecular function regulator activity (GO:0098772)
- molecular transducer activity (GO:0060089)
- structural molecule activity (GO:0005198)
- transcription regulator activity (GO:0140110)
- transporter activity (GO:0005215)


CD38 : [Somatic Mutation Rate: 0.81%]
NM_001775
5
1
Rib_hydrolase
0
50
100
150
200
250
300
Missense_Mutation

04

DISCUSSION

Significance of our findings

Compared to literature

Hypothesis Not Supported

We found that high CD38 expression is correlated with higher survival rates.

- Other genes impact CD38 expression
- Small sample size

Medical Implications

Could CD38 reduce efficiency of biological processes?

Gene Ratio

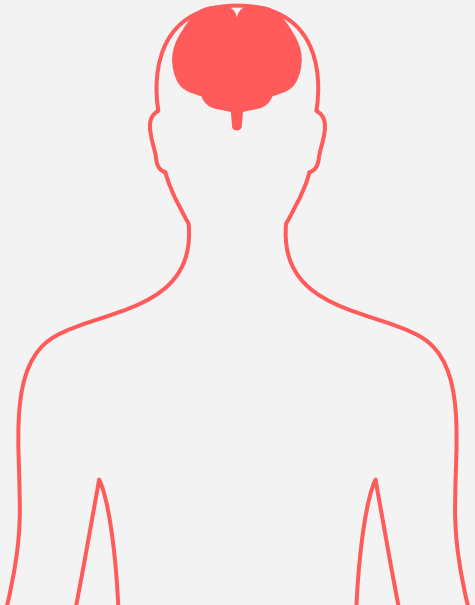
Total Upregulated Genes = 2436
Total Downregulated Genes = 1490

Upregulated and downregulated genes perform similar functions. By ratio, we identified twice as many upregulated genes than downregulated genes in RNA data. However, this is not reflected in the PANTHER bar graph.

Future Directions (pathways)

Treatments

Current treatments are limited by blood brain barrier.



Comparison Between Cancers

Examine why high CD38 expression is correlated with lower survival rates in glioblastoma, but improves prognosis in hepatocellular carcinoma (HCC) and breast cancer.

1. Run differential analysis expression on high/low CD38 cohorts in HCC and breast cancer

2. Input upregulated and downregulated genes of both cancers into PANTHER

3. Compare pathways with glioblastoma

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Questions?

Thank you for your time and attention!