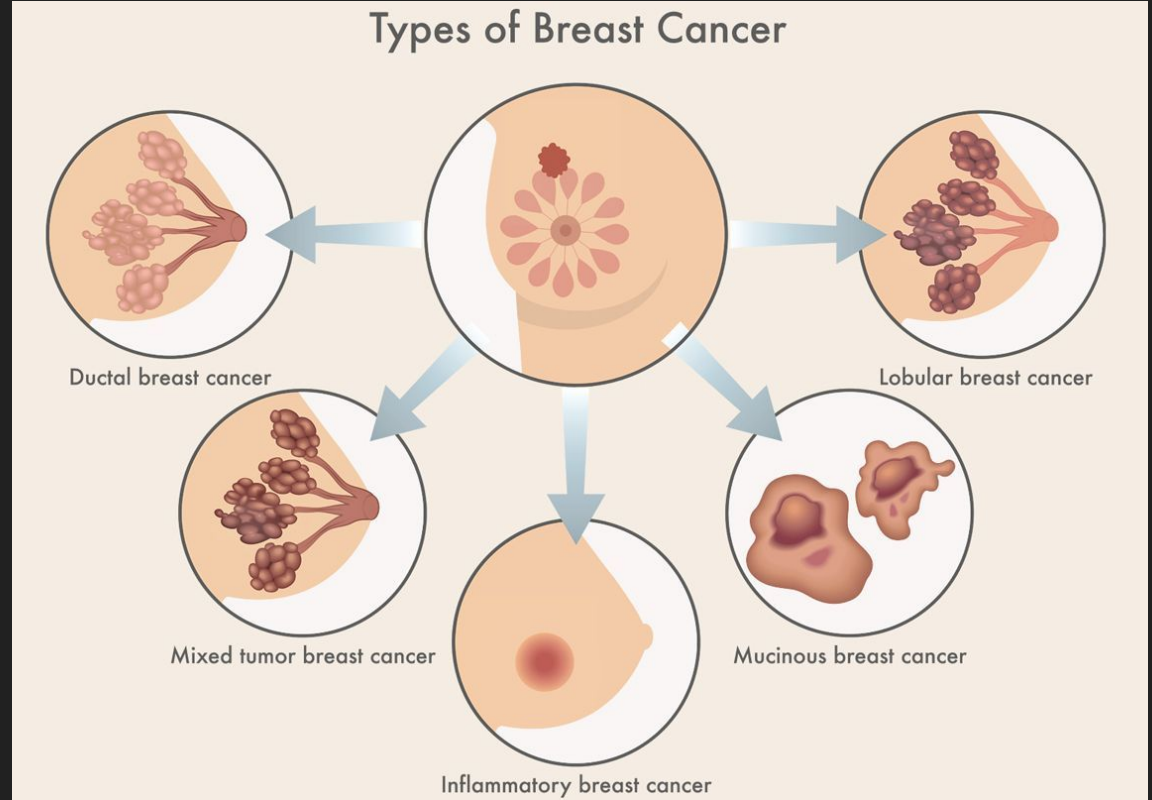
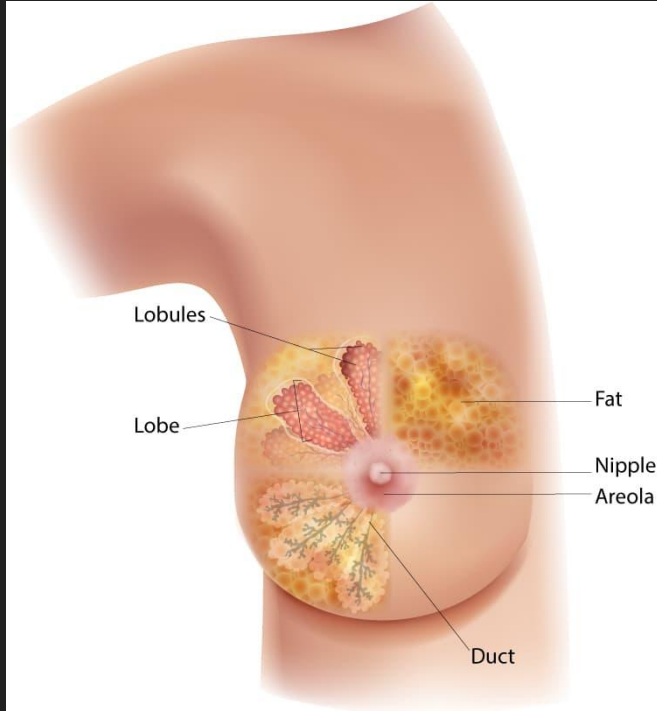



The Role of TP53 Co-Mutations in Breast Cancer Patient Survival

Kailin Liu, Chloe Liu, Colin Yeo

Introduction - Breast Cancer



Introduction - Breast Cancer Statistics

In 2022, an estimated
287,500 new cases
of invasive breast cancer
will be diagnosed in
women in the U.S. 



1 in 8
women

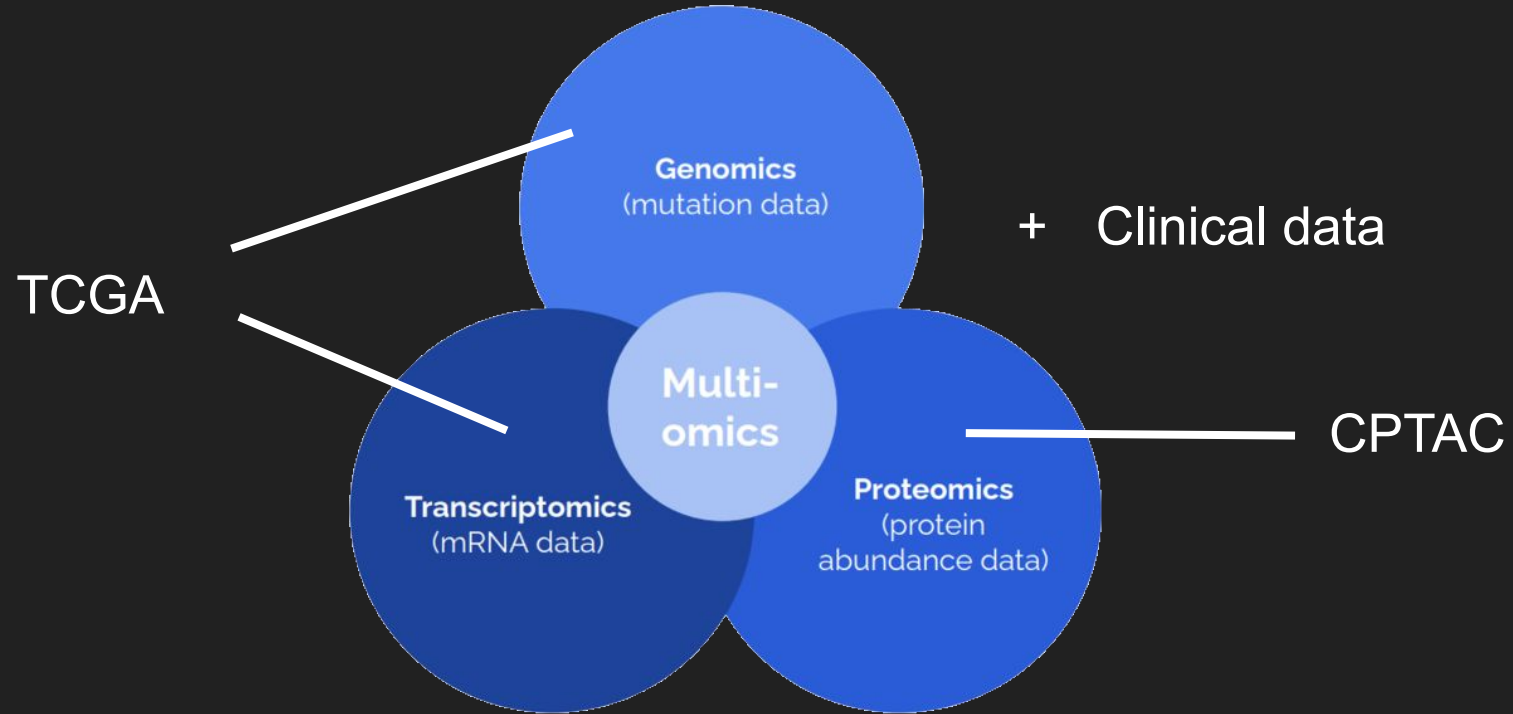
in the United States will develop
breast cancer in her lifetime.



Introduction - Datasets



Introduction - Multi-omic Data Analysis



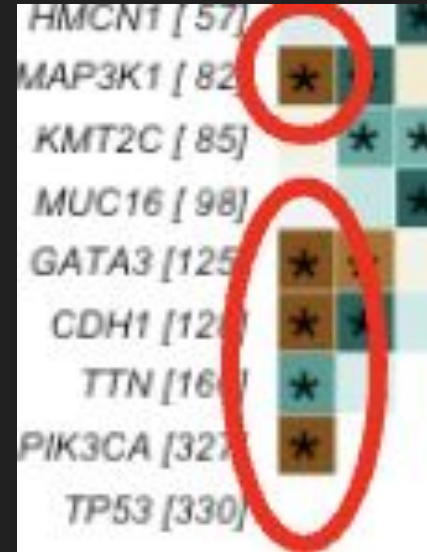
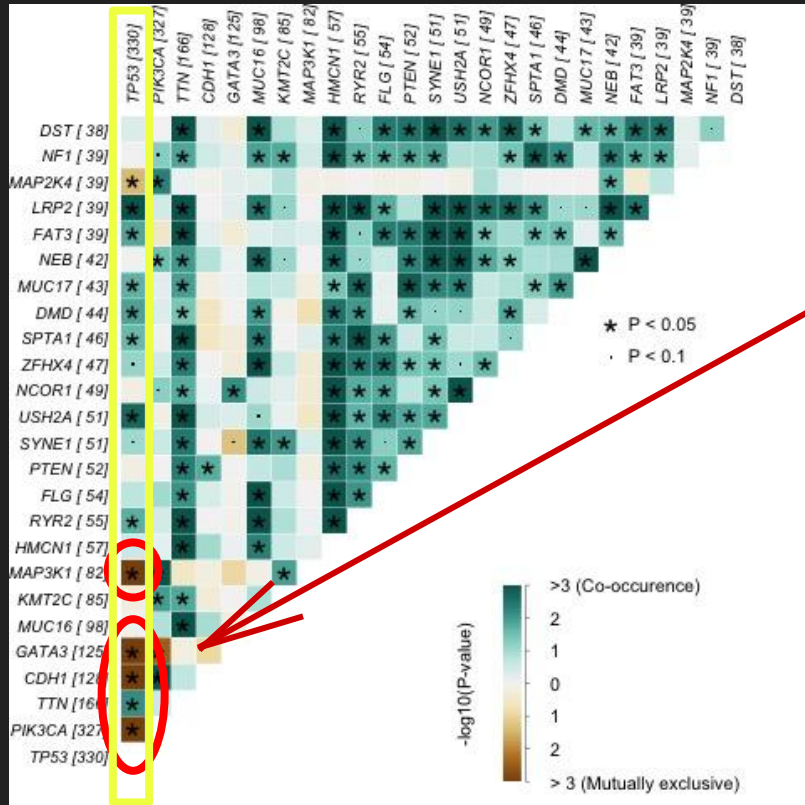
Research Question:

How does TP53 co-mutation influence survival in breast cancer patients and interact with other genes/protein production?

Methods

- R
 - TCGA (~1100 patients)
 - BiocManager, Summarized Experiment
 - Maftools, ggplot2, survival, survminer
- Python
 - CPTAC (122 patients)
 - Numpy, Pandas, Scipy, Matplotlib, Seaborn

4 Genes Show Mutual Exclusivity with TP53 (Fig 1)

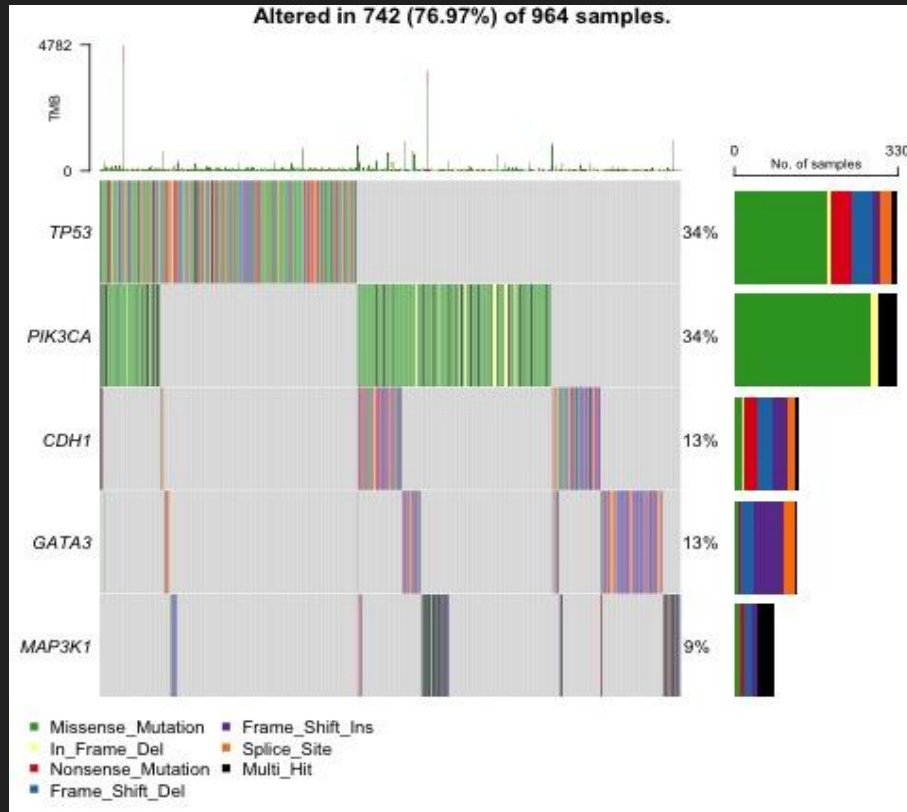


Somatic Interaction Plot that highlights 4 mutually exclusive genes with TP53.

Our 4 Chosen Genes

- MAP3K1 (cell migration/survival), GATA3 (cell development/function), CDH1 (tumor suppression), PIK3CA (cell growth)
- TP53 & GATA3 implicated in early onset breast cancer (Grote et al., 2021)
- TP53 & CDH1 involved in familial breast cancer (Rahim et al., 2022)

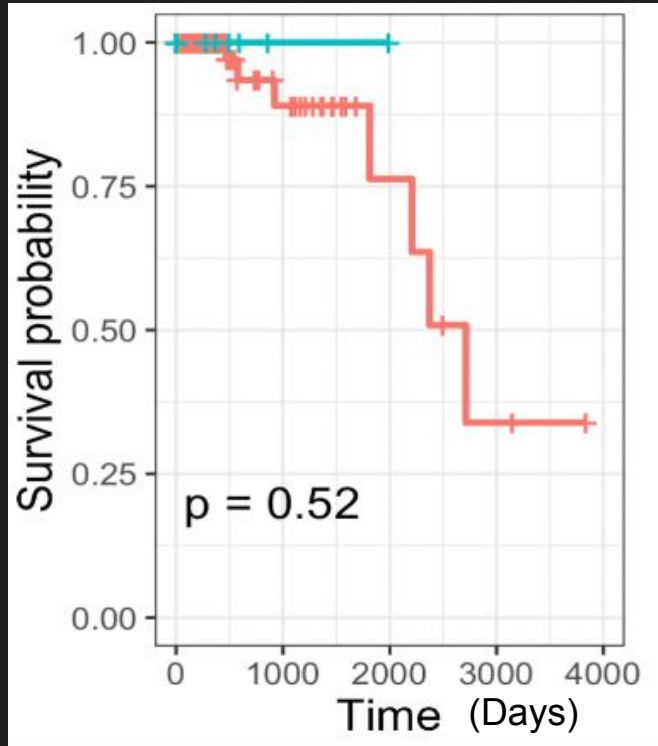
Oncoplot Shows Slight Overlap between Genes (Fig 2)



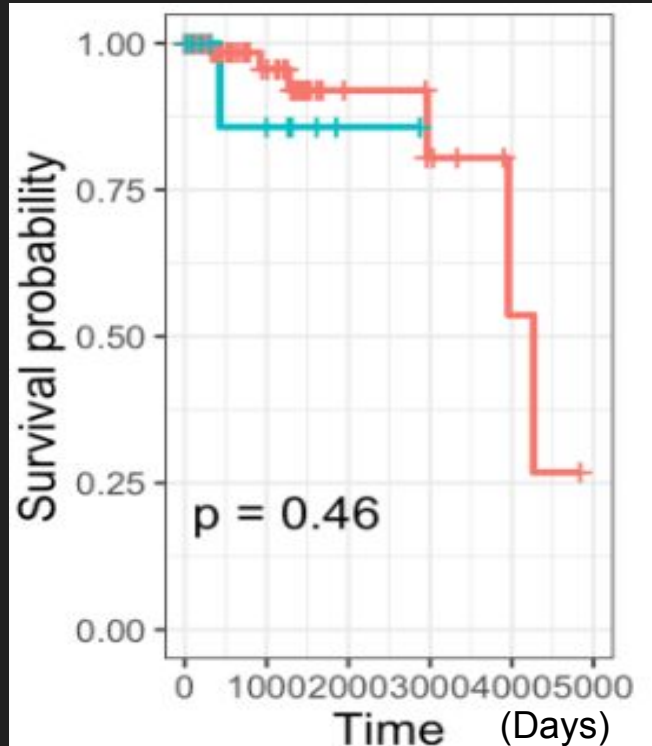
Key Takeaways:

- Certain genetic mutations are caused disproportionately by one type of mutation
- The number of overlaps between the gene mutations is minor

KM Plot Shows Higher Survival Probability for TP53+/CDH1+ and TP53+/MAP3K1+ Patients (Figs 3-4)



MAP3K1 (TP53-: 113; TP53+: 9)

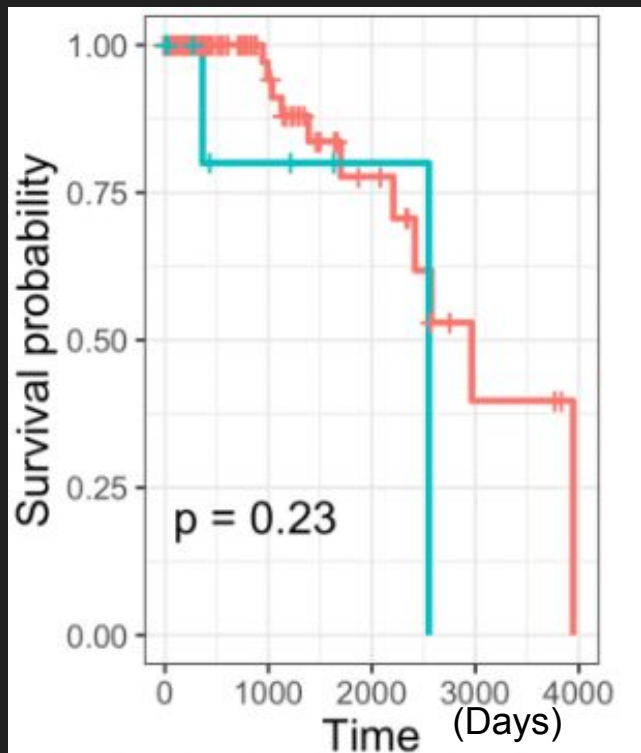


CDH1 (TP53-: 123; TP53+: 11)

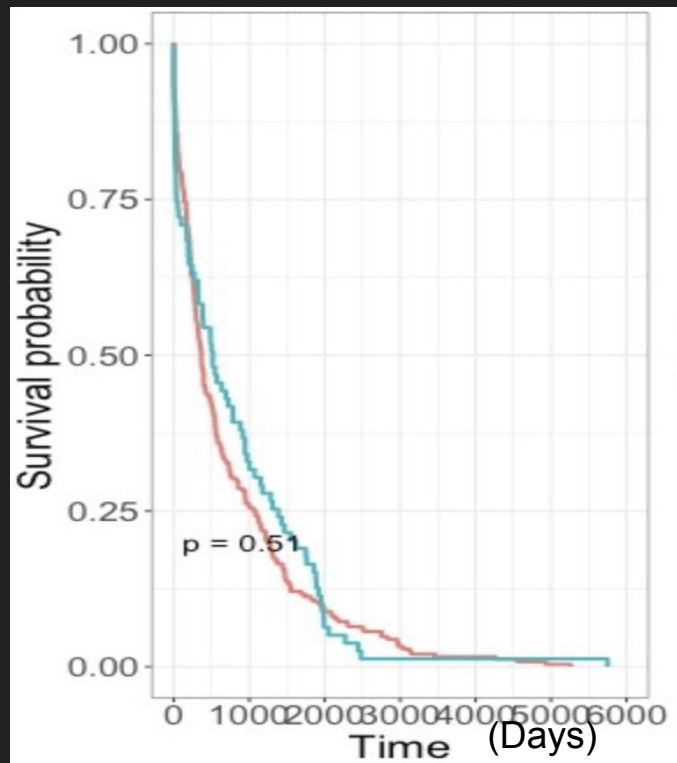
RED = TP53-

BLUE = TP53+

KM Plot Shows Non-Differential Survival for GATA3+ and PIK3CA+ Patients (Figs 5-6)



GATA3 (TP53-: 118; TP53+: 9)

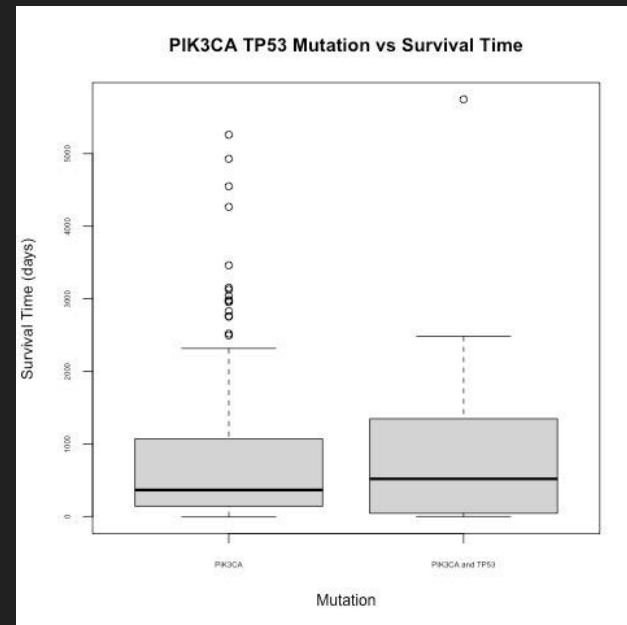
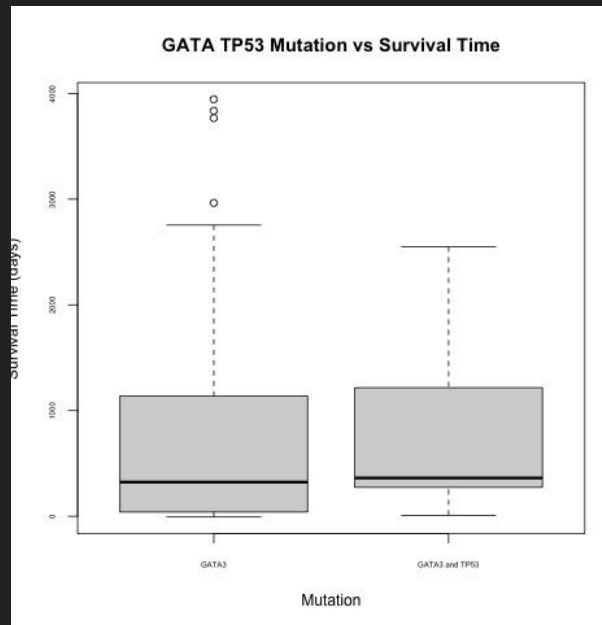
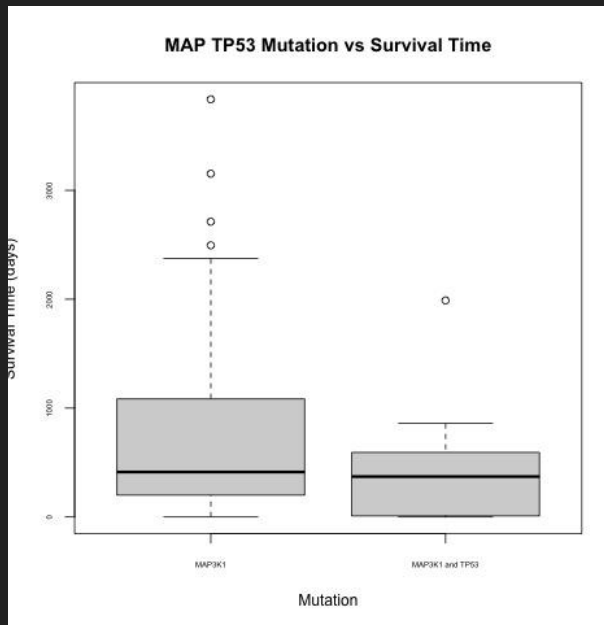


PIK3CA (TP53-: 289; TP53+: 79)

RED = TP53-

BLUE = TP53+

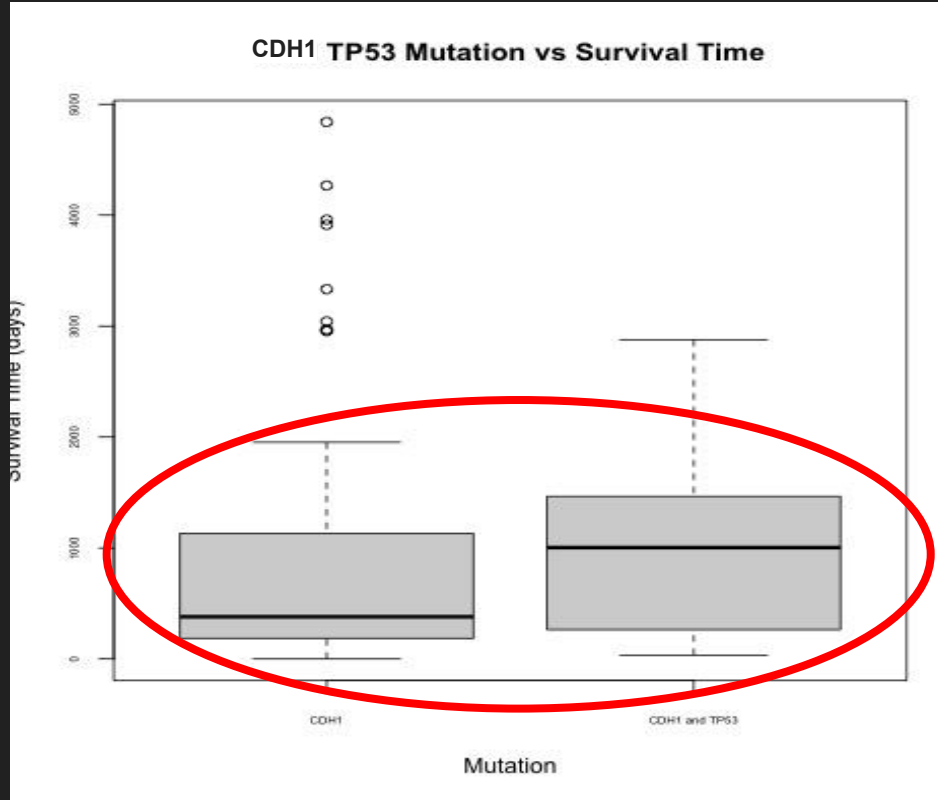
Survival Time Comparable for 3 Genes (Figures 7, 9, 10)



Left = Single Mutation

Right = TP53 Co-mutation

CDH1/TP53 Co-Mutation → Longer Survival (Fig 8)

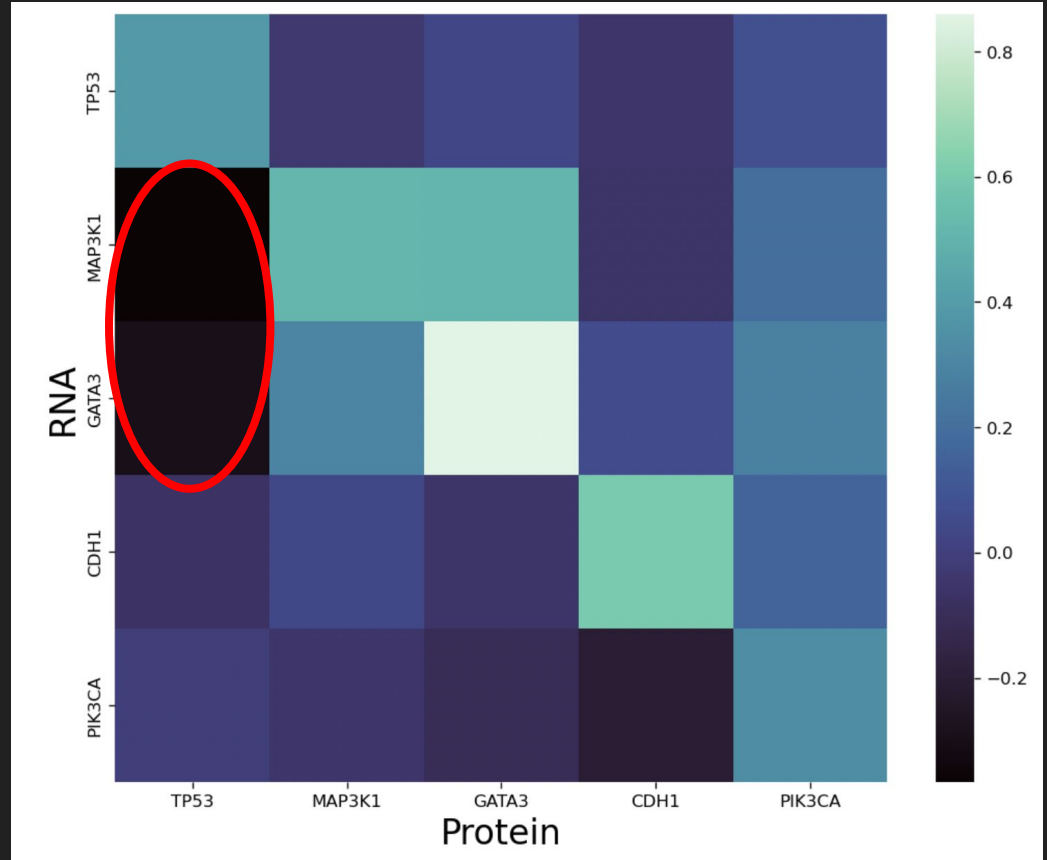


Left = Single Mutation

Right = TP53 Co-mutation

RNA/Protein Expression Heatmap (Fig 11)

Negative Relationship
between TP53 Protein &
GATA3/MAP3K1 RNA



Notable Takeaways

- TP53+/CDH1+ patients survival time > TP53-/CDH1+ patients in our dataset
 - These mutations are correlated with increase breast cancer risk (Shabnaz et al., 2015)
 - $P > 0.05$ for this finding, suggests potential statistical weakness
- Low presence of TP53 protein correlated with high expression of GATA3, MAP3K1 genes/RNA
 - Recent article (ovarian cancer) suggests GATA3 may cause apoptosis of TP53-producing cells (El-Arabey et al., 2022)

Future areas of study

- Consider the interactions between other genes (outside of the genes chosen for this study)
- Repeat this study on a bigger dataset (i.e. TCGA only contained ~1100 patients), might address the statistical significance issues

Why does this matter?

- Clinicians may push for more individualized treatments for patients with various combinations of mutated genes
- Understanding co-mutations' influence on survival may provide families with a loved one's prognosis

Works Cited

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Questions?