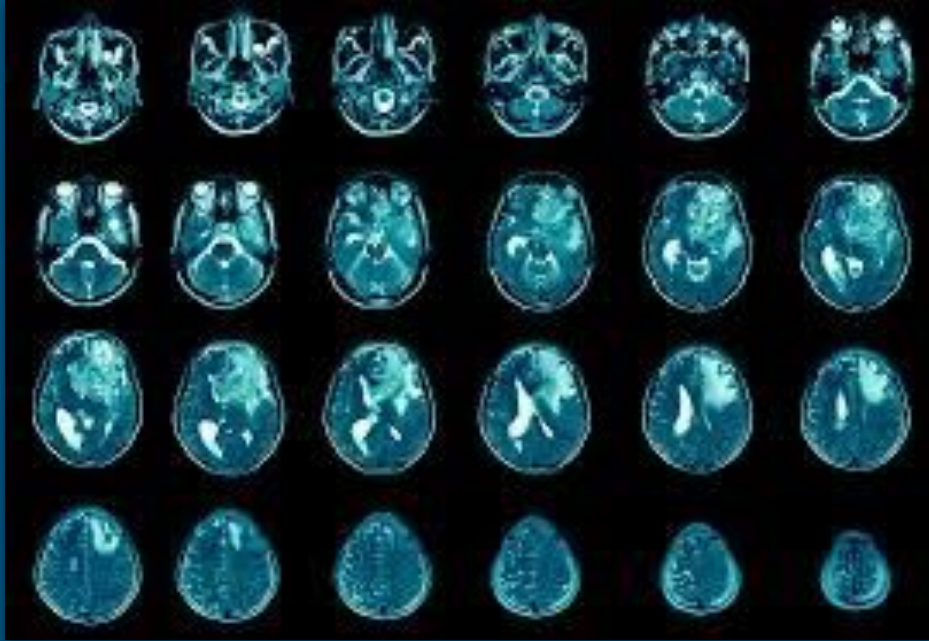


An Investigation into Glioblastoma Multiforme Survival

Kayla Xu, Joshua Gabbay, Jenna
Jacobs

Glioblastoma Multiforme (GBM)



The uncontrolled division of cells in the central nervous system

Kills 13,000 Americans annually

Risk factors:

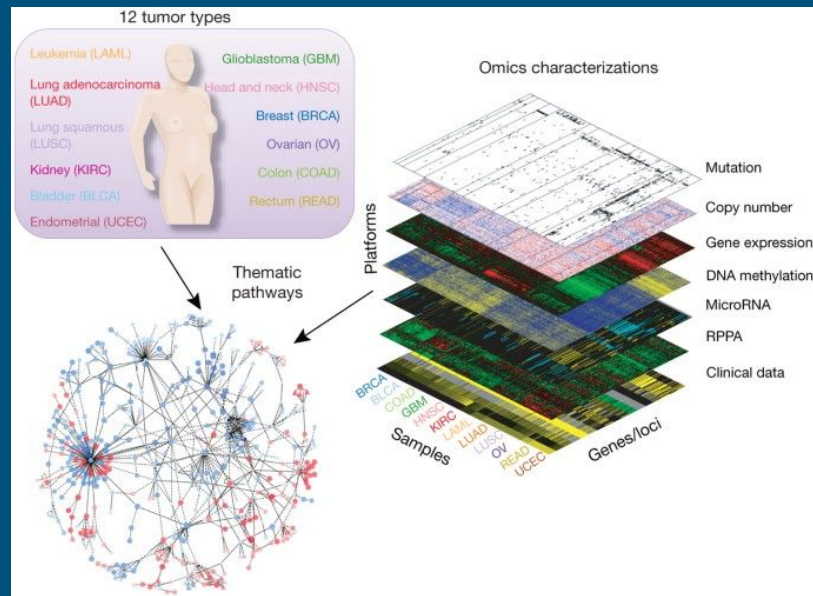
- Genetic
 - PTEN, EGFR, CDKN2A, CDH1
- Environmental
 - Radiation exposure

The Data

What is TCGA and how will we be using it?

What is CPTAC?

Analysing problems from a multi-omic perspective.

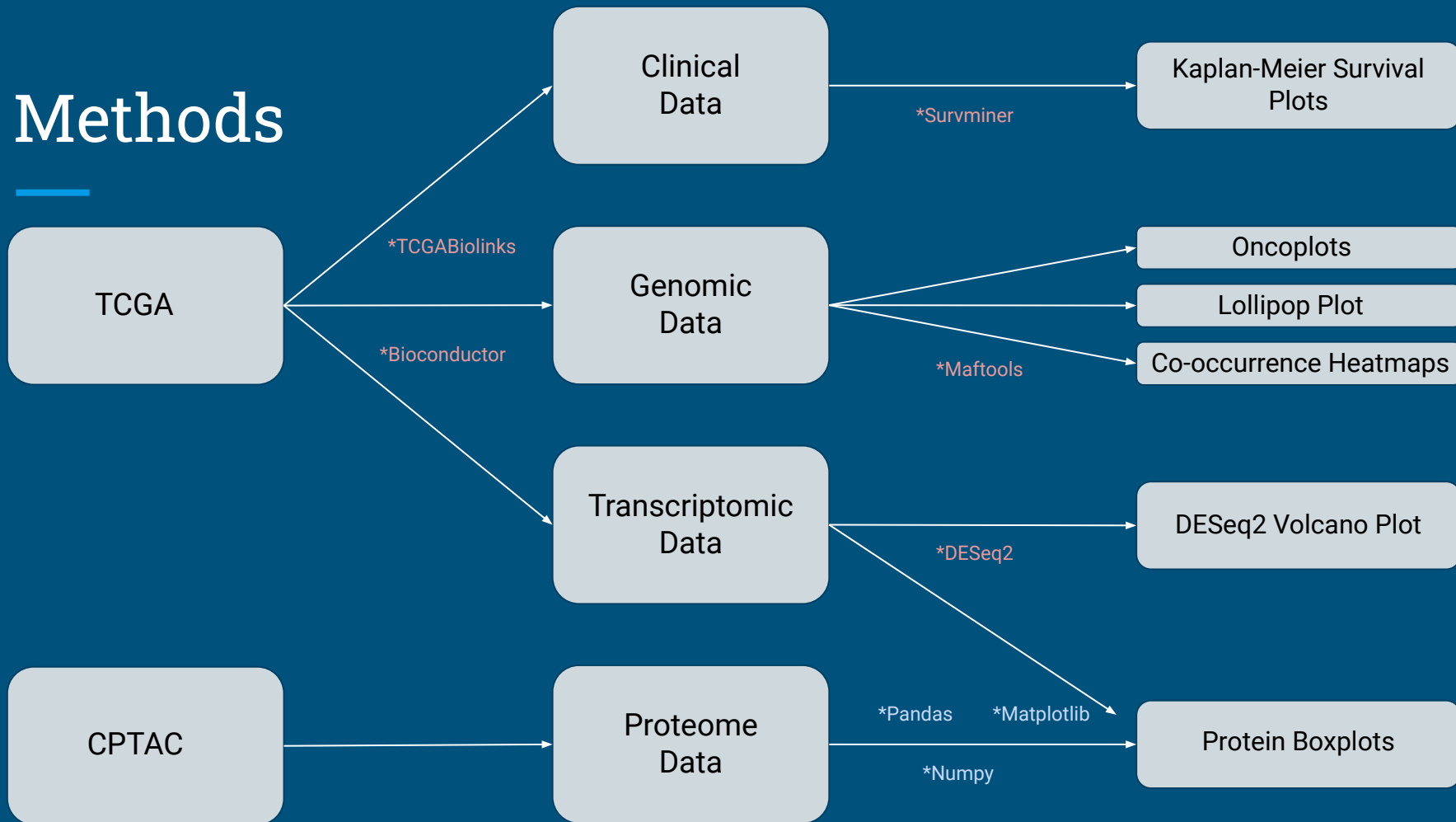


<https://www.nature.com/articles/ng.2764>

The Investigation

Hypothesis: There will be significant differences in genomic, transcriptomic, proteomic, and clinical profiles between surviving patients and non-surviving patients.

Methods

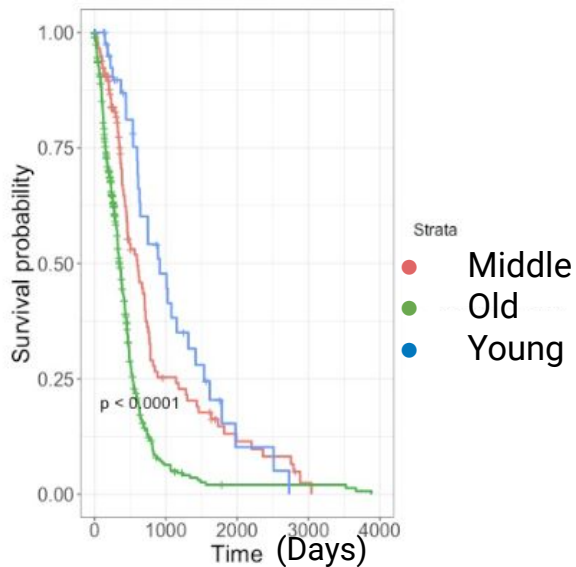


Dataset Breakdown

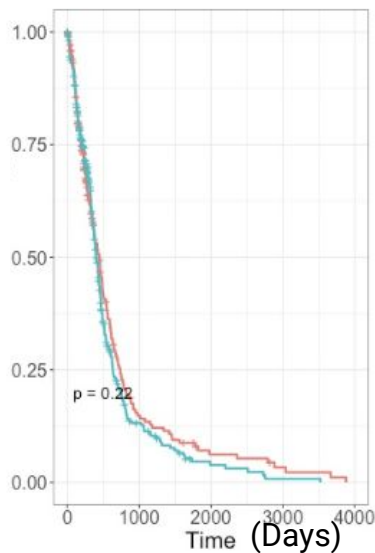
Age	Sex	Race
Old patients = 556	Male patients = 368	White patients = 509
Middle-aged patients = 119	Female patients = 231	Black patients = 52
Young patients = 44		Asian patients = 13

Kaplan-Meier plots show age and, possibly, race impact a patient's survival rate

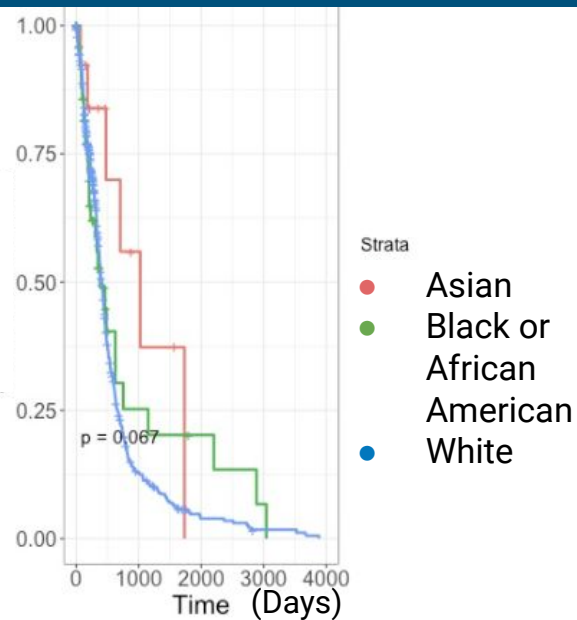
Figure 1. 1a: Age



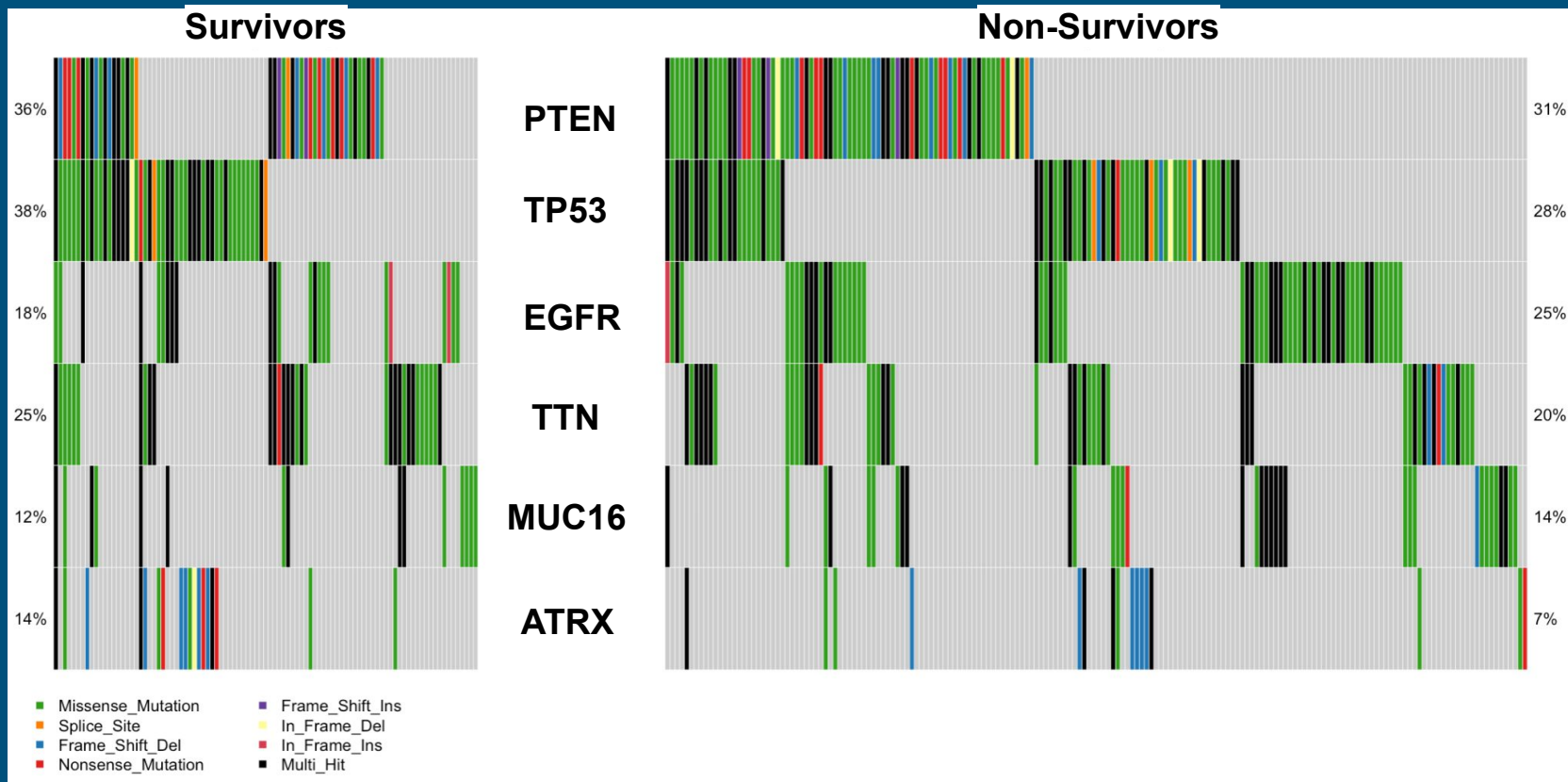
1b: Sex



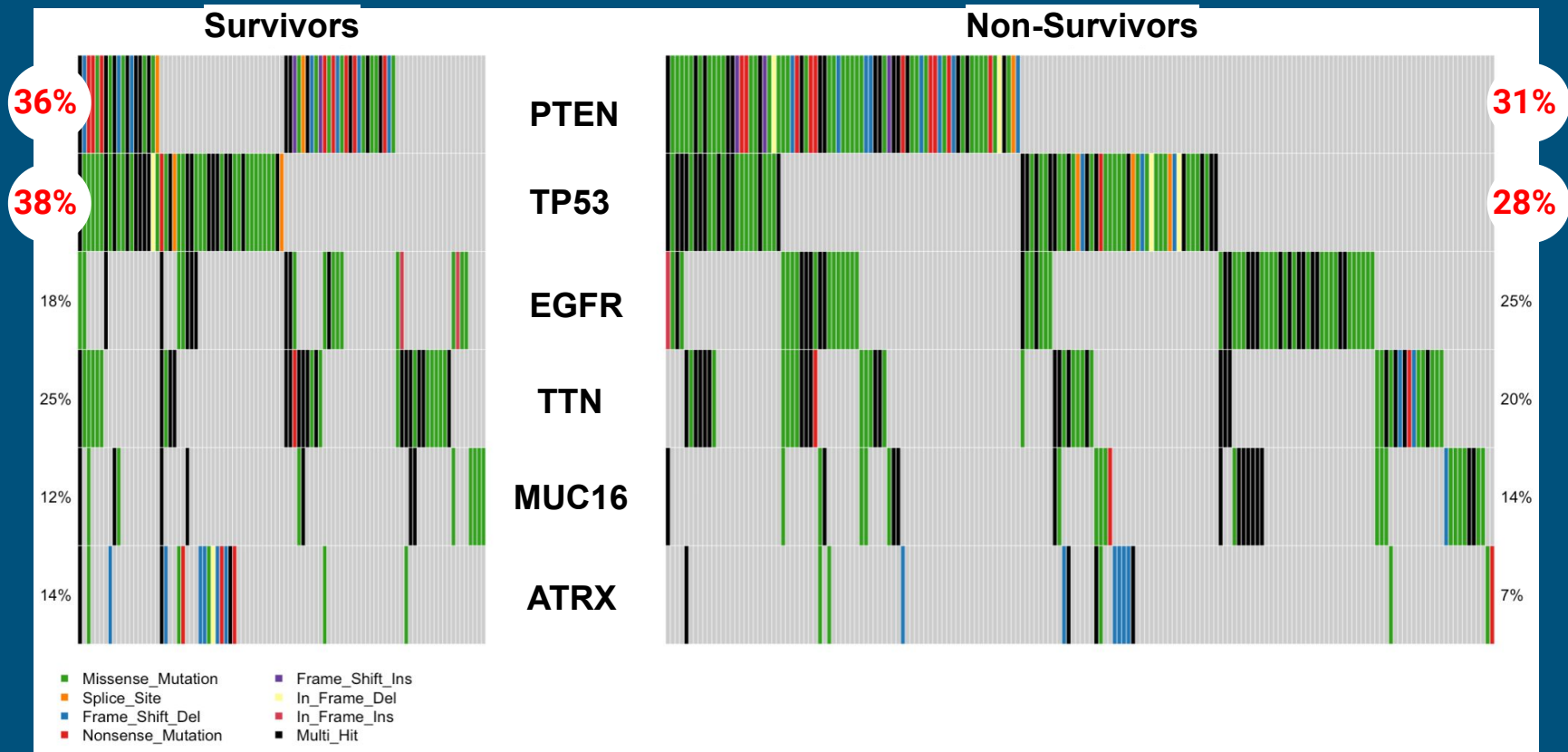
1c: Race



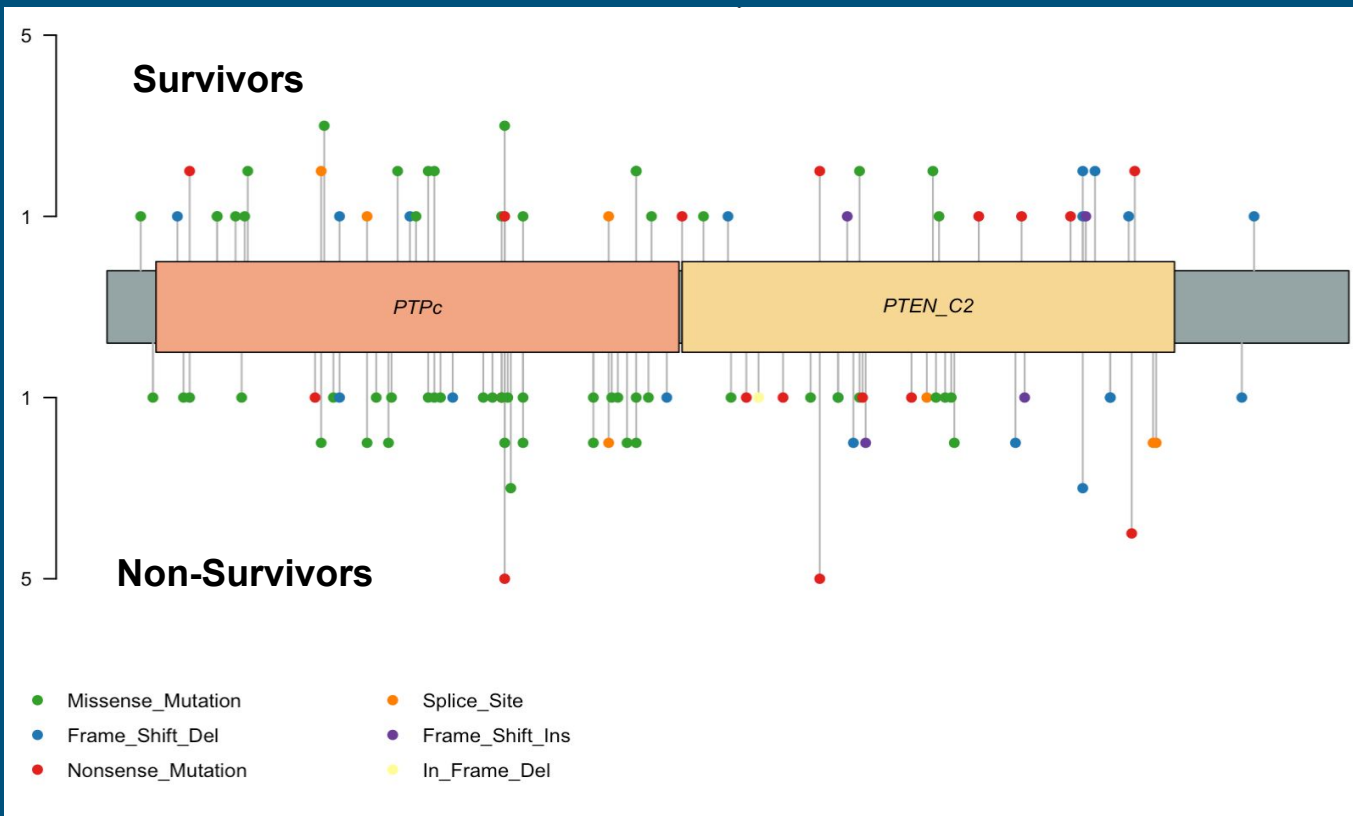
Oncoplots Between Survivors and Non-survivors



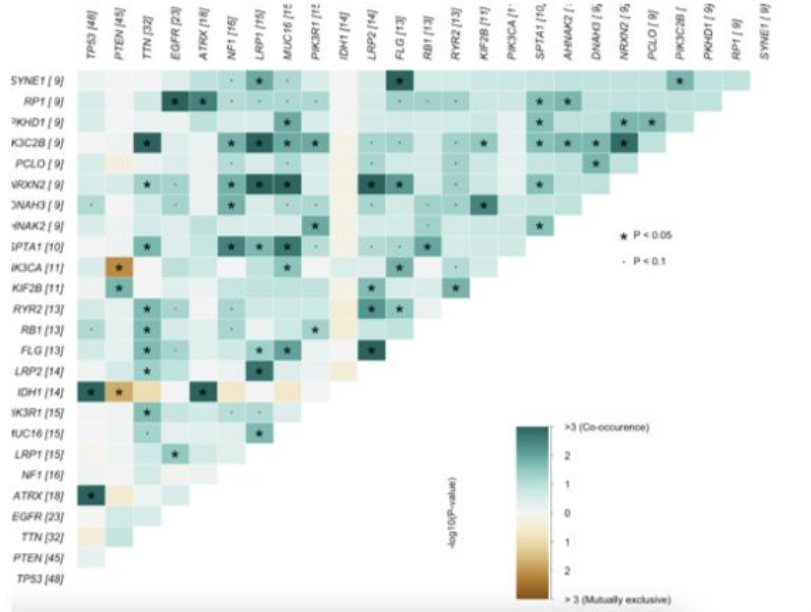
Oncoplots Between Survivors and Non-survivors



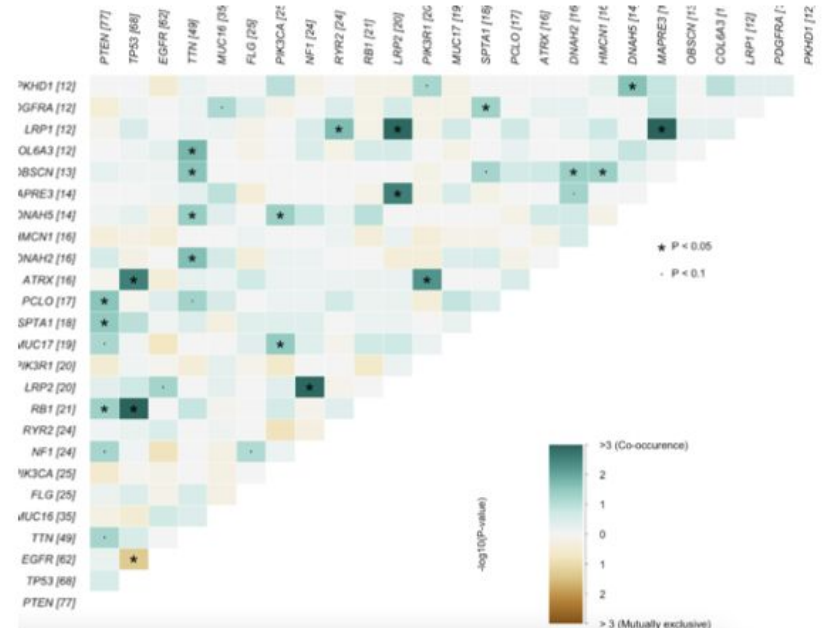
Gene Mutations: PTEN



Mutation Co-occurrence



Survivors

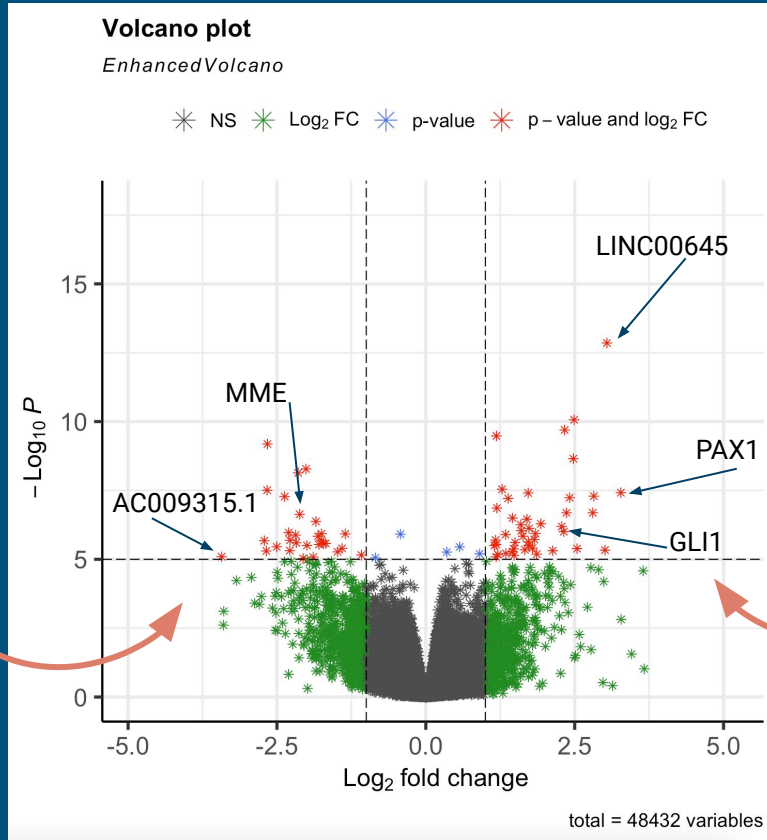


Non-Survivors

Volcano plot between survivors and non-survivors shows several upregulated genes in each group

- upregulation in non-survivors

- upregulation in survivors

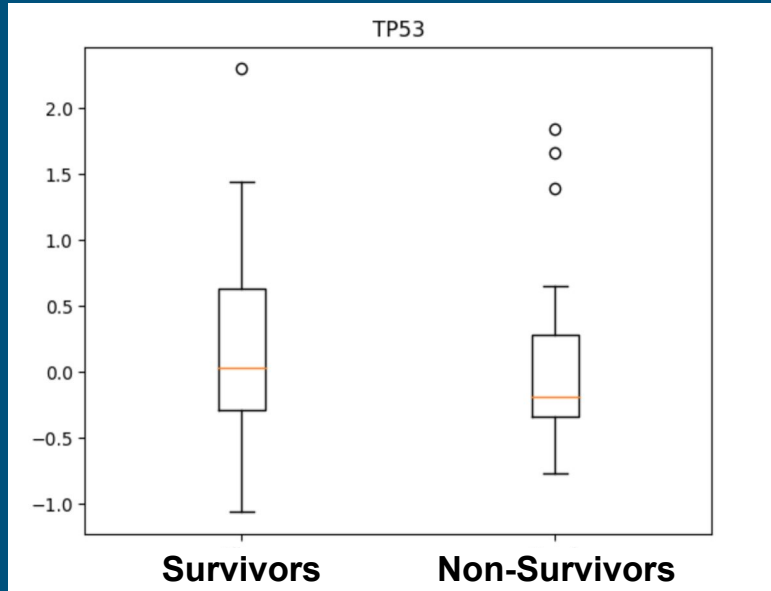


- Mostly non-coding RNAs
- Differences from oncoplots

Figure 5.

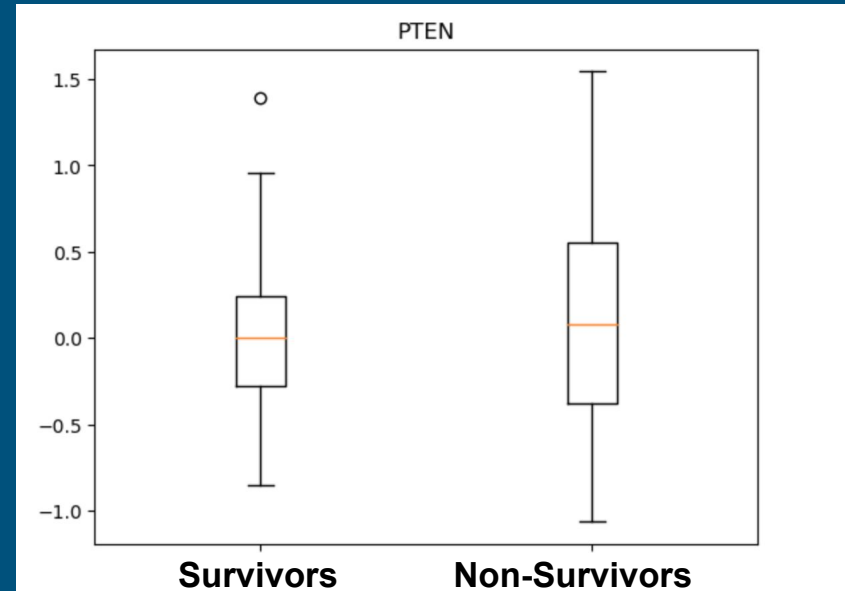
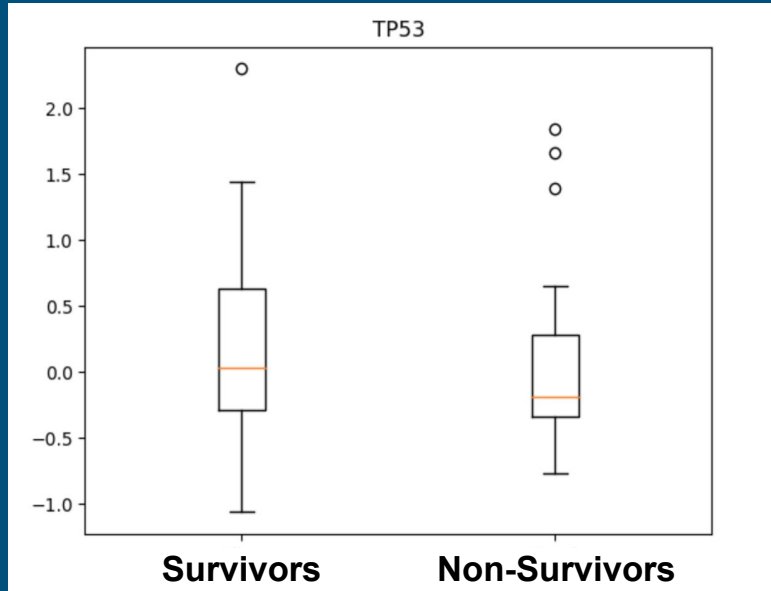
Protein Expression

For commonly mutated genes



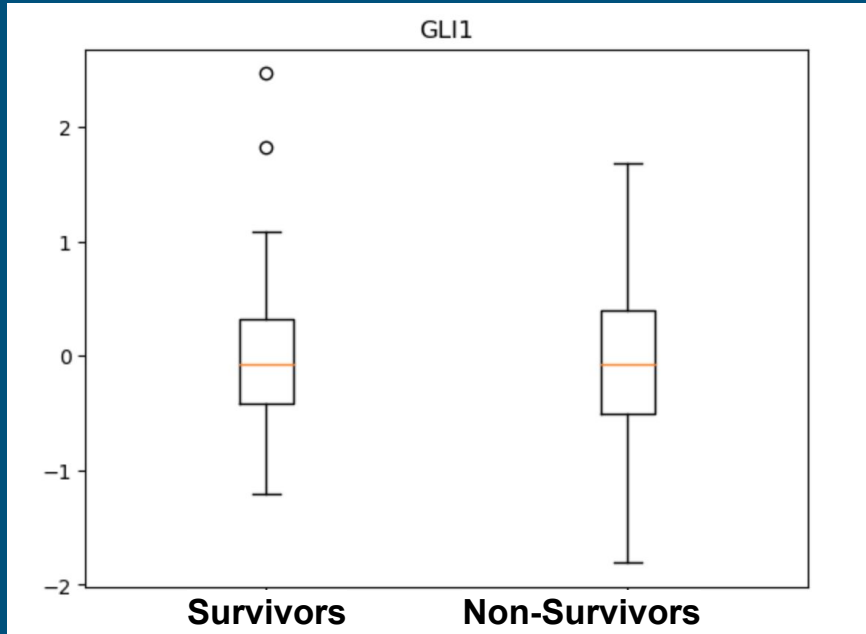
Protein Expression

For commonly mutated genes



Protein Expression

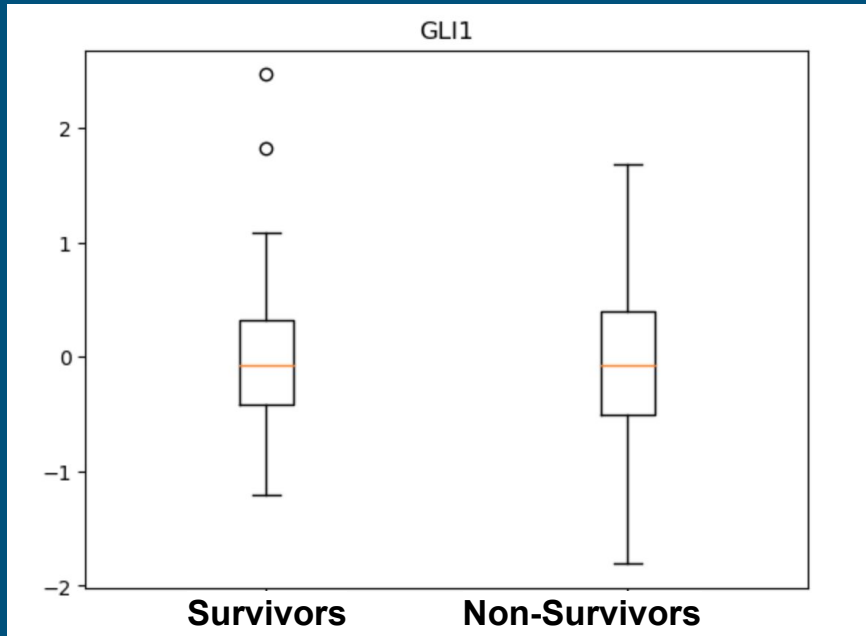
For differentially expressed RNA



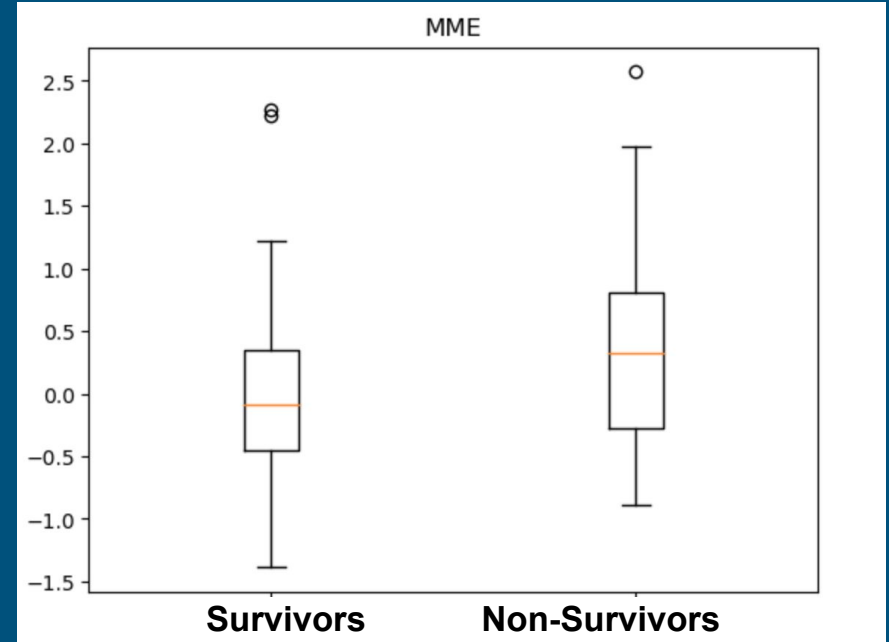
Survivor - upregulated

Protein Expression

For differentially expressed RNA



Survivor - upregulated



Non-Survivor - upregulated

Key Takeaways

- Differences between age and race
- Transcriptomic Differences -> non-coding RNAs
 - PAX1 and AC009315.1 importance
- Differences in mutations
 - PTEN PTPc domain
- Limited continuity between mutations, RNA, protein
 - Exception: MME

Moving Forwards

Non-coding upregulated gene

-(LINC00645)

Demographics and survivals

-African-American/Black and Asian patients

Larger sample size

Works Cited

Angelopoulou, Efthalia, et al. "Emerging Pathogenic and Prognostic Significance of Paired Box 3 (PAX3) Protein in Adult Gliomas." *Translational Oncology*, vol. 12, no. 10, 2019, pp. 1357–1363.,

<https://doi.org/10.1016/j.tranon.2019.07.001>.

Avery, Justin T., et al. "GLI1: A Therapeutic Target for Cancer." *Frontiers in Oncology*, vol. 11, 2021, <https://doi.org/10.3389/fonc.2021.673154>.

"The Cancer Genome Atlas (TCGA)." *Genome.gov*, <https://www.genome.gov/Funded-Programs-Projects/Cancer-Genome-Atlas>.

Förster, Alisa, et al. "Rare germline variants in the E-cadherin gene *CDH1* are associated with the risk of brain tumors of neuroepithelial and epithelial origin." *Acta Neuropathologica*, vol. 142, 2021, pp. 191-210.,

<https://doi.org/10.1007/s00401-021-02307-1>

Gan, Hui K et al. "The epidermal growth factor receptor variant III (EGFRvIII): where wild things are altered." *The FEBS journal* vol. 280,21 (2013): 5350-70. doi:10.1111/febs.12393

Li, C., Zheng, H., Hou, W. et al. Long non-coding RNA linc00645 promotes TGF- β -induced epithelial–mesenchymal transition by regulating miR-205-3p-ZEB1 axis in glioma. *Cell Death Dis* 10, 717 (2019).

<https://doi.org/10.1038/s41419-019-1948-8>

Lin, Dongdong, et al. "Trends in Intracranial Glioma Incidence and Mortality in the United States, 1975-2018." *Frontiers in Oncology*, vol. 11, 2021, <https://doi.org/10.3389/fonc.2021.748061>.

Nguyen, Ha S et al. "Molecular Markers of Therapy-Resistant Glioblastoma and Potential Strategy to Combat Resistance." *International journal of molecular sciences* vol. 19,6 1765. 14 Jun. 2018, doi:10.3390/ijms19061765

Rasheed, Sumbal, et al. "An Insight into the Risk Factors of Brain Tumors and Their Therapeutic Interventions." *Biomedicine & Pharmacotherapy*, vol. 143, 2021, p. 112119., <https://doi.org/10.1016/j.biopha.2021.112119>.

Shen, Yaoqing, et al. "Comprehensive Genomic Profiling of Glioblastoma Tumors, Btics, and Xenografts Reveals Stability and Adaptation to Growth Environments." *Proceedings of the National Academy of Sciences*, vol. 116, no. 38, 2019,

pp. 19098–19108., <https://doi.org/10.1073/pnas.1813495116>.

Wang, Haiwei, et al. "Analysis of the EGFR Amplification and CDKN2A Deletion Regulated Transcriptomic Signatures Reveals the Prognostic Significance of spats2l in Patients with Glioma." *Frontiers in Oncology*, vol. 11, 2021,

<https://doi.org/10.3389/fonc.2021.551160>.

Yang, Jr-M, et al. "Characterization of PTEN Mutations in Brain Cancer Reveals That PTEN Mono-Ubiquitination Promotes Protein Stability and Nuclear Localization." *Oncogene*, vol. 36, no. 26, 2017, pp. 3673–3685.,

<https://doi.org/10.1038/onc.2016.493>.



Thank You For Listening



Questions?

