

C³ Cancer Clustering Collaborative

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<https://github.com/SVAI/C3>



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Aims

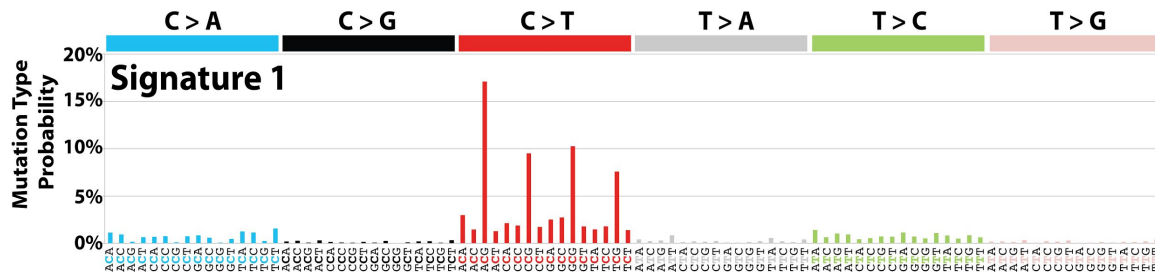
NF2 is a rare benign cancer characterized by NF2 gene mutations.

- Find a subset of well studied cancers that are biologically similar to the NF2 patient
- Suggest treatments based on existing therapeutics in well known tumors

Approach

Two data sources:

- Provided VCF
- TCGA brain cancers



Features:

- [mutational signatures](#) : indicate biological processes causing mutations in the genome
- GO Terms of mutated genes : indicate functional changes in the tumor

Methods:

- Counting trinucleotide changes (e.g. AAA > ATA) and extracting known mutational signatures (deconstructSigs R package)
- Dimensionality reduction and clustering all cancers (PCA + k-means)

Results: VCF processing to filter mutations

Criteria:

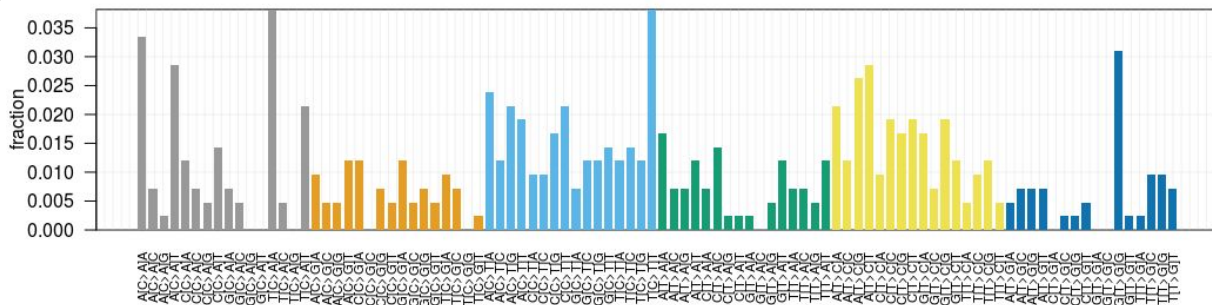
- Variant quality score > 30
- > 15 reads supporting the alternate allele
- Variant not present in the normal (blood) tissue

9.6K mutations

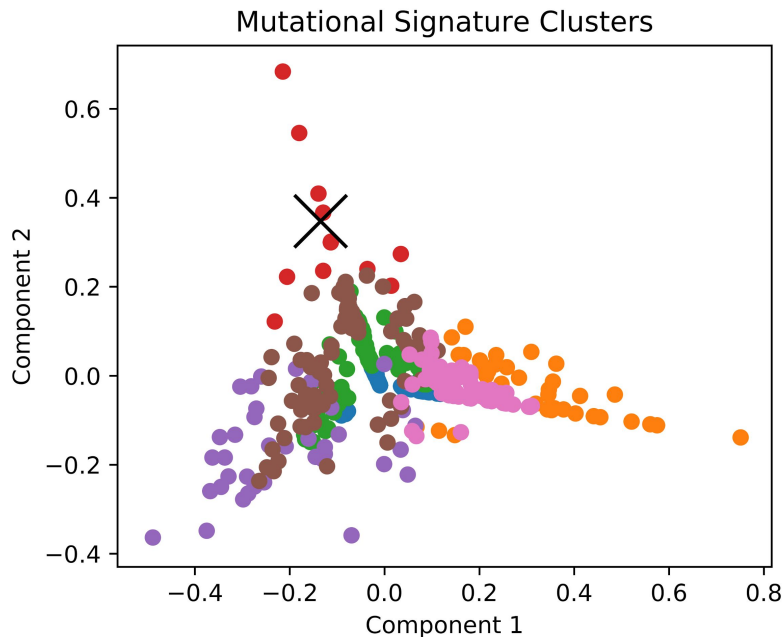
229 protein coding mutations

43 mutated genes

Onno's mutational pattern

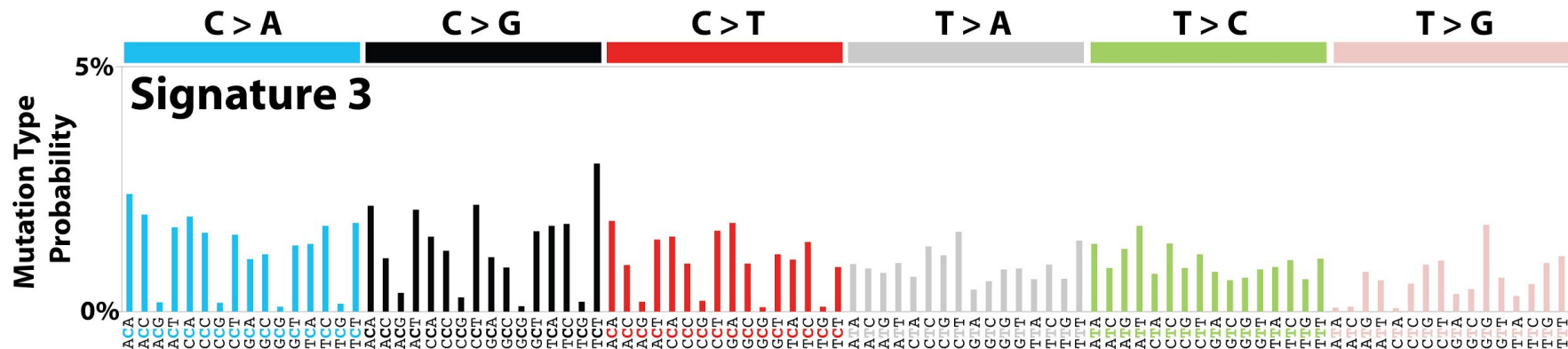


Results: Clustering of Mutation Signatures



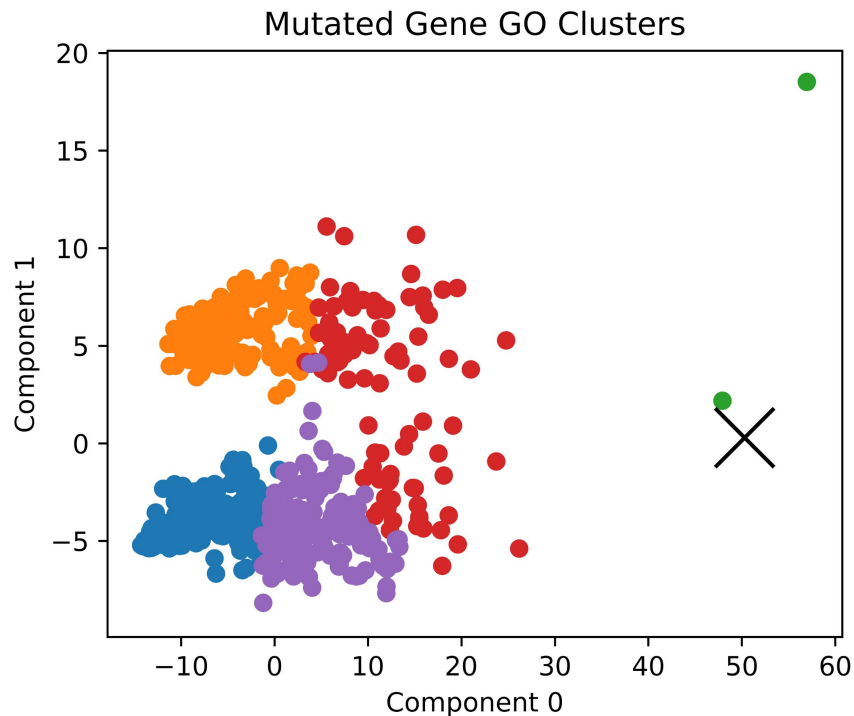
- 7 clusters of brain cancer based on mutational signatures
- Onno's tumor maps to the least populated cluster
- Mostly glioblastoma
- Have Signature 3

Results: Signature 3



- Found in hereditary (BRCA+) breast cancers
- Defective in homologous repair pathway
- Can be treated by PARP inhibitors

Results: Functional Clustering



- 5 clusters based on functions of mutated genes
- Onno's tumor is a clear outlier to known brain cancers

Future Directions

Broaden: Extend analysis to non-brain cancers

Deepen: Examine similarity of Onno to other patients assigned to the same cluster

Explore: Possible therapeutics. Mutational characteristics of Onno's tumor are similar to BRCA+ breast cancer with well known therapeutics.