

Elucidating tumor evolutionary patterns using high- depth molecular data

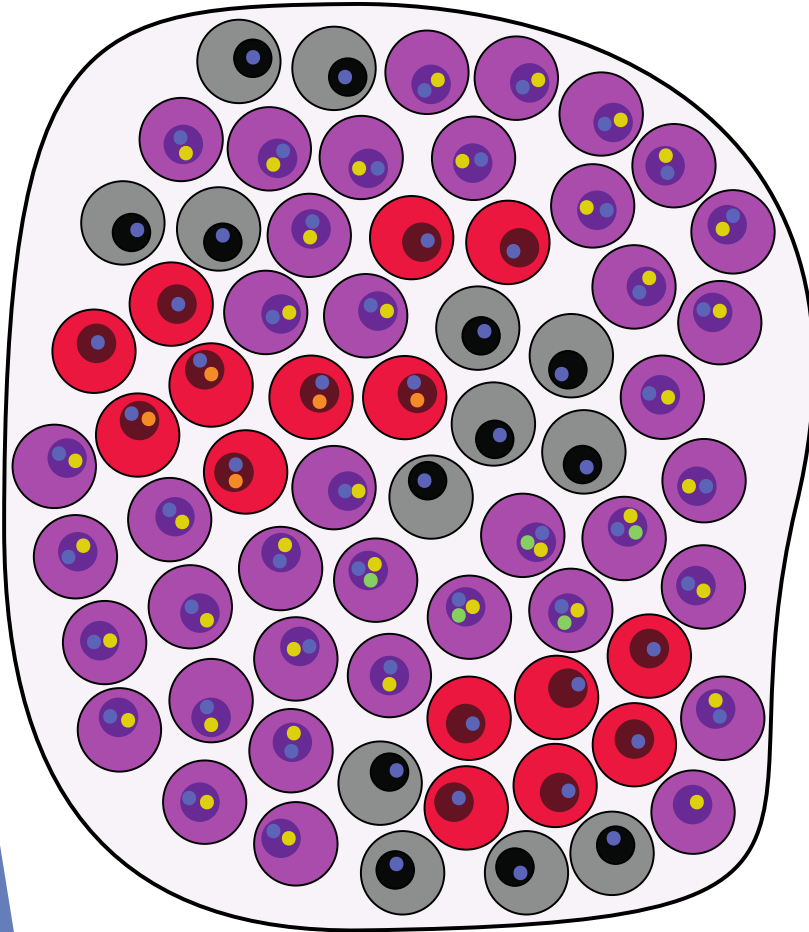
Caitlin Guccione

Mentor: Dr. Hossein Khiabani

Background on Research

- ▶ Tumor
 - ▶ Abnormal growth of tissue
 - ▶ Focus on cancerous growths
- ▶ Cancer
 - ▶ A genetic disease
 - ▶ A mutation in DNA that leads to cells dividing without control and other cellular processes breaking down
- ▶ Evolution of Cancer Cells
 - ▶ **Do they follow normal patterns of cellular evolution?**
- ▶ High Depth Molecular Data
 - ▶ A closer look at sequencing data from DNA, specifically in cancer tumors

High-depth clinical DNA sequencing



Tumor purity of 58%



Non-tumor stromal cell; 19%



Clone 1, mutated tumor cell; 51%



Clone 2, mutated tumor cell; 7%



Non-tumor hematopoietic cell; 15%



Heterozygous germline variant; VAF = 50%

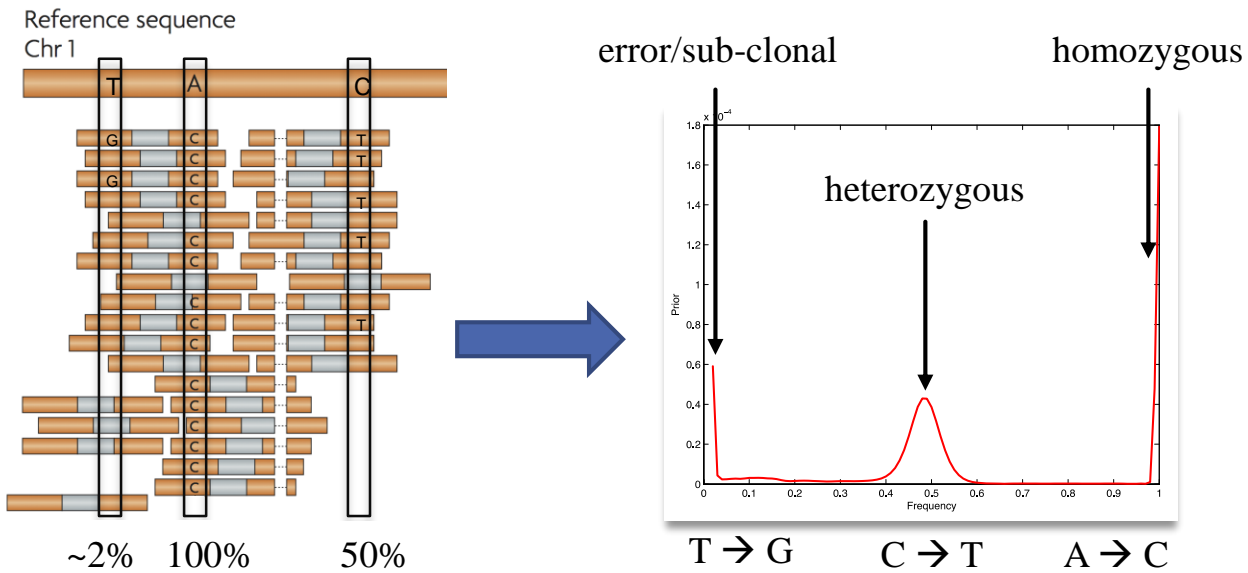


Heterozygous somatic variant; VAF = 29%

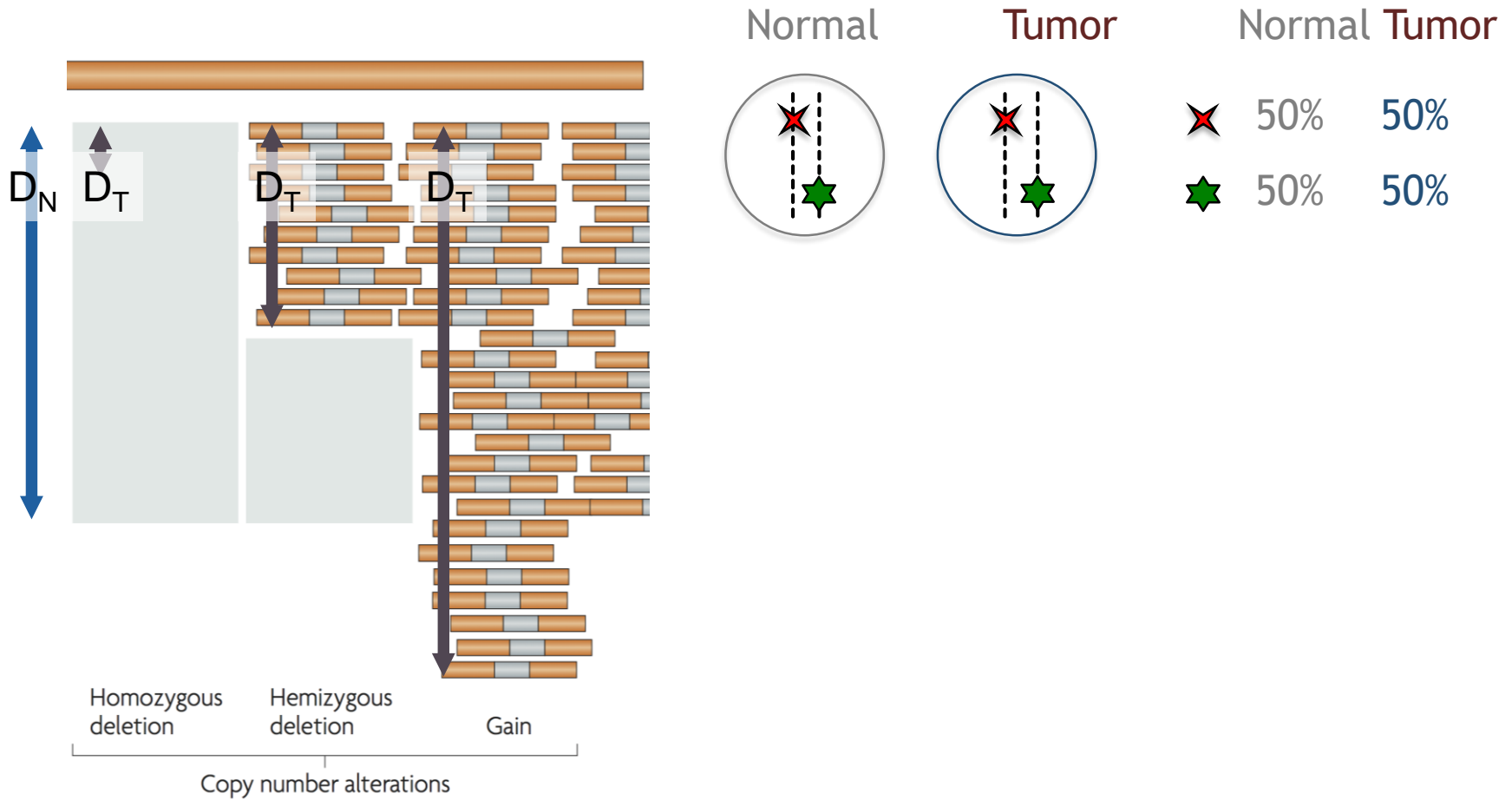


Heterozygous somatic variant; VAF = 3.5%

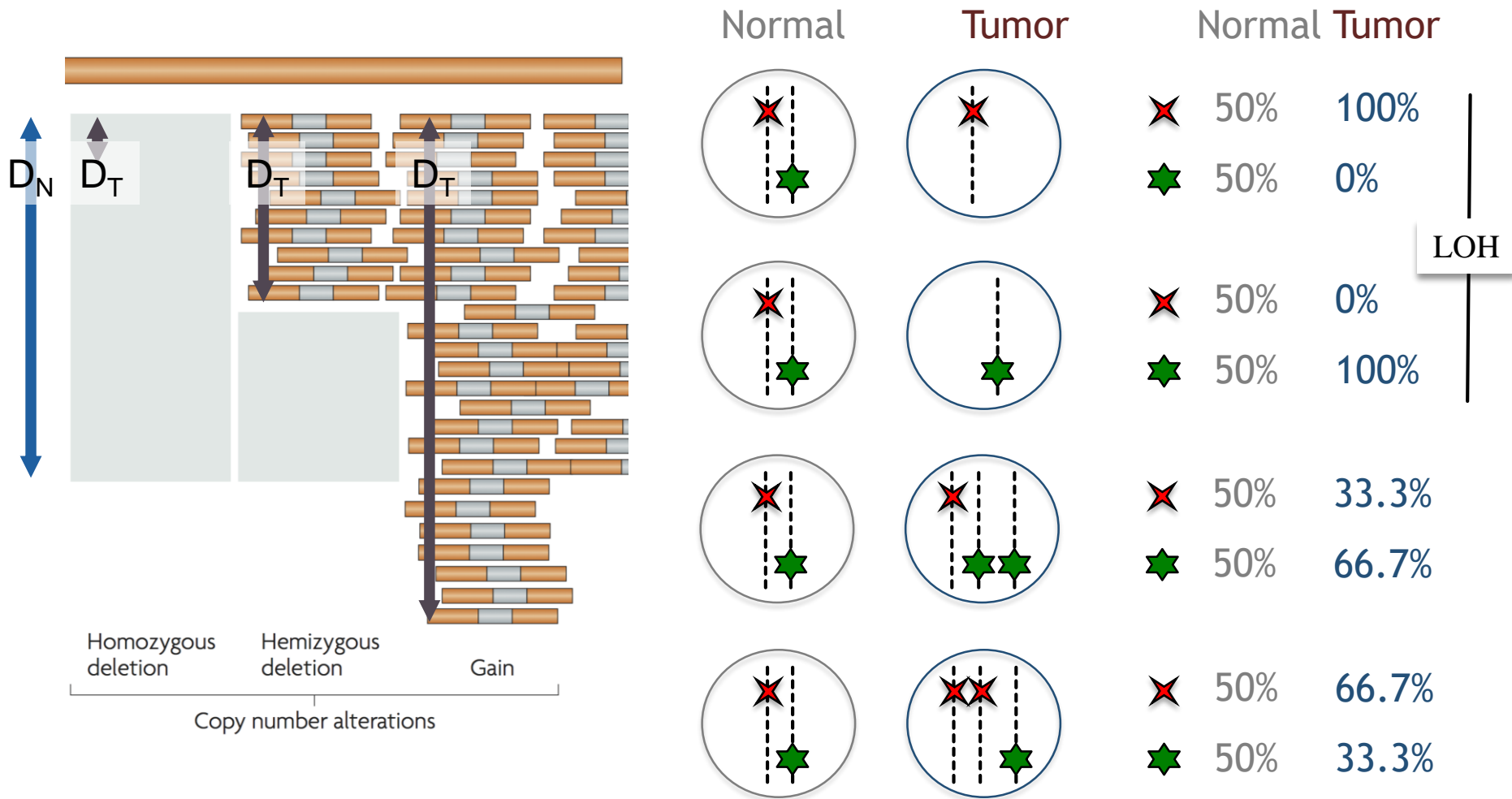
Confidence in variant allele frequency (VAF) estimates



Effect of copy number changes on variants



Effect of copy number changes on variants



Modeling mutational status

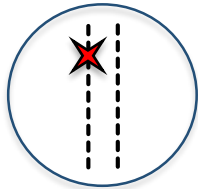
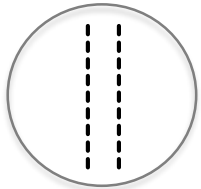
Somatic mutation

Normal

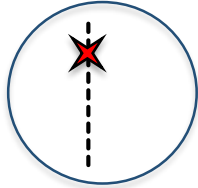
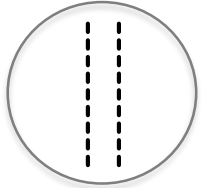
Tumor

$1-p$

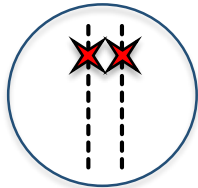
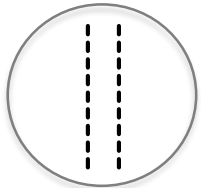
p



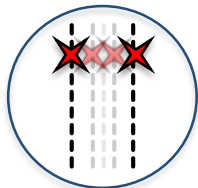
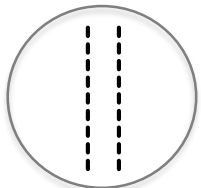
$$\langle \text{VAF} \rangle = \frac{p}{2}$$



$$\langle \text{VAF} \rangle = \frac{p}{2-p}$$



$$\langle \text{VAF} \rangle = p$$



$$\langle \text{VAF} \rangle = \frac{c_{\text{mut}}p}{2(1-p) + Yp}$$

Modeling mutational status

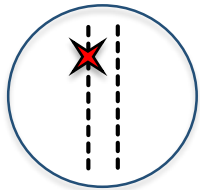
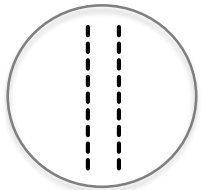
Somatic mutation

Normal

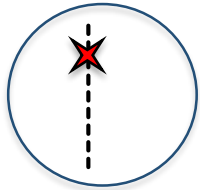
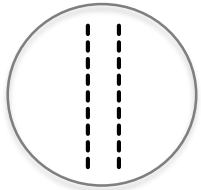
Tumor

$1-p$

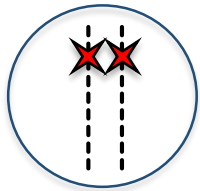
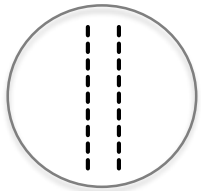
p



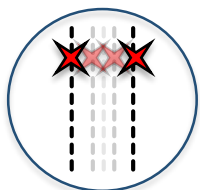
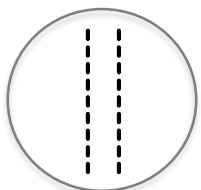
$$\langle \text{VAF} \rangle = \frac{p}{2}$$



$$\langle \text{VAF} \rangle = \frac{p}{2-p}$$



$$\langle \text{VAF} \rangle = p$$



$$\langle \text{VAF} \rangle = \frac{c_{\text{mut}}p}{2(1-p) + Yp}$$

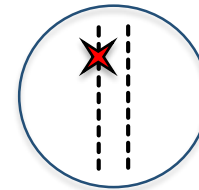
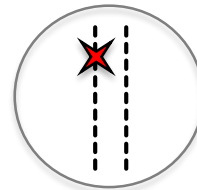
Germline mutation

Normal

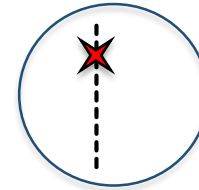
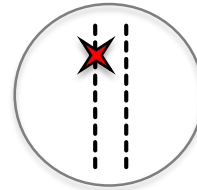
Tumor

$1-p$

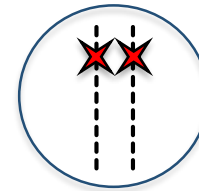
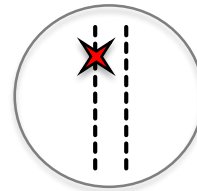
p



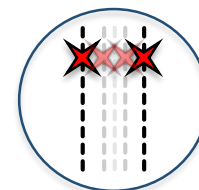
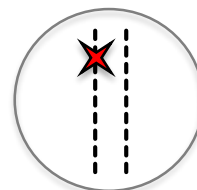
$$\langle \text{VAF} \rangle = \frac{1}{2}$$



$$\langle \text{VAF} \rangle = \frac{1}{2-p}$$

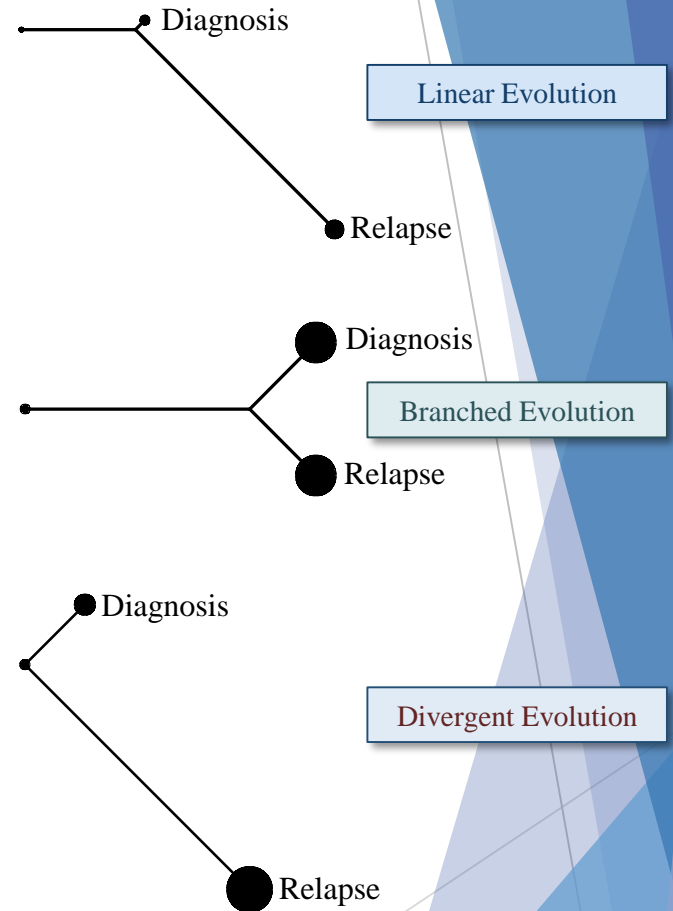
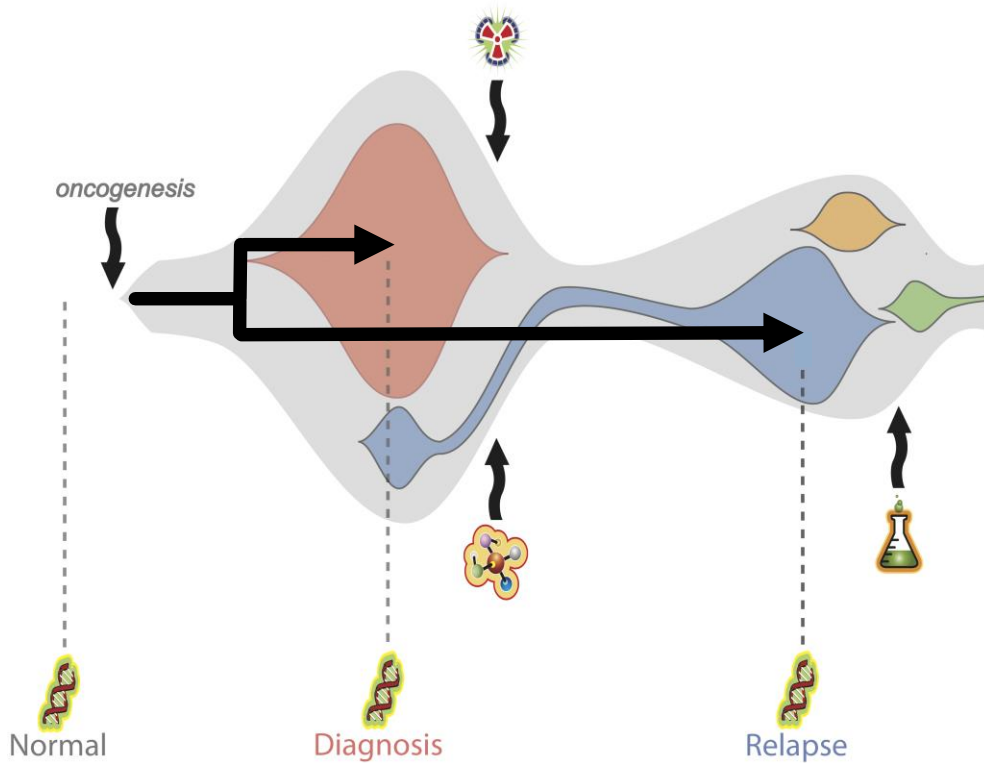


$$\langle \text{VAF} \rangle = \frac{1+p}{2}$$



$$\langle \text{VAF} \rangle = \frac{(1-p) + c_{\text{mut}}p}{2(1-p) + Yp}$$

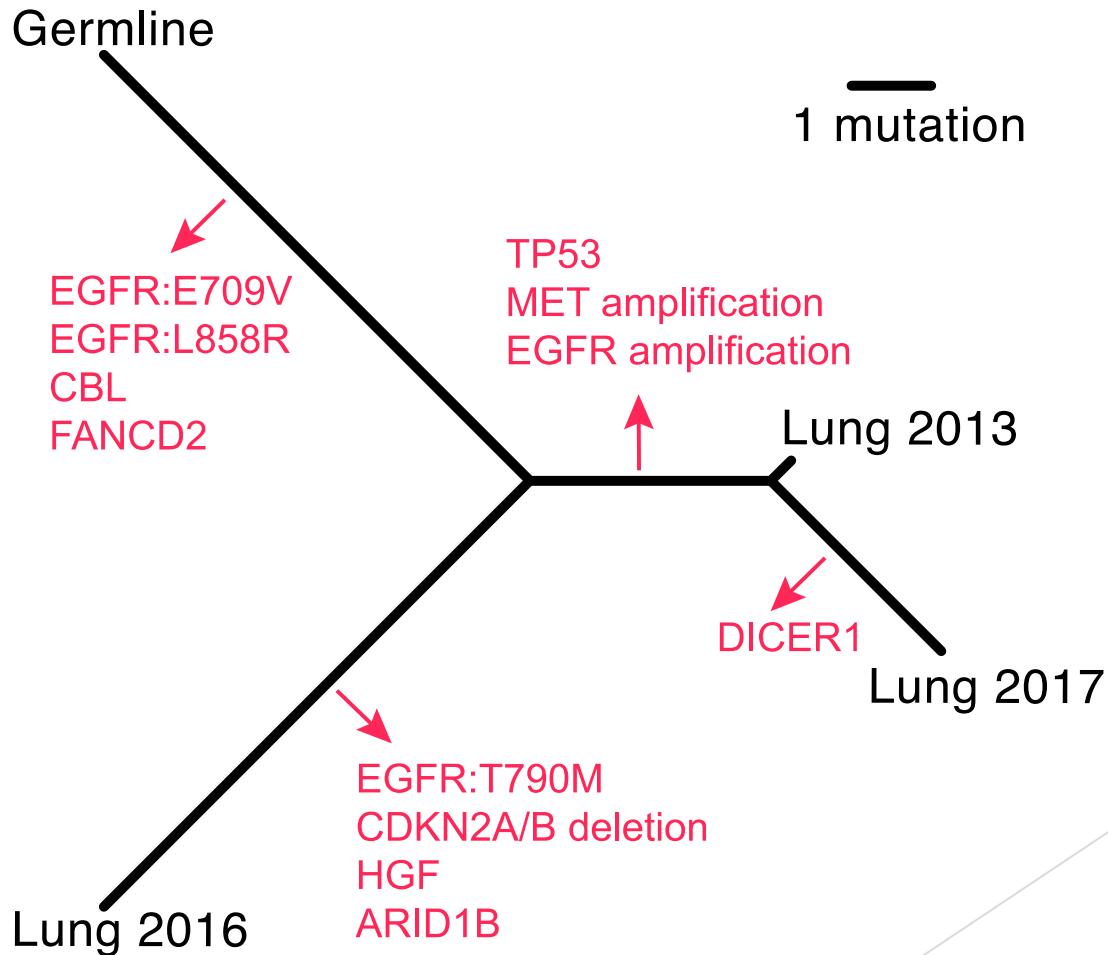
Evolution of tumor from diagnosis to relapse



- A **phylogenetic tree** that relates the genomic information at remission, diagnosis, and relapse shows the molecular history of each relapsed tumor.

Evolution of tumor from diagnosis to relapse

- Evolution of a patient under treatment



Goals for the Summer

1. Get a better understanding of all the biology that ties into the project
2. Determine an efficient way to organize the trees of 300 patients
3. Discover patterns within the trees that could lead to a better understanding of cancer cell evolution
4. Learn more graph theory and phylogenetic analysis to be able to manipulate the trees easily

Works Cited

Khiabani et al, JCO Precision Oncology 2018

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