



# BIMM 143

## Cancer Genomics & Immunoinformatics

Lecture 18

Barry Grant  
UC San Diego

<http://thegrantlab.org/bimm143>

# Today's Menu

## Cancer Genomics

Brief review of cancer fundamentals,  
What is cancer and what causes it?

## Mining Cancer Genomic Data

**Hands-on analysis** to identify genomic  
changes in different cancers and identify  
new targets for therapy

## Towards personalized cancer treatments

Recap on how the immune system normally  
detects cancer cells and how we can predict  
mutations that can be recognized by T cells

## Cancer Immunoinformatics

**Hands-on analysis** to design personalized  
cancer vaccines

# What is Cancer?

“Cancer is a name given to a collection of related diseases, where some of the body’s cells begin to divide without stopping and spread into surrounding tissue”

Source: <https://www.cancer.gov>

It is estimated that cancer will strike 40% of people at some point in their lifetime with frequently devastating effects.

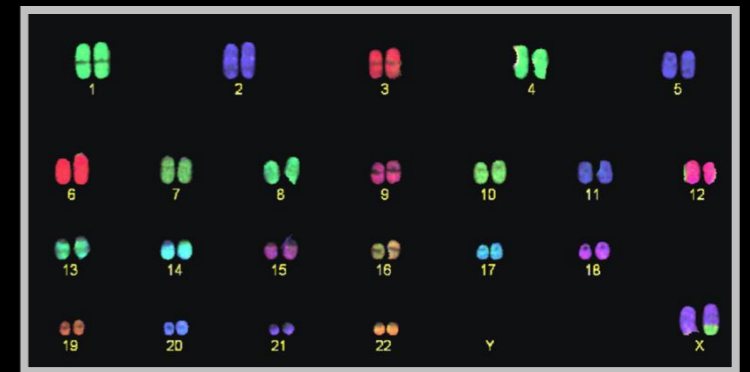
# What is Cancer?

“Cancer is a name given to a collection of related diseases, where some of the body’s cells begin to divide without stopping and spread into surrounding tissue”

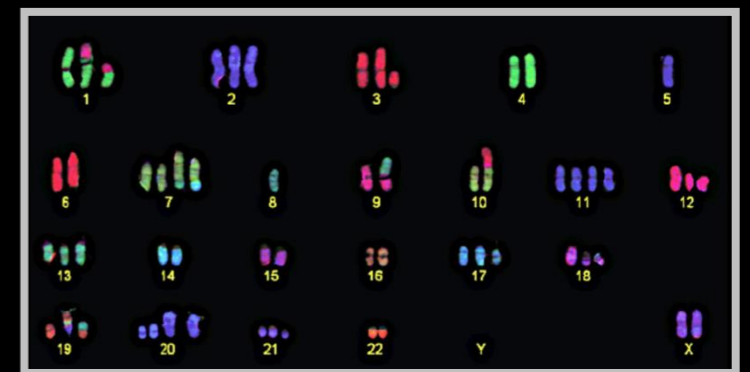
Source: <https://www.cancer.gov>

# Cancer is a disease of the Genome

- Caused by changes to genes that control the way our cells function, especially how they **grow and divide**.
- A major challenge in treating cancer is that every tumor is different: Each person's cancer has a unique combination of genetic changes (both “driver” & “passenger”).
- As the cancer continues to grow, additional changes will occur.



**Healthy 46  
chromosomes**



**Example cancer 59  
chromosomes**

# Goals of Cancer Genome Research

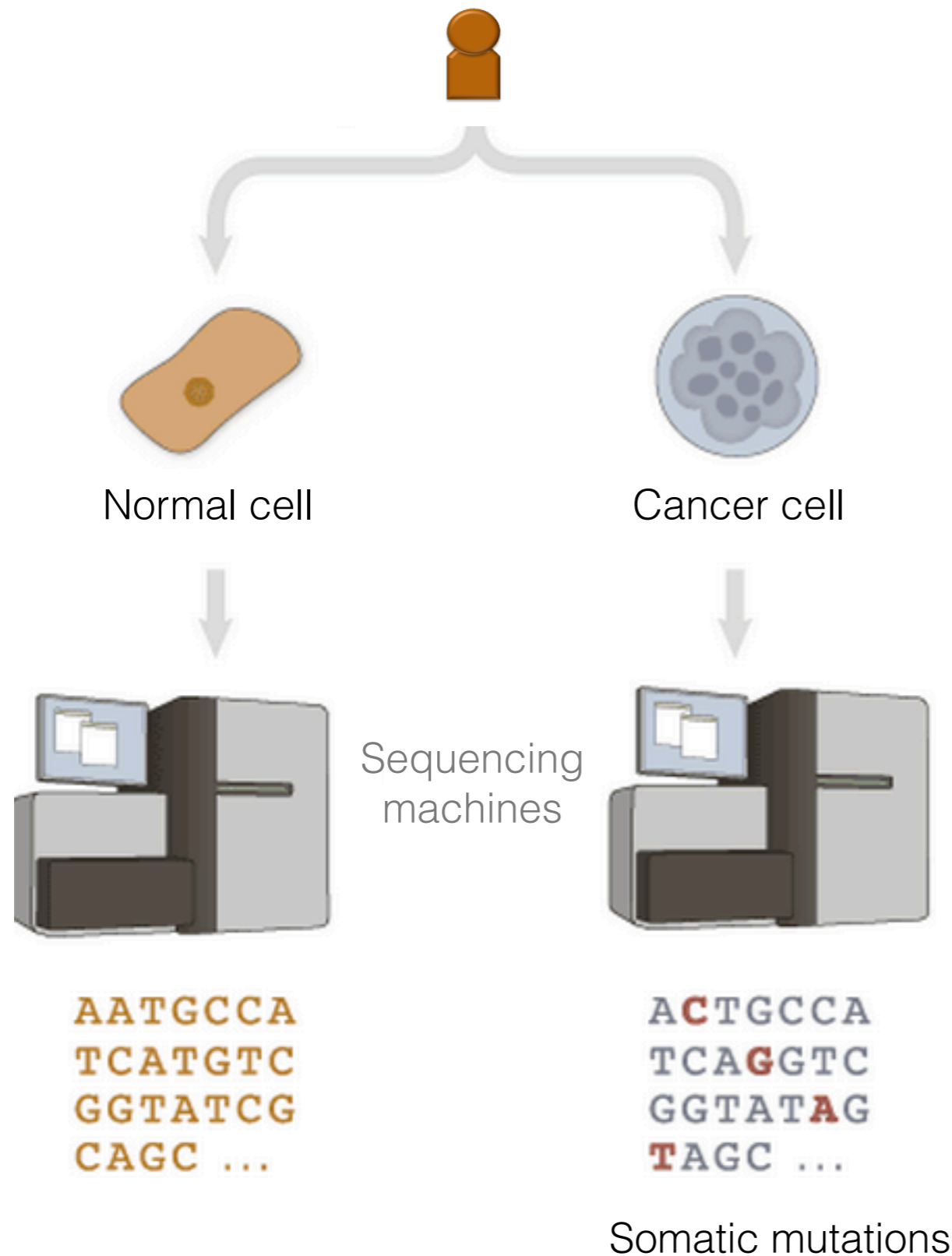
- Identify changes in the genomes of tumors that drive cancer progression
- Identify new targets for therapy
- Select drugs based on the genomics of the tumor
- Provide early cancer detection and treatment response monitoring
- Utilize cancer specific mutations to derive neoantigen immunotherapy approaches



# Finding Cancer Drivers



# Finding Cancer Associated Mutations



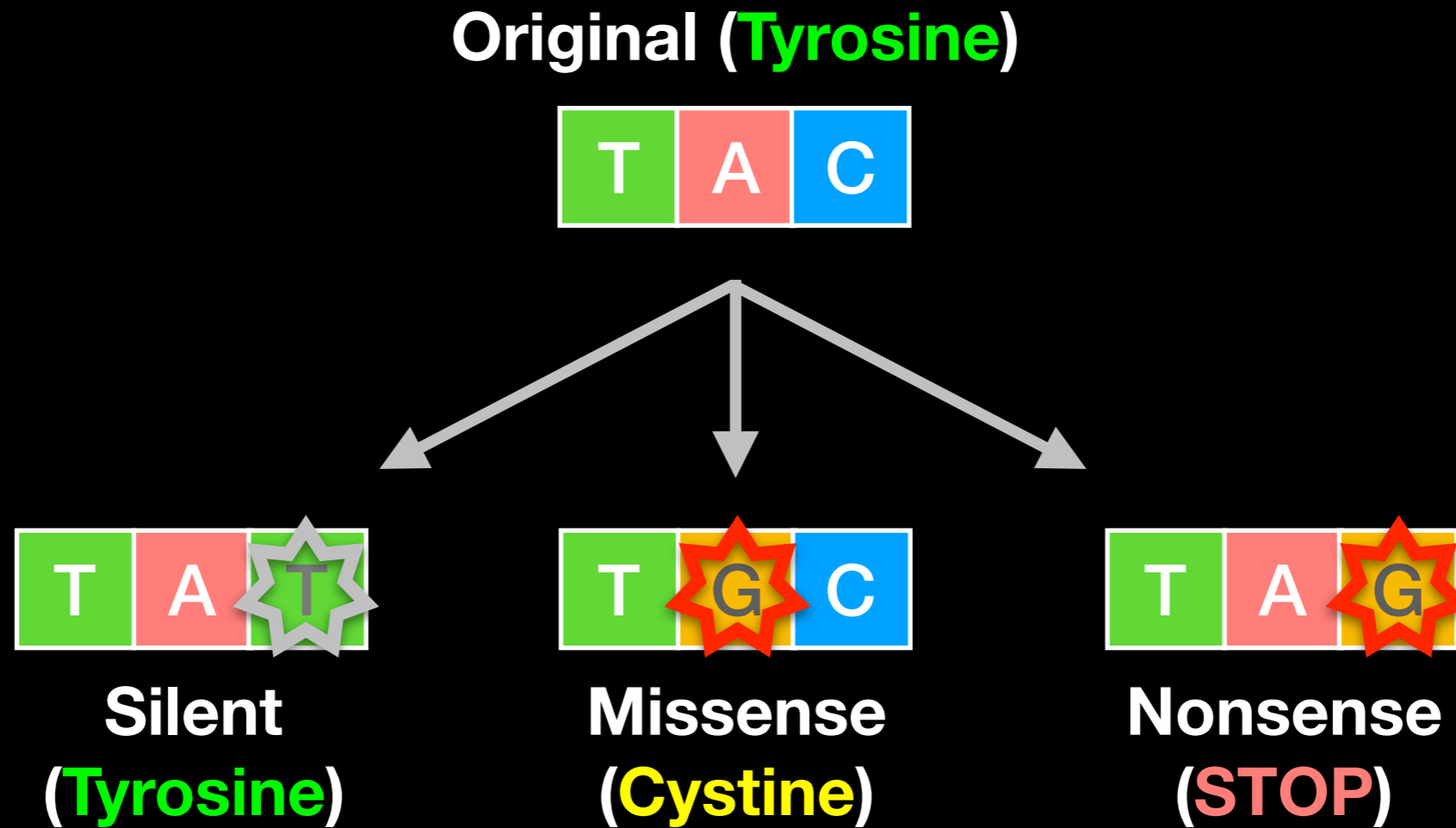
Identify all mutations specific to tumor cells



Filter out silent mutations



# Mutations detected: Point mutations

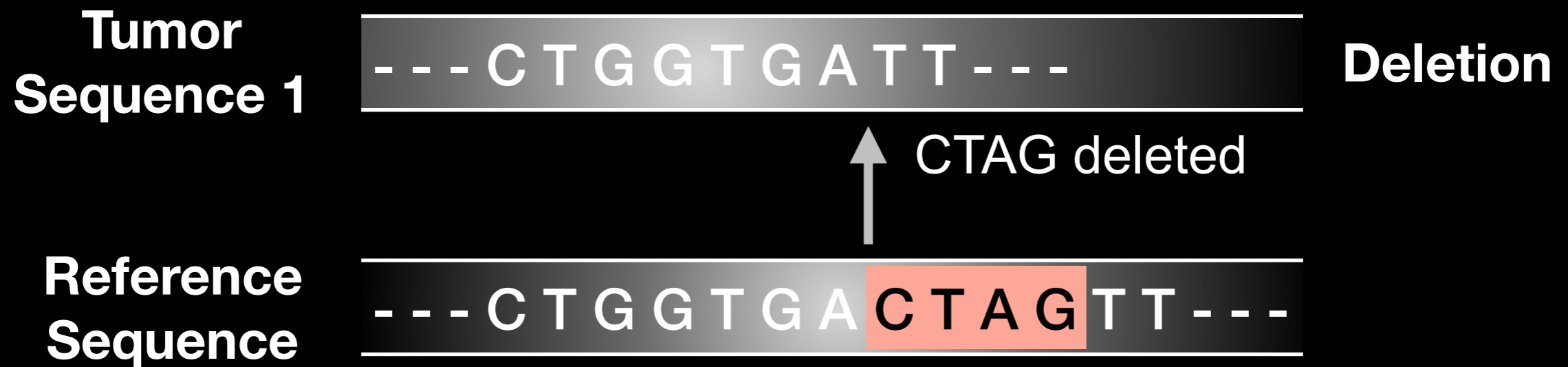


# Mutations detected: Indels

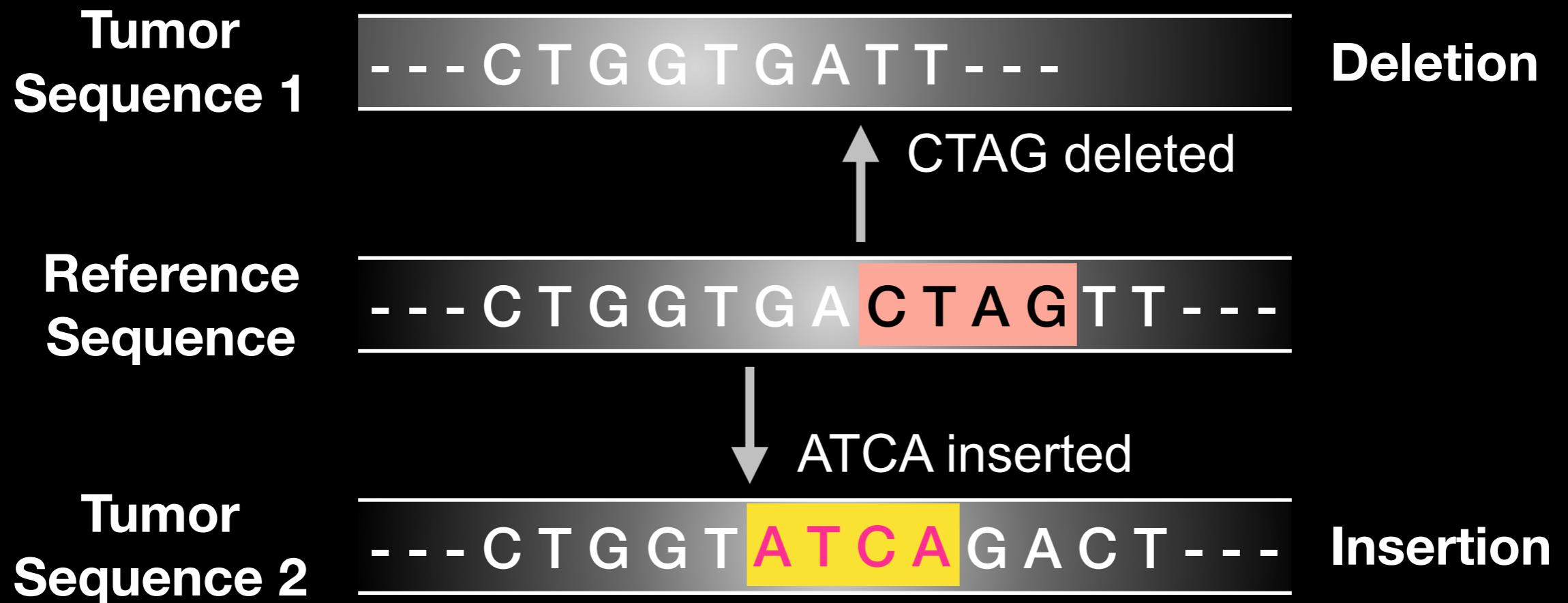
Reference  
Sequence

---CTGGTGACTAGTT---

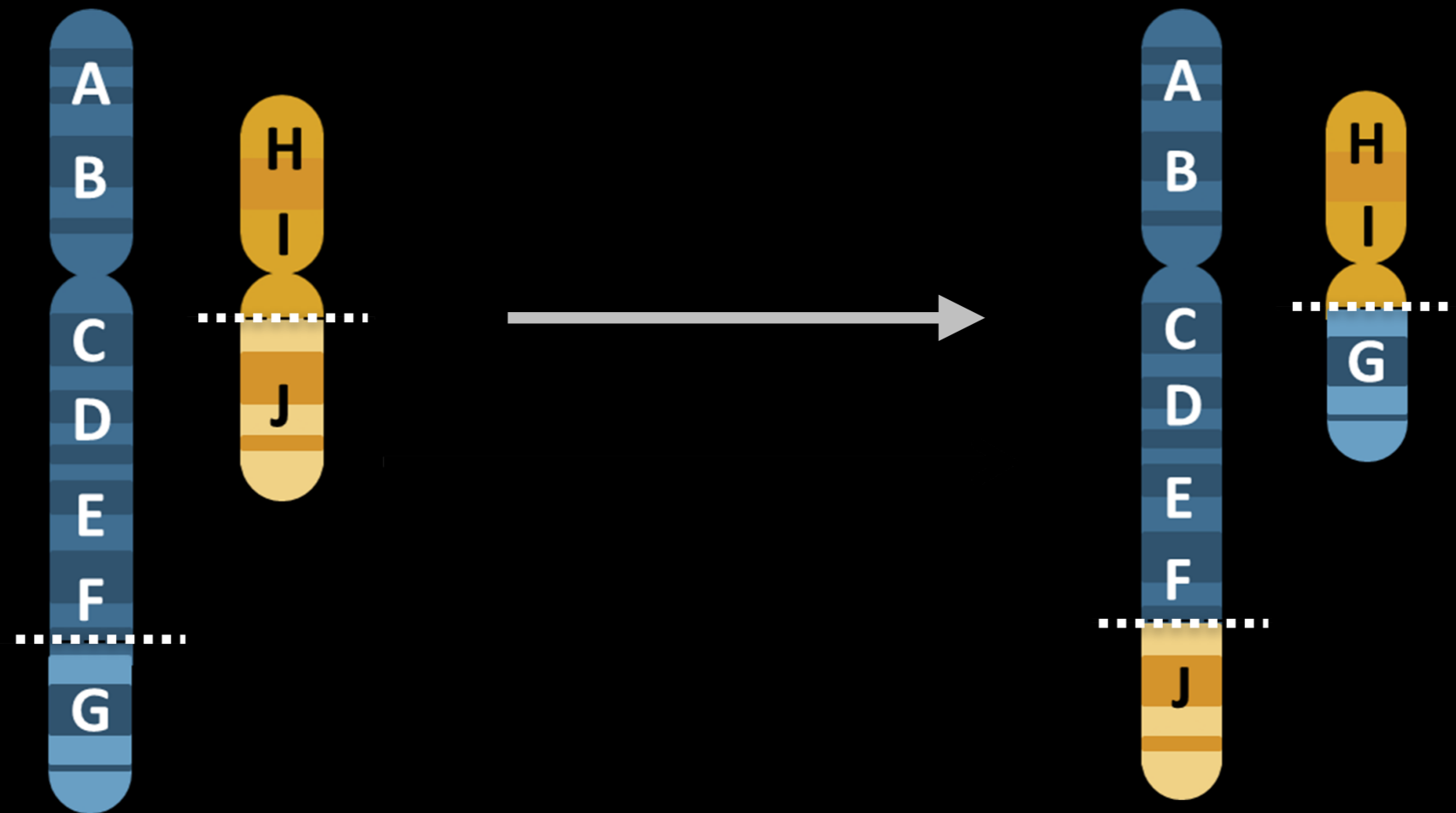
# Mutations detected: Indels



# Mutations detected: Indels



# Mutations detected: Translocations



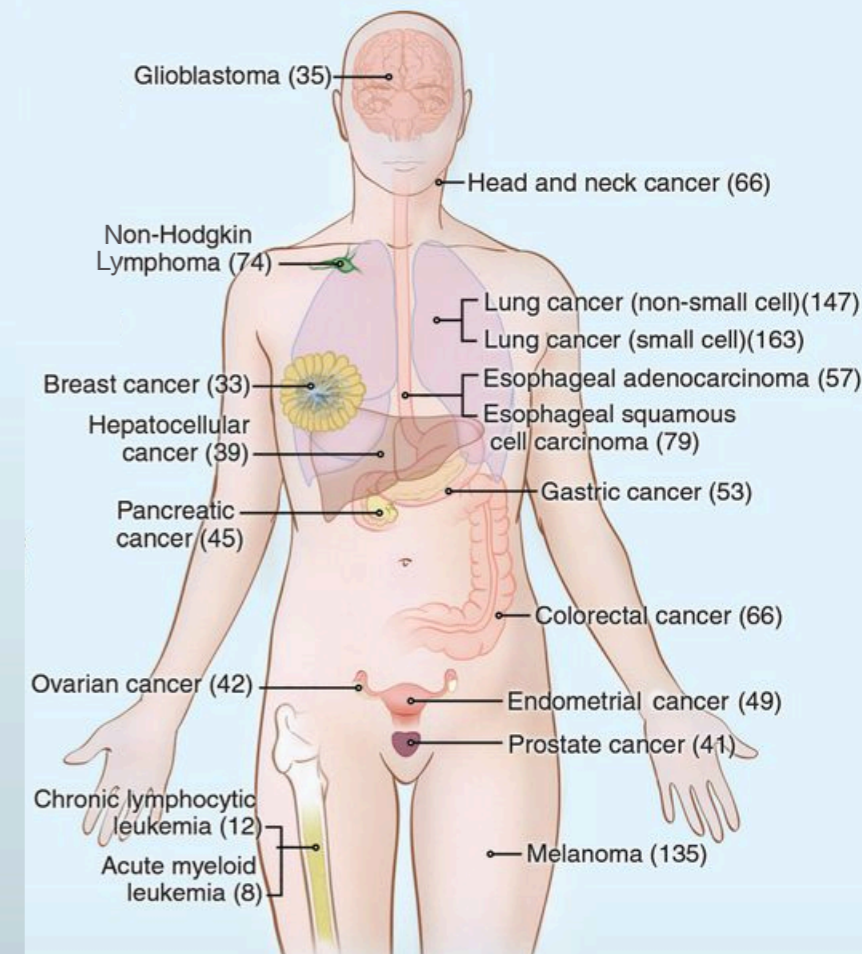
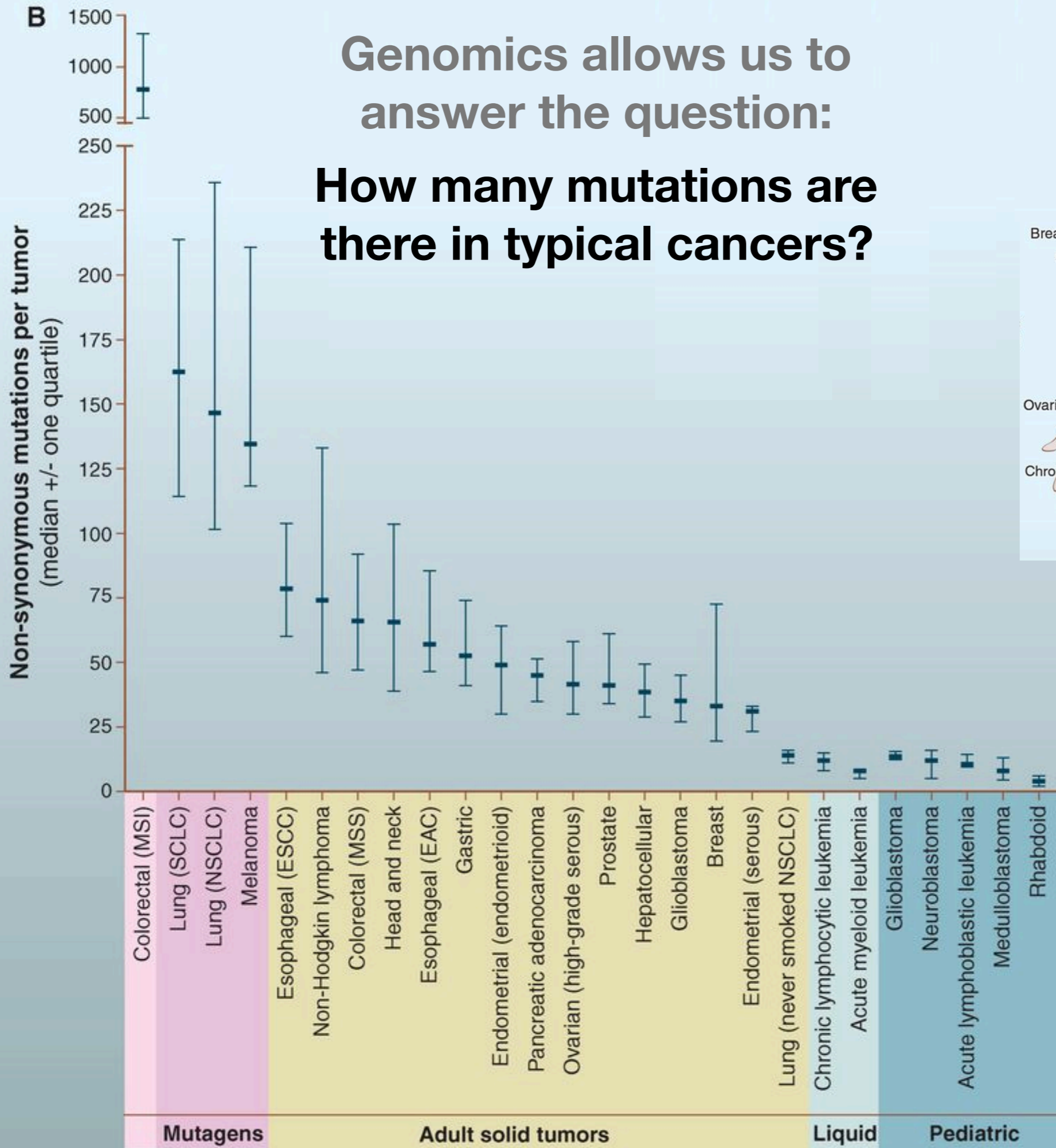
# What can go wrong in cancer genomes?

Type of change	Some common technology to study changes
DNA mutations	WGS, WXS
DNA structural variations	WGS
Copy number variation (CNV)	CGH array, SNP array, WGS
DNA methylation	Methylation array, RRBS, WGBS
mRNA expression changes	mRNA expression array, RNA-seq
miRNA expression changes	miRNA expression array, miRNA-seq
<i>Protein expression</i>	Protein arrays, mass spectrometry

WGS = whole genome sequencing, WXS = whole exome sequencing

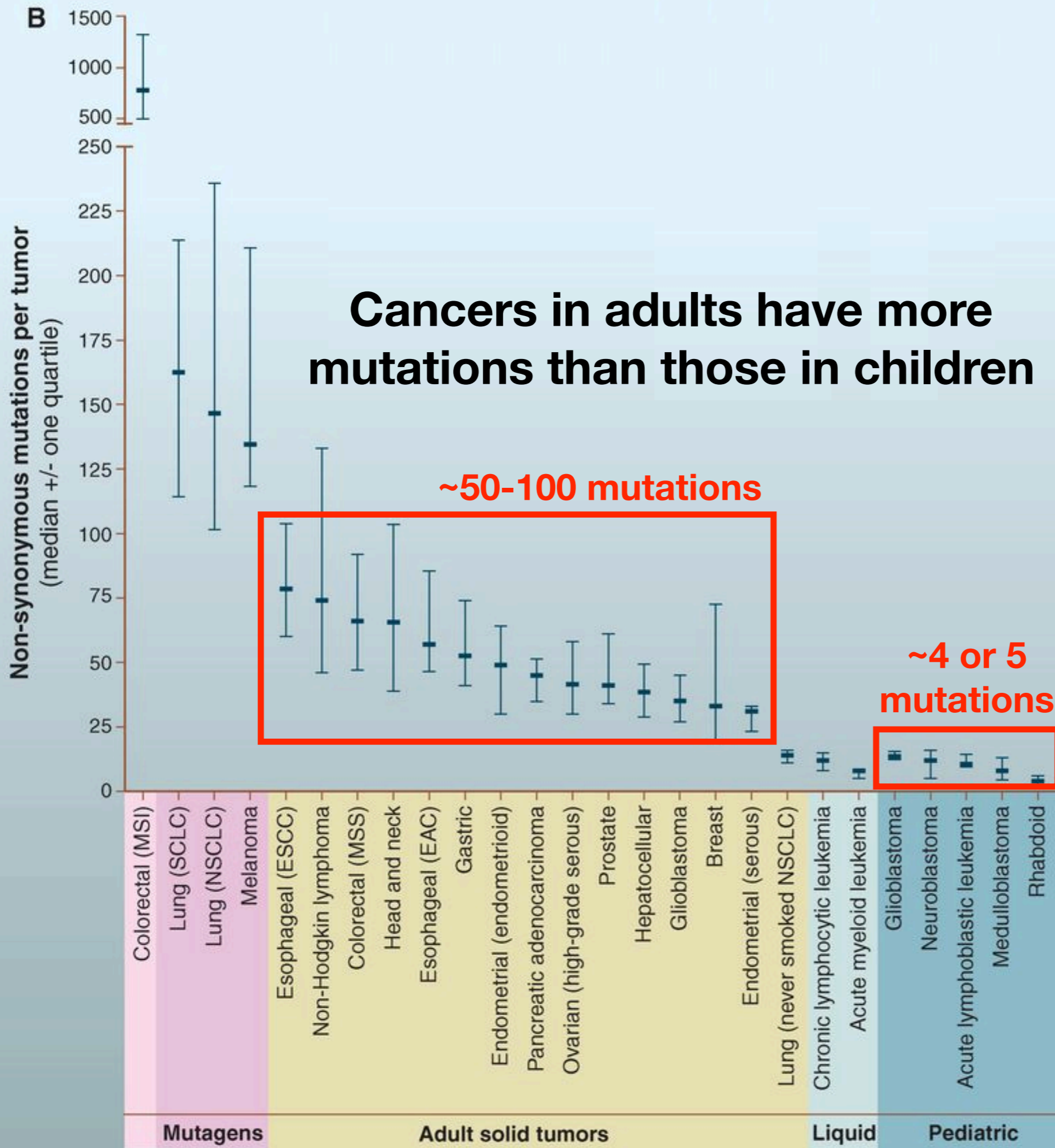
RRBS = reduced representation bisulfite sequencing, WGBS = whole genome bisulfite sequencing

**Genomics allows us to answer the question: How many mutations are there in typical cancers?**



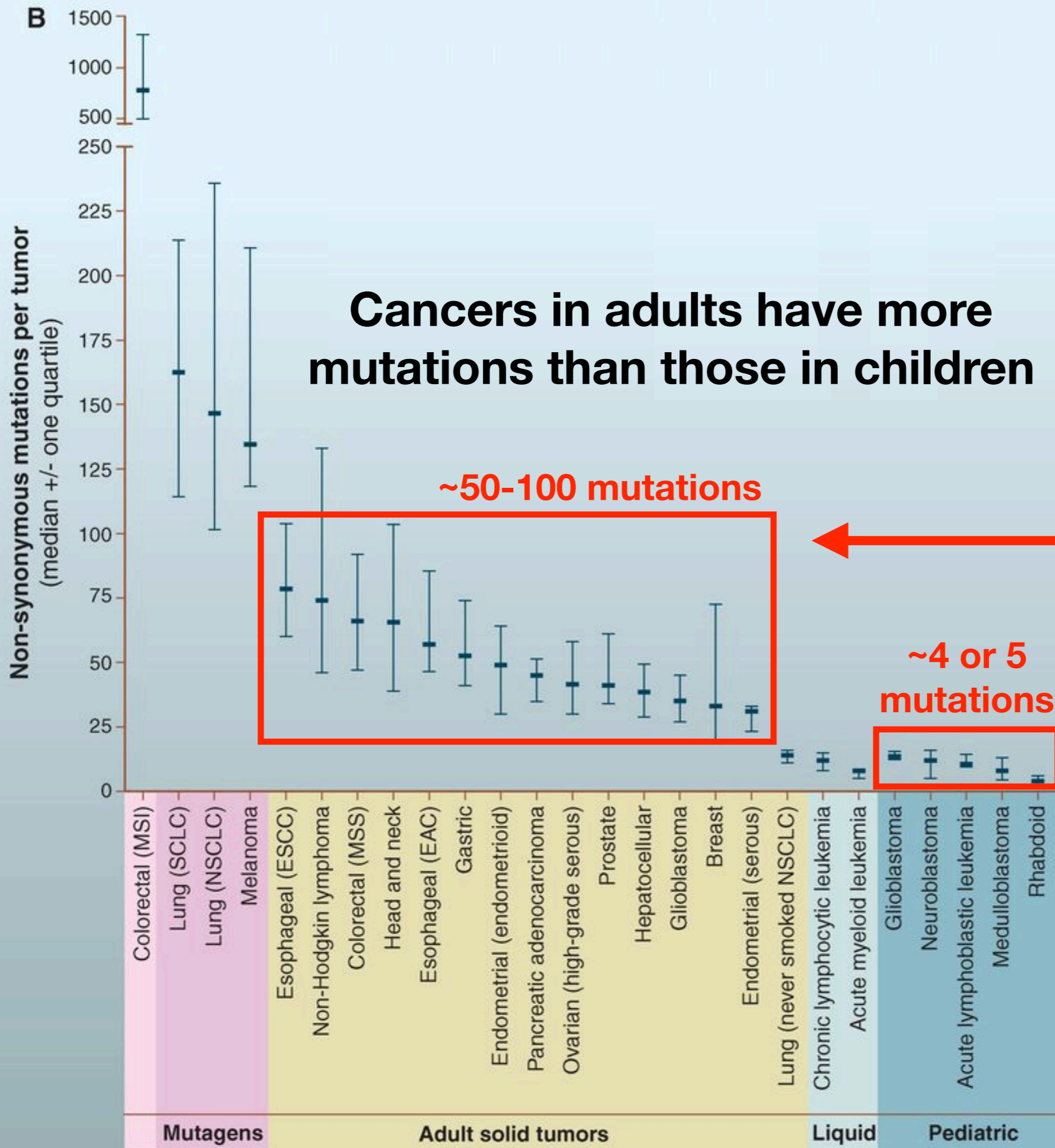
**Number of somatic mutations in representative human cancers, detected by genome-wide sequencing studies**

**Vogelstein et al. Science (2013)**

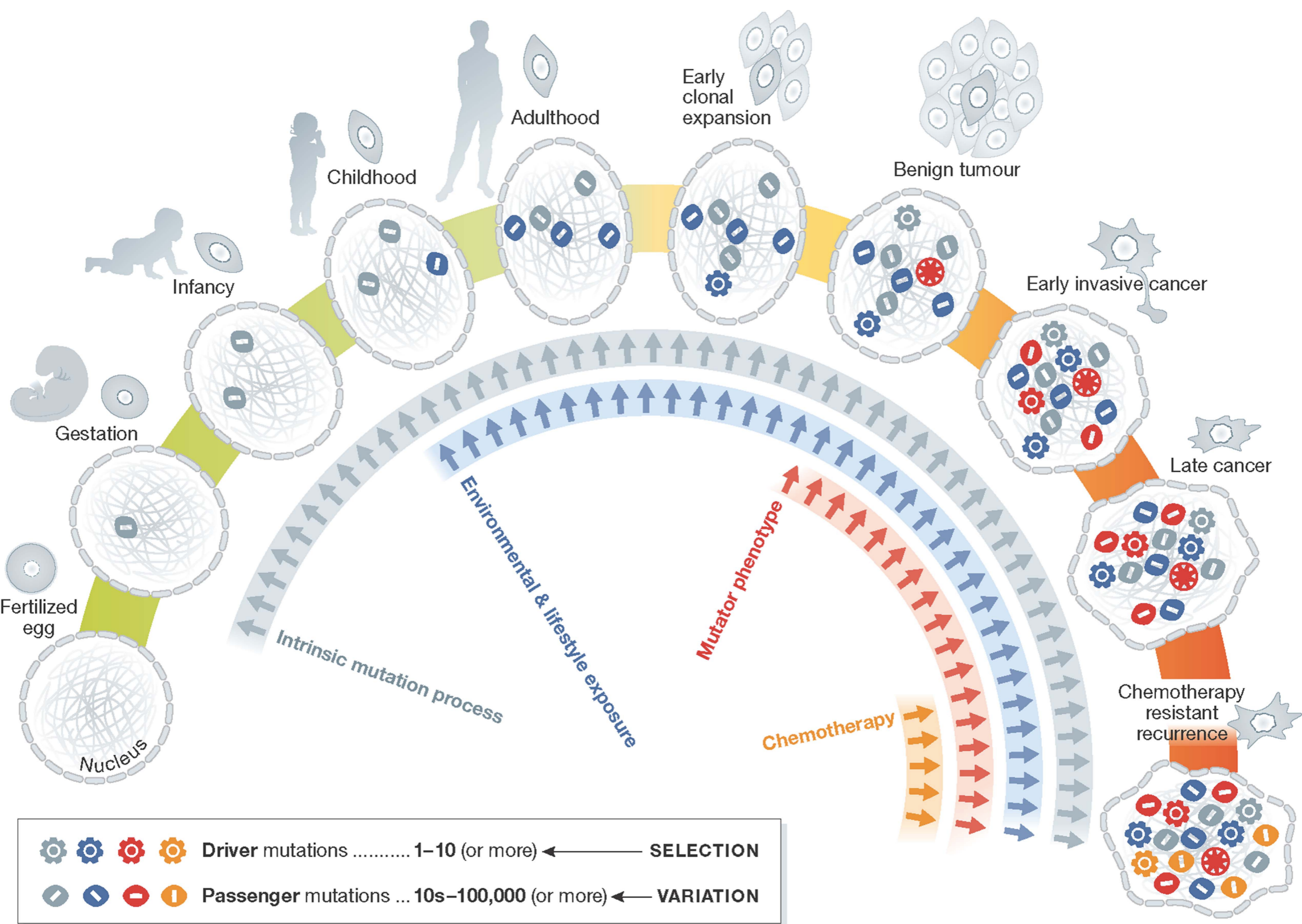


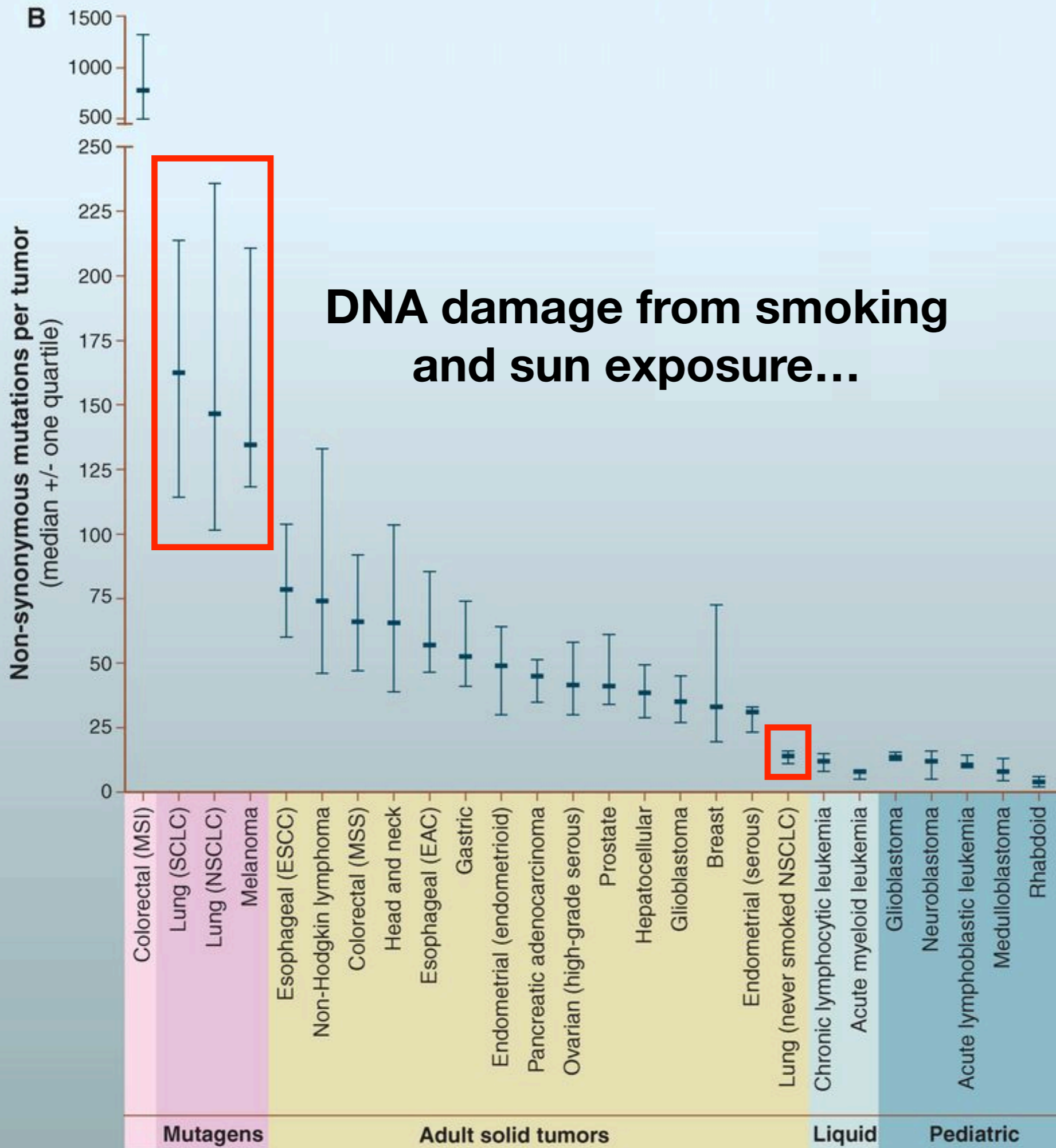
**Vogelstein et al.  
Science (2013)**





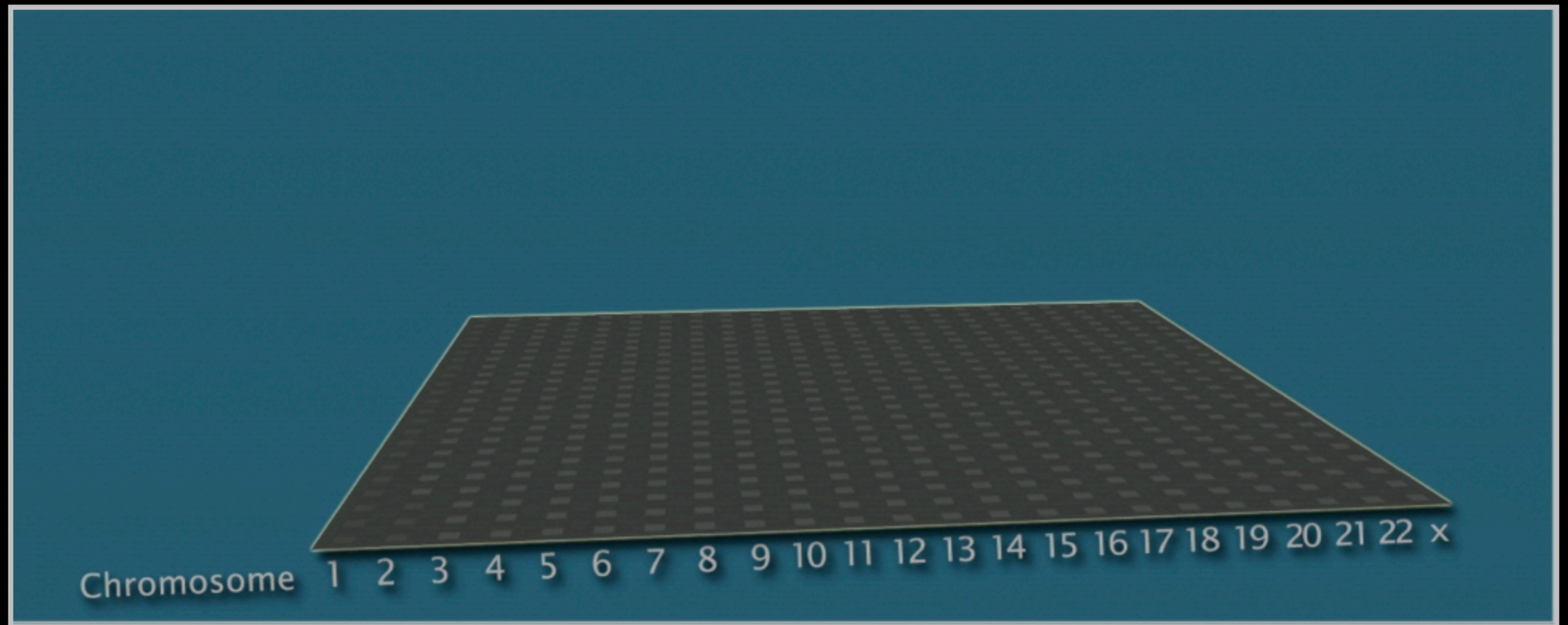
**Vogelstein et al.  
Science (2013)**





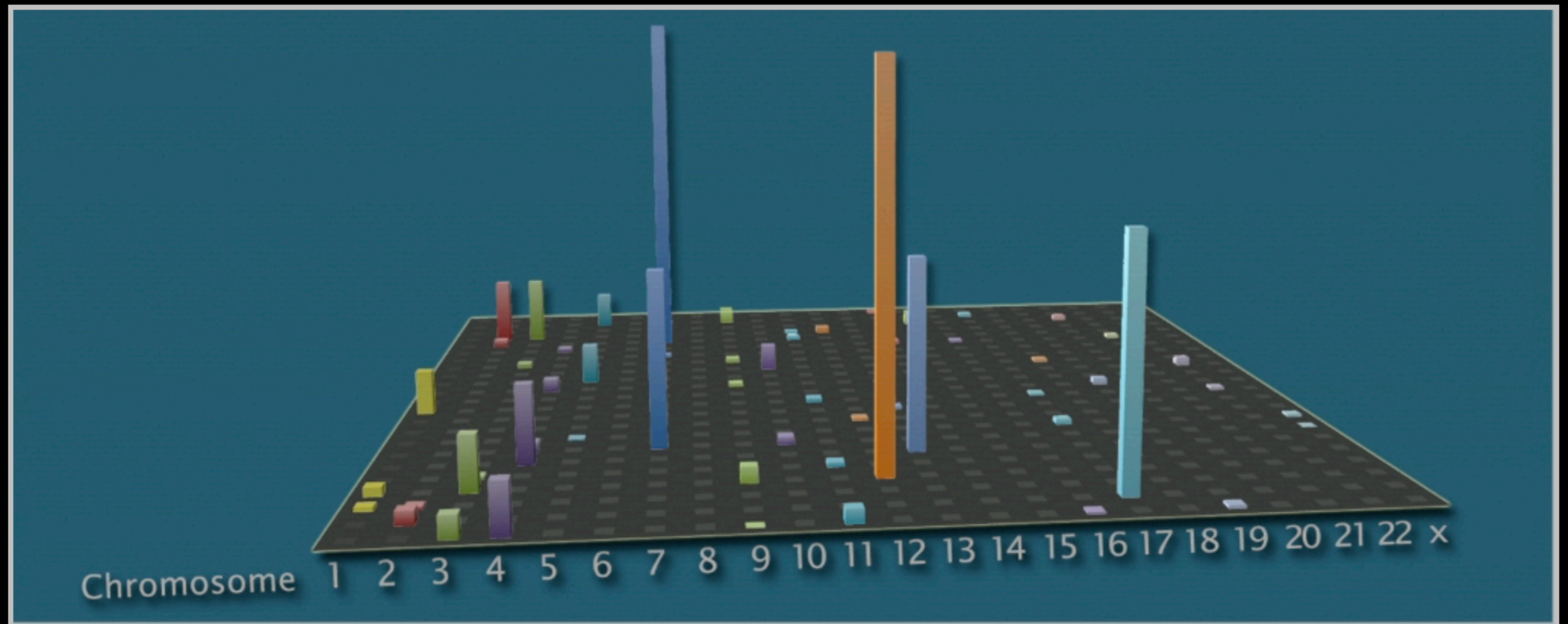
Vogelstein et al.  
Science (2013)

# Genomic approaches can identify the genes most commonly mutated in cancer



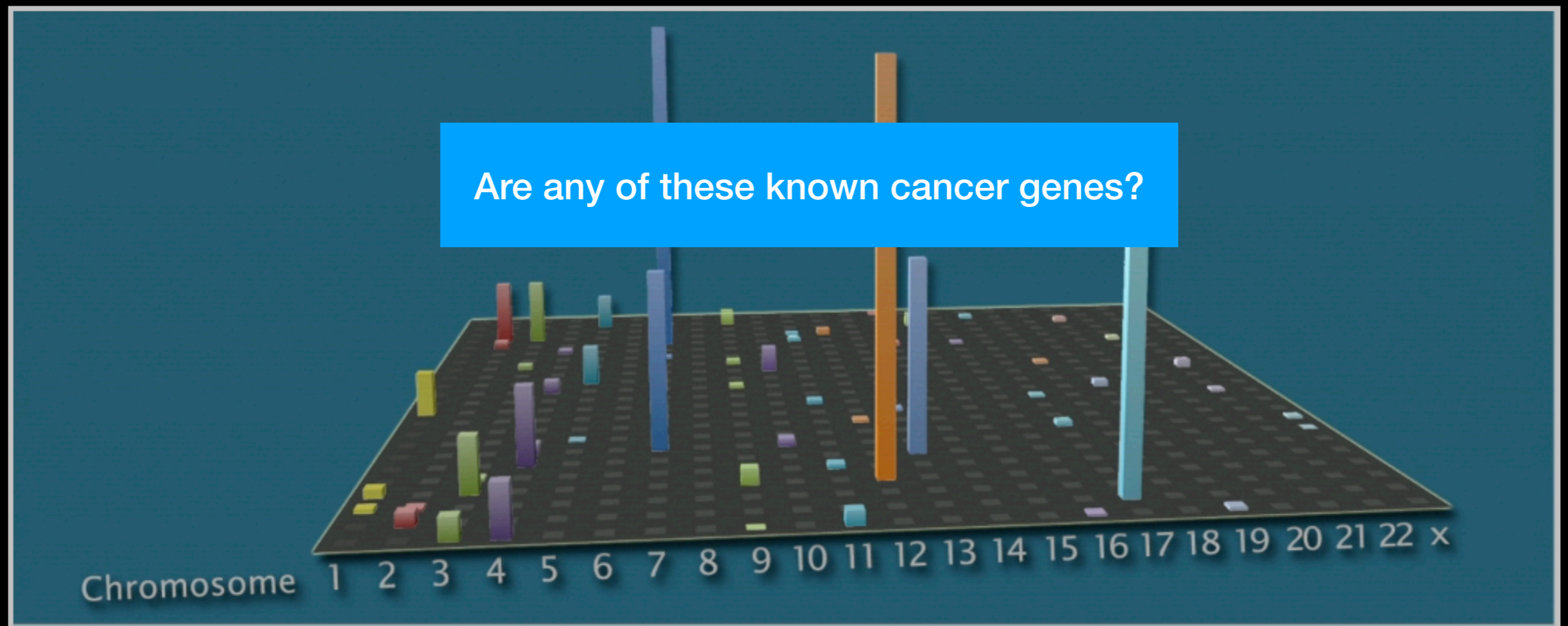
**Arrange all genes in a matrix, ordered by chromosomes**

# Identifying genes most commonly mutated in cancer



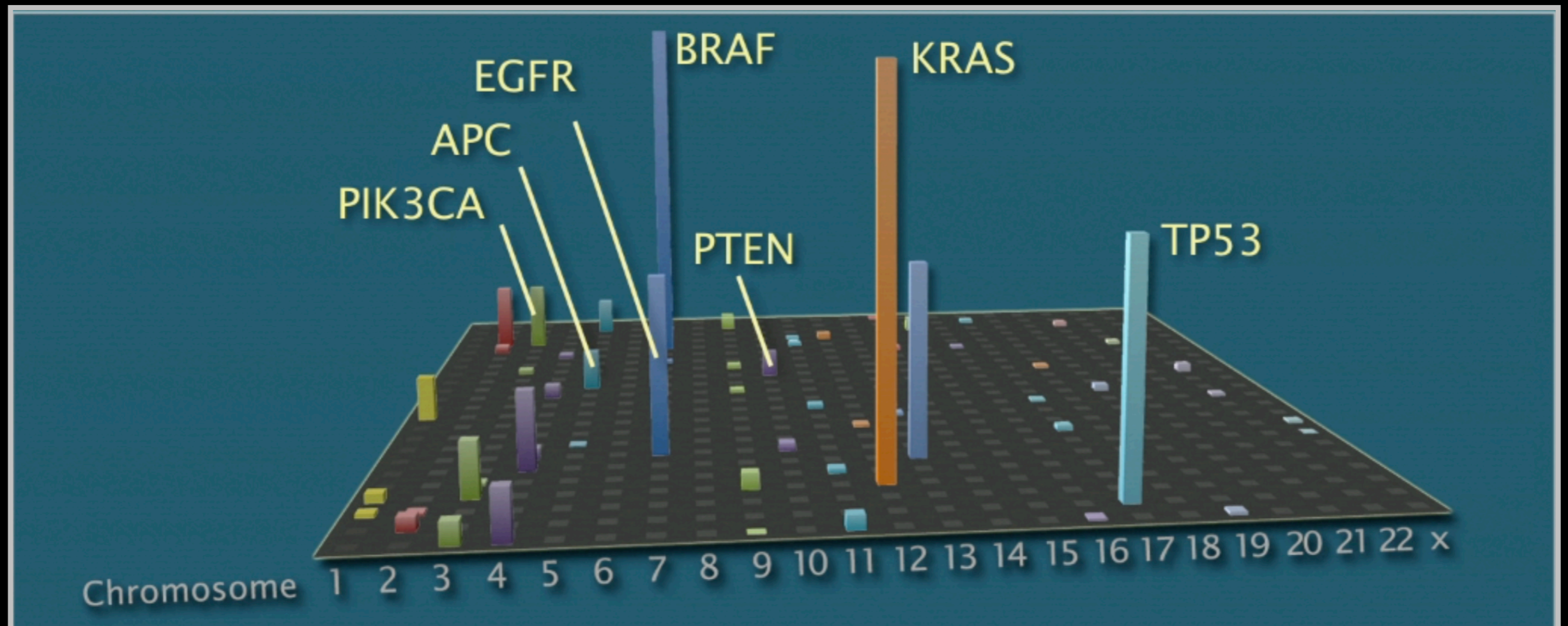
**Add all data together to see which genes are most often mutated**

# Identifying genes most commonly mutated in cancer



**Add all data together to see which genes are most often mutated**

# Identifying genes most commonly mutated in cancer



**Many are famous proto-oncogenes, many others are new cancer genes!**

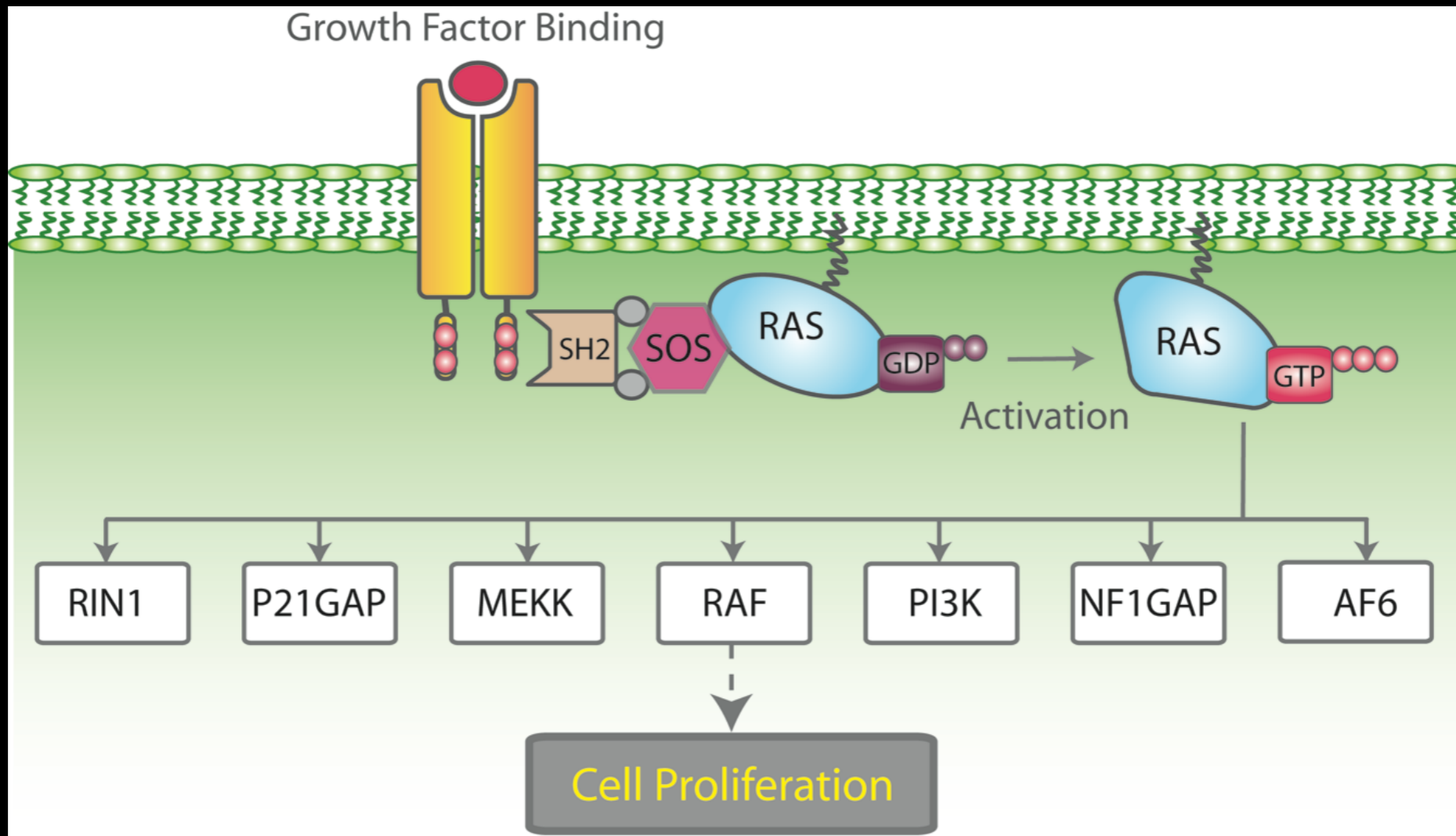
# Three Main Types of Cancer Genes:

- **Oncogenes**, such as **Ras**, normally function to accelerate cell division and growth. They can be mutated to act like stuck gas pedals.
- **Tumor suppressor genes**, such as **p53** normal act like breaks. Mutations can cause these breaks to fail.
- **DNA repair genes**, such as **BRCA1 & 2**, normally function to fix minor damage to DNA when it replicates. When these genes are mutated, DNA damage can accumulate and lead to cancer.



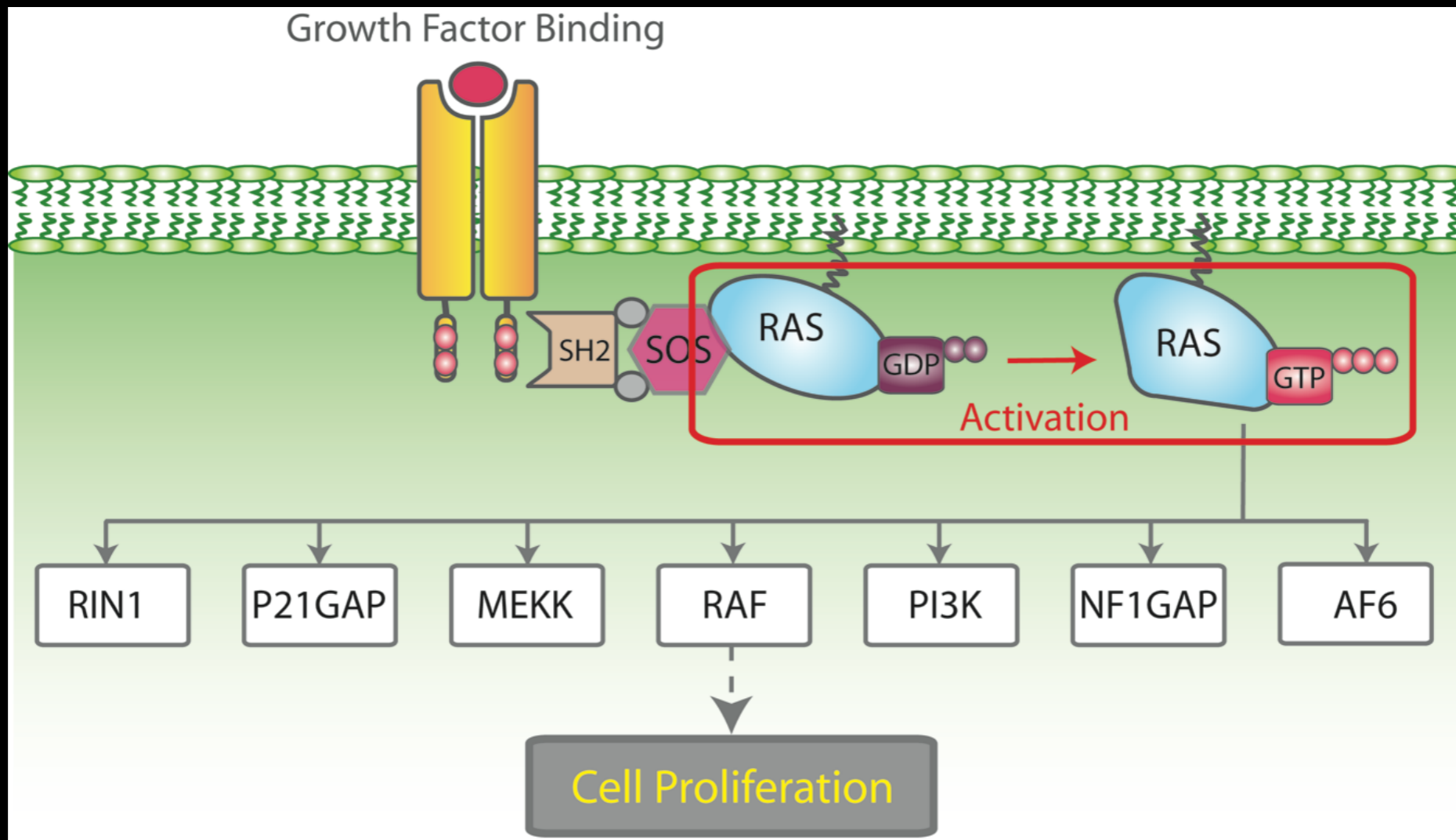
# Cell growth and survival genes

Many participate in signaling pathways that promote cell proliferation  
(E.G. EGFR, Ras, BRAF, MEK etc.)

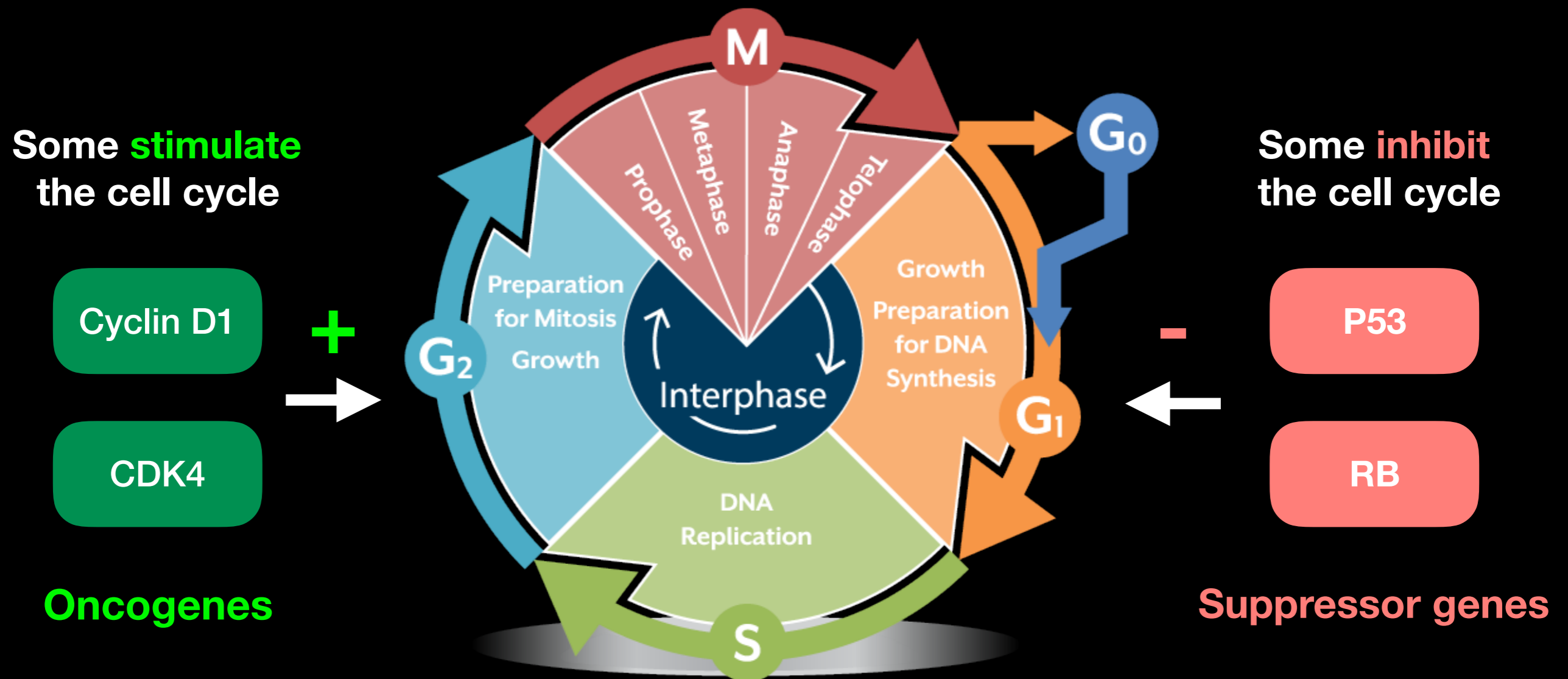


# Cell growth and survival genes

Many participate in signaling pathways that promote cell proliferation  
(E.G. EGFR, Ras, BRAF, MEK etc.)



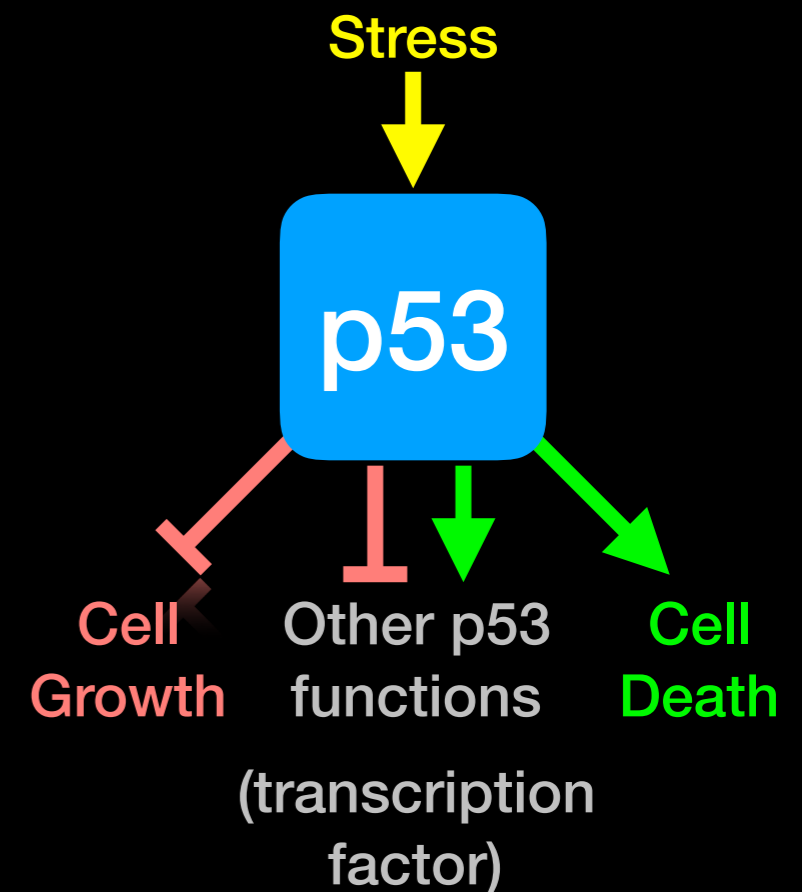
# Regulators of Cell Cycle and Cell Death



# p53 Regulates Cell Division

Probably the most famous cancer gene that is mutated in about half of all tumors. Often called the '*guardian of the genome*'

- p53 normally shuts down cell division when a cell is stressed (e.g. by DNA damage)
- When DNA is damaged, p53 activates genes that stop cell growth or trigger the cell to die.
- Thus, p53 guards against changes to cells that might lead to tumor formation.
- It appears necessary to inactivate p53 to develop many forms of cancer.



Do it Yourself!

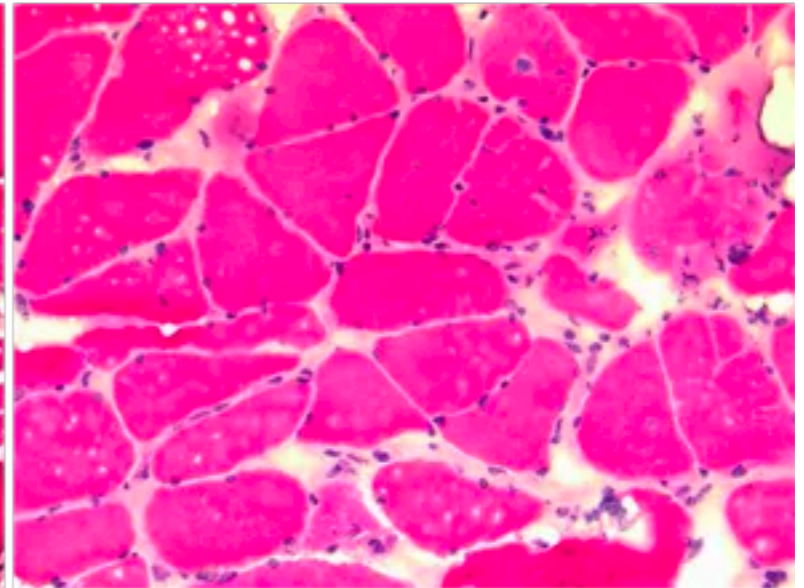
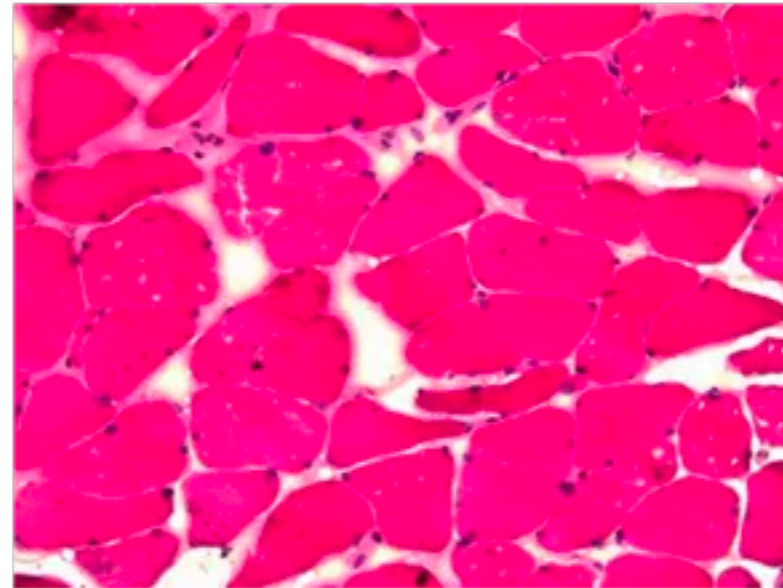
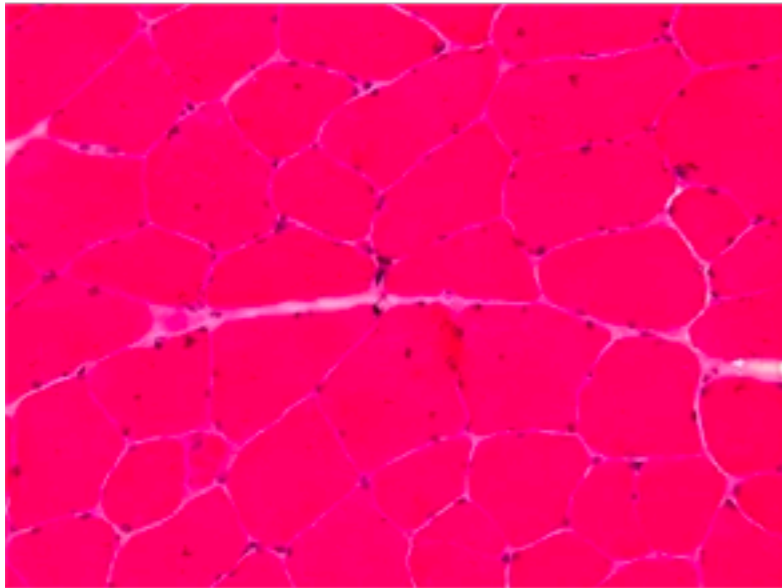
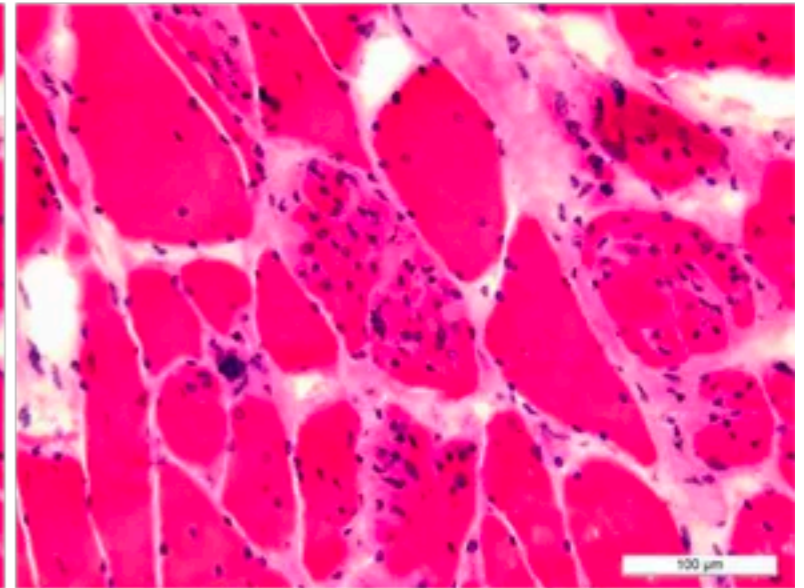
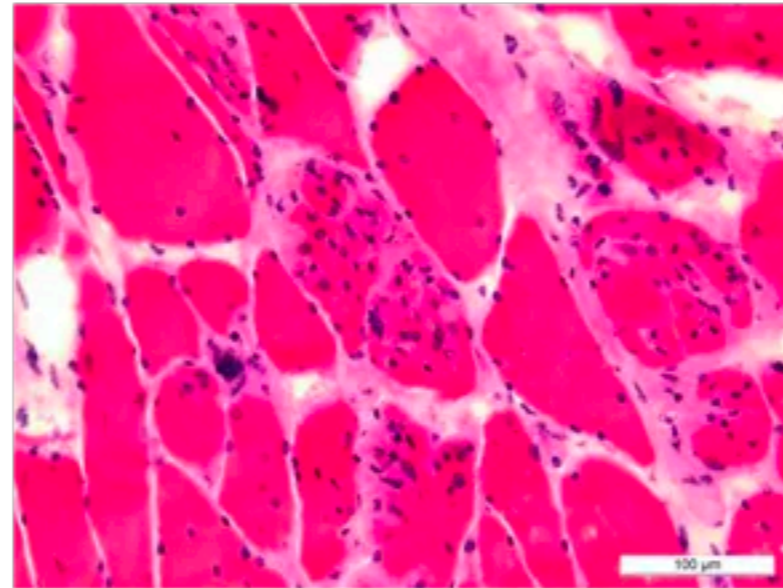
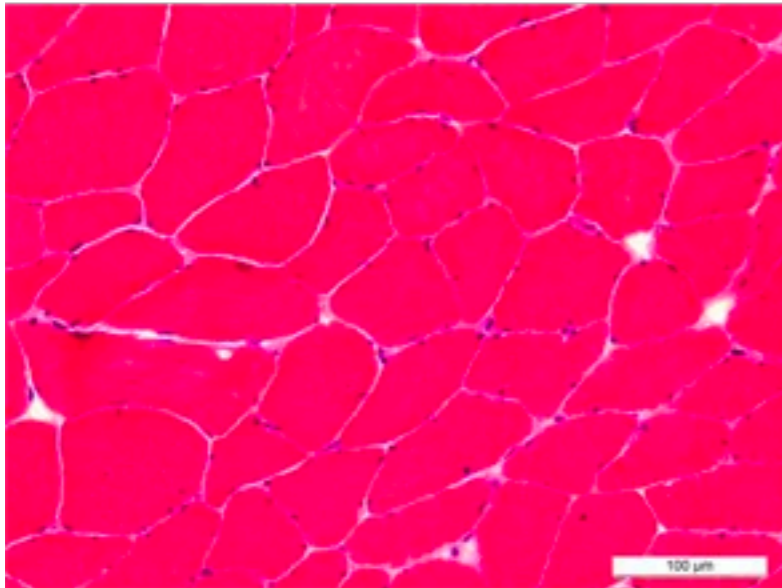
# Hands-on time!

[https://bioboot.github.io/bimm143\\_W19/lectures/#17](https://bioboot.github.io/bimm143_W19/lectures/#17)

**Part 1 Only Please**

## Control

## Pancreatic Cancer



Representative H&E micrographs of rectus abdominis biopsies are displayed for two patients without cancer (*left*) and four patients with pancreatic cancer (*right*)

# Today's Menu

## Cancer Genomics

Brief review of cancer fundamentals,  
What is cancer and what causes it?

## Mining Cancer Genomic Data

**Hands-on analysis** to identify genomic  
changes in different cancers and identify  
new targets for therapy

## Towards personalized cancer treatments

Recap on how the immune system normally  
detects cancer cells and how we can predict  
mutations that can be recognized by T cells

## Cancer Immunoinformatics

**Hands-on analysis** to design personalized  
cancer vaccines

Next Up: