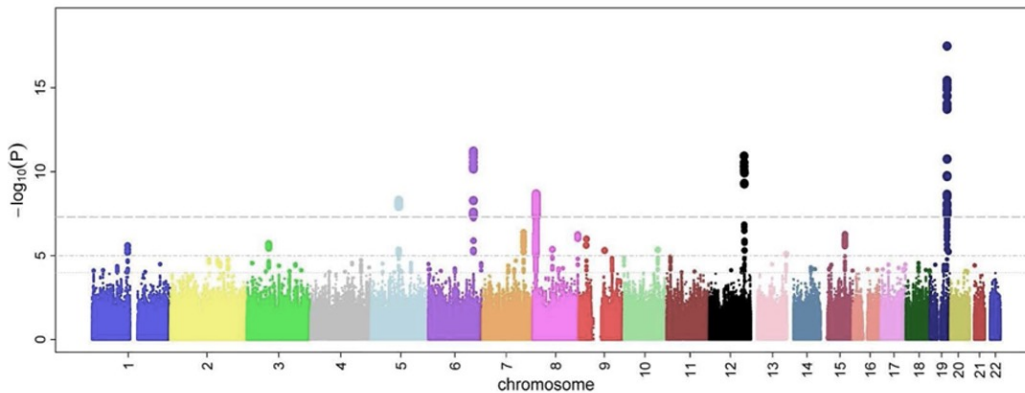


# **NGS - variant analysis**

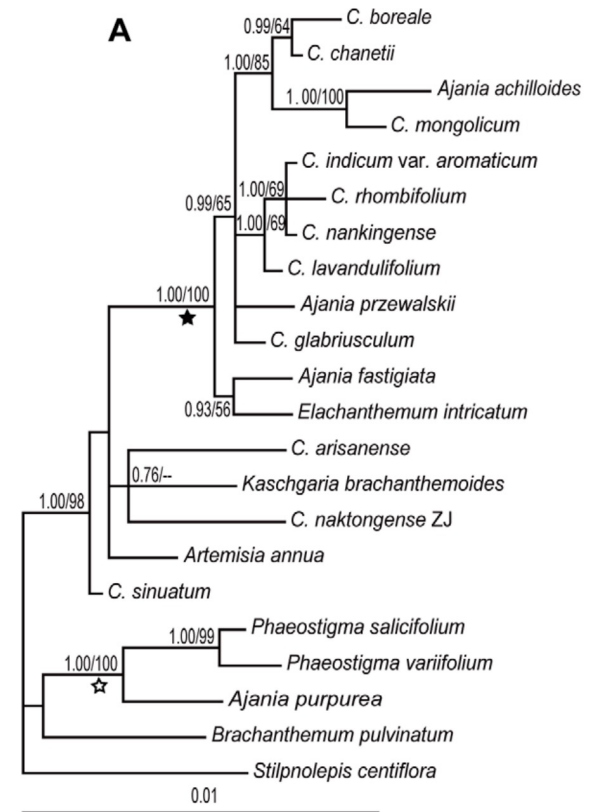
Introduction to variant analysis

# Why study variants?

- Find causes for phenotypic variation
- Understand relatedness



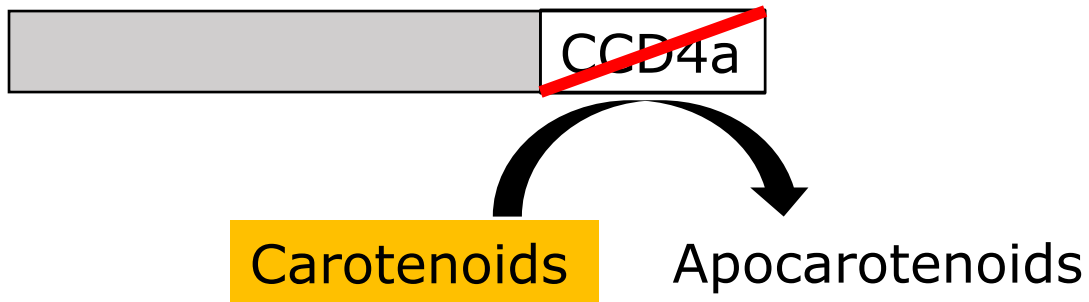
[https://en.wikipedia.org/wiki/Genome-wide\\_association\\_study](https://en.wikipedia.org/wiki/Genome-wide_association_study)



# Mutation

Causes variation

Change in DNA sequence



# Mutations - causes

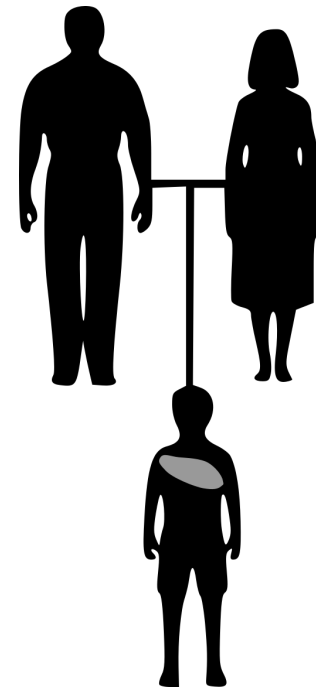
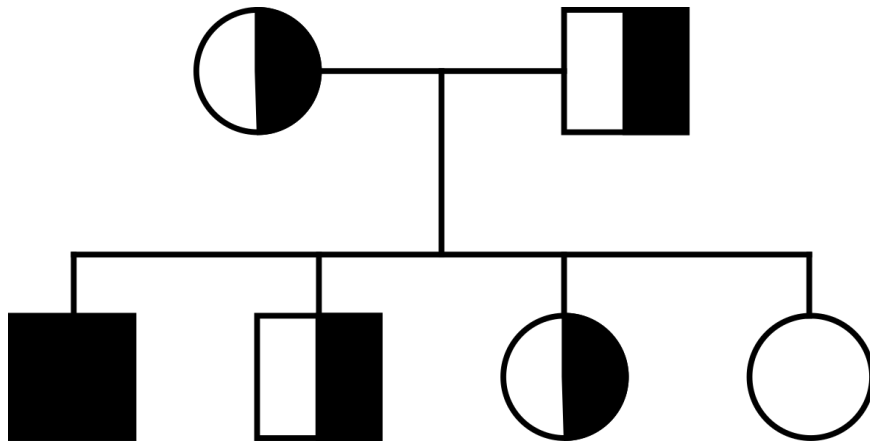
- Repair mistakes
- Unbalanced cell division
- Transposable elements



[https://nl.wikipedia.org/wiki/Springend\\_gen](https://nl.wikipedia.org/wiki/Springend_gen)

# Mutations - types

- inherited – germline variant
- cells – caused by somatic mutation



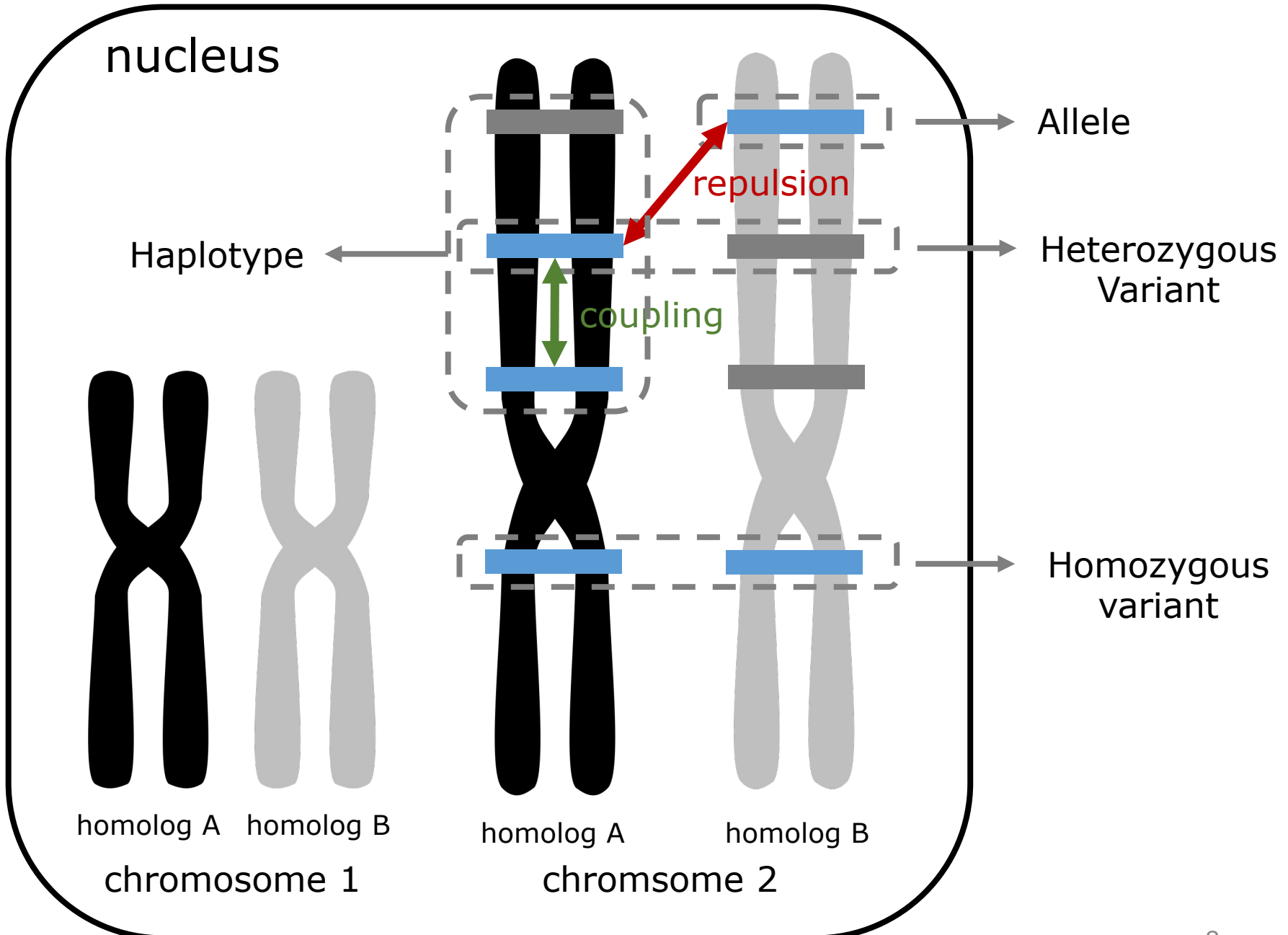


# Question

# Some definitions..

- **Mutation:** a change in DNA
- **Variant:** any difference that exists between any DNA
- **Polymorphism:** variation that is common in a population (often AF > 1%)

Variant vs polymorphism can be problematic: depends on the population

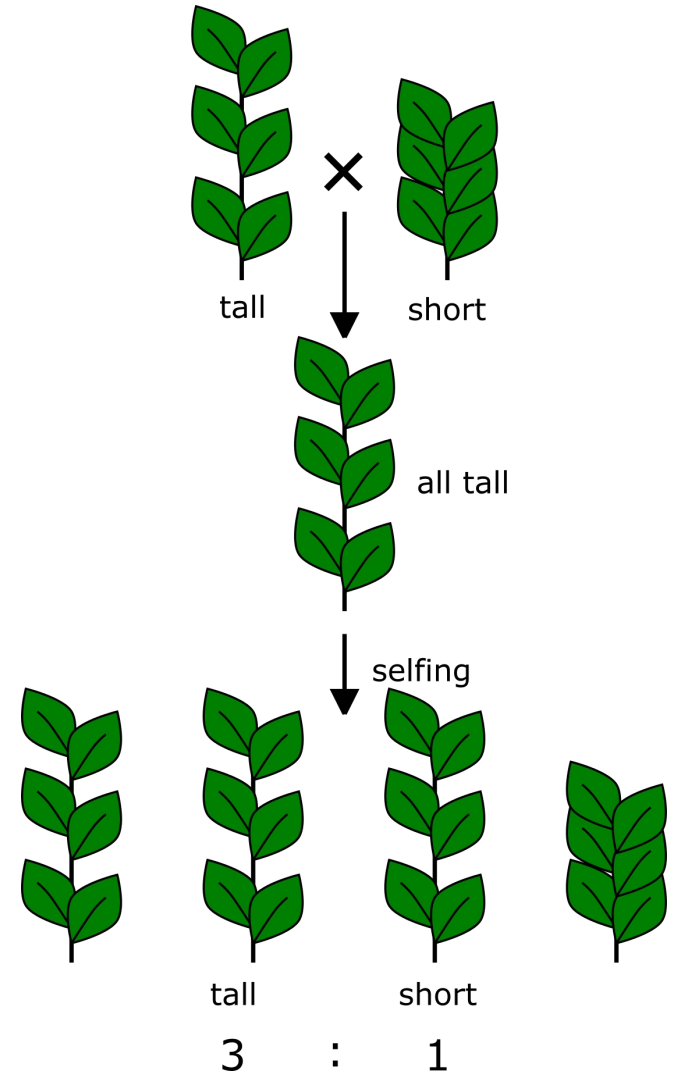
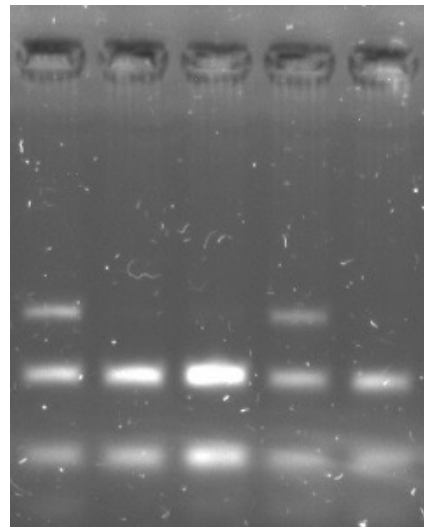
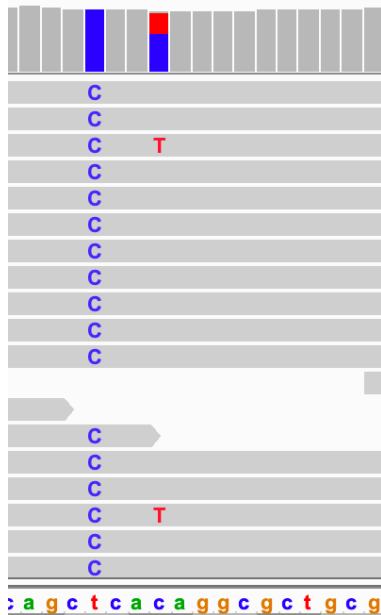




# Question

# Detecting variants

- Phenotypic analysis
- Molecular analysis
  - Sequencing



# Small variants

- Single nucleotide variant (SNV)

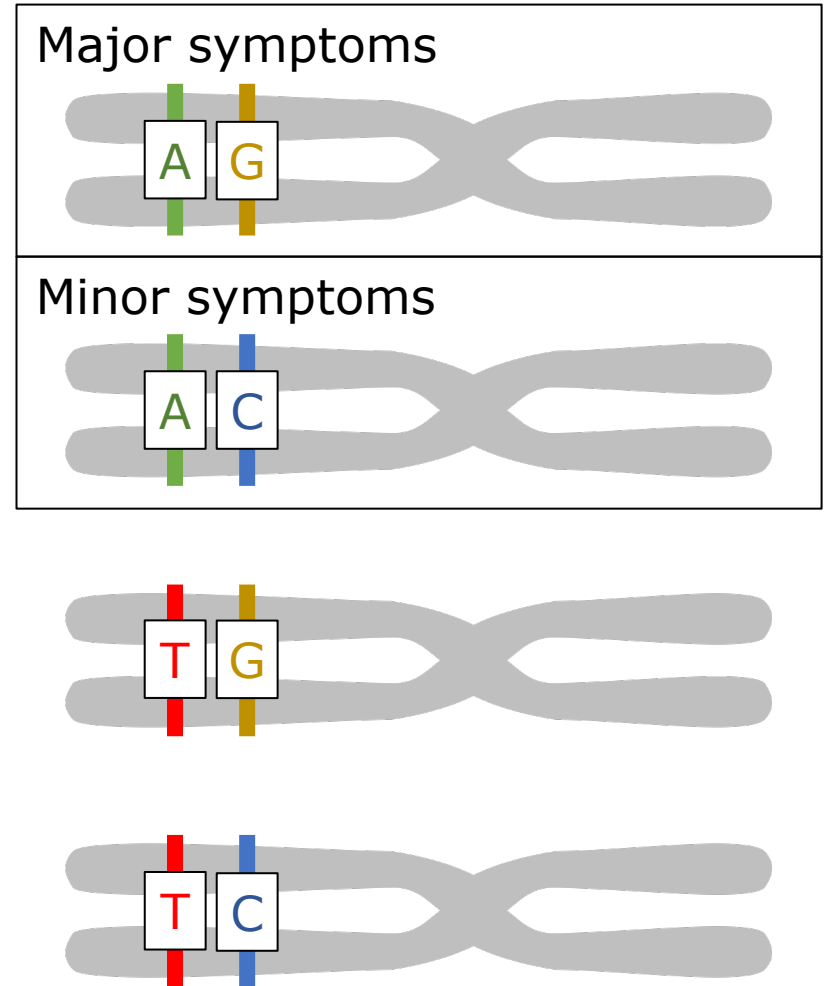
ATCATG**A**CCGTCA  
ATCATG**T**CCGTCA

- Insertion/deletion (INDEL)

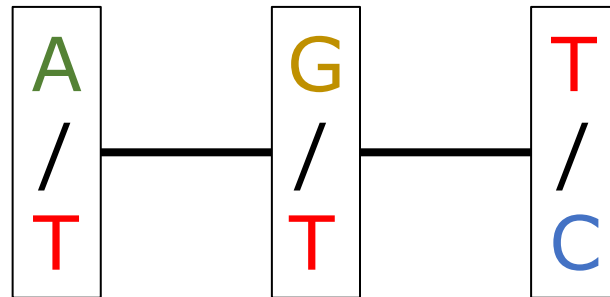
ATCATG**ACC**GTCA  
ATCATG**- - -**GTCA

# Haplotypes

- NGS variants: mostly SNP
- Most SNPs are bi-allelic e.g. [A/T], [G/C]
- Genetic variation is often multi-allelic

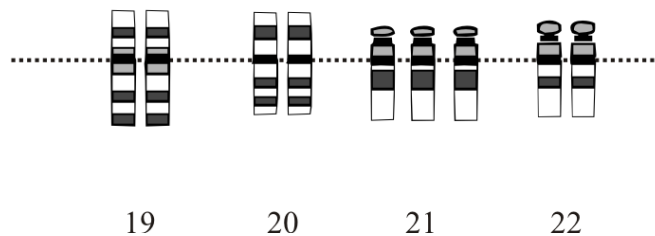


# Question



# Large variants

- Structural variance ( $> 1,000$  base pairs)
  - Copy number variation
  - Translocations
  - Inversions
  - Deletions/insertions
- Chromosomal aberration

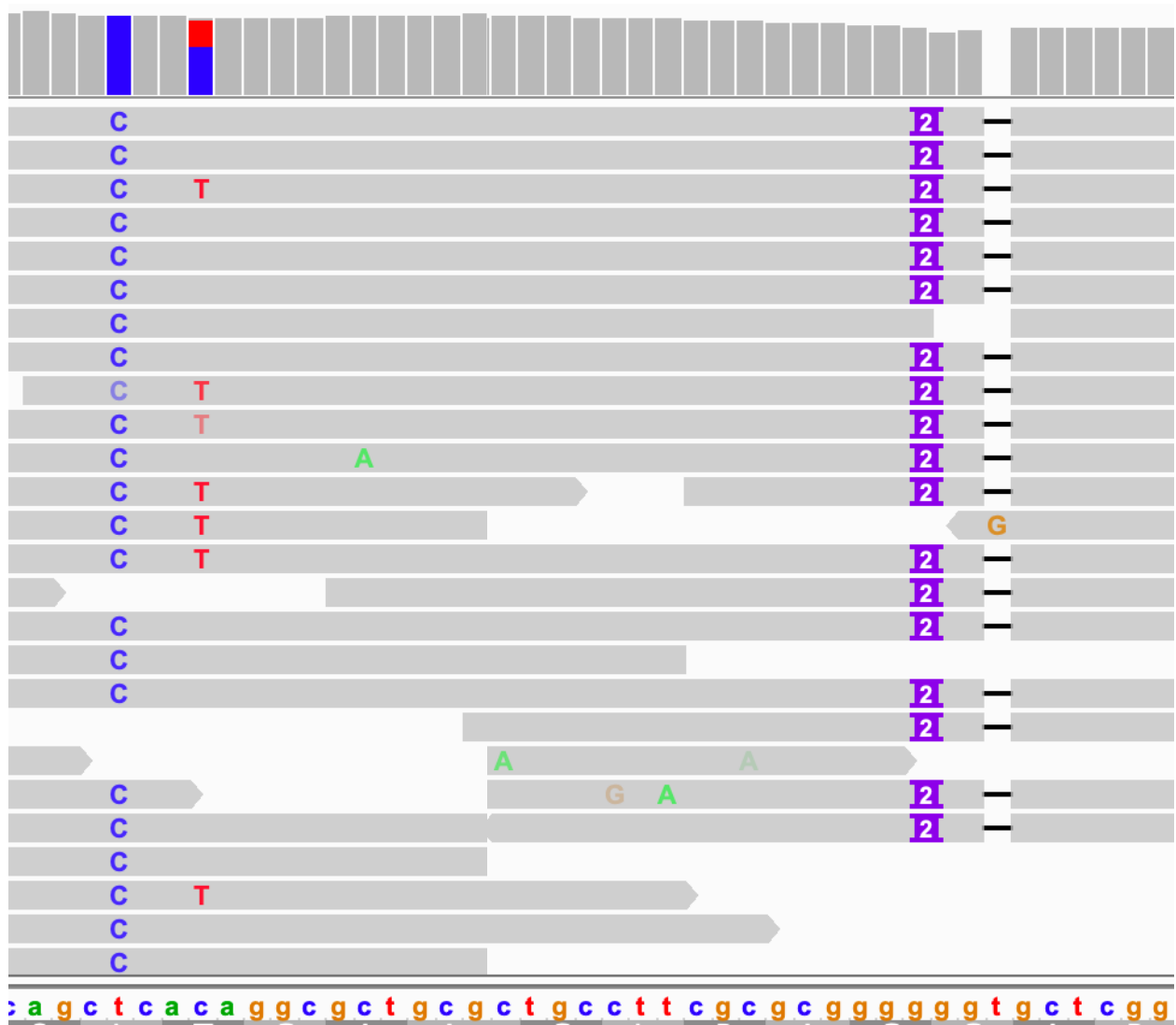


<https://en.wikipedia.org/wiki/Aneuploidy>



# This course

- Inherited (germline) small variants
- Detection by next generation sequencing (NGS)





# GATK

