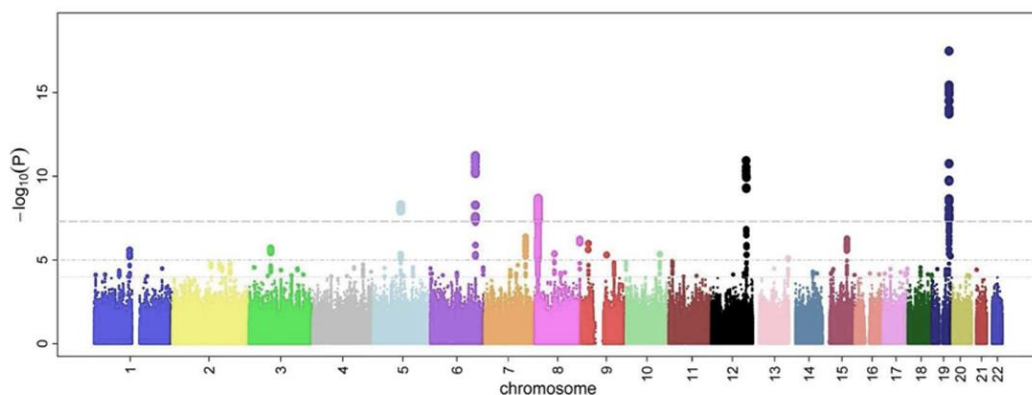


NGS - variant analysis

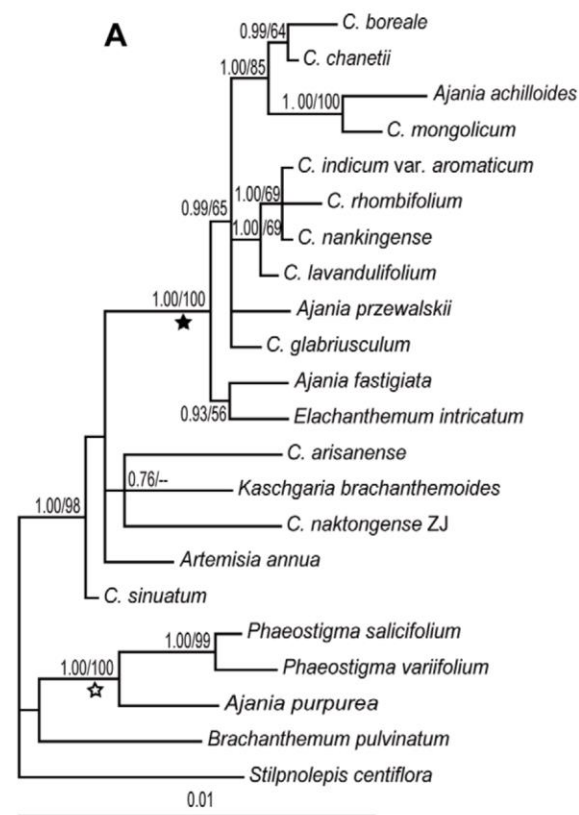
Introduction to variant analysis

Why study variants?

- Find causes for phenotypic variation
- Understand relatedness



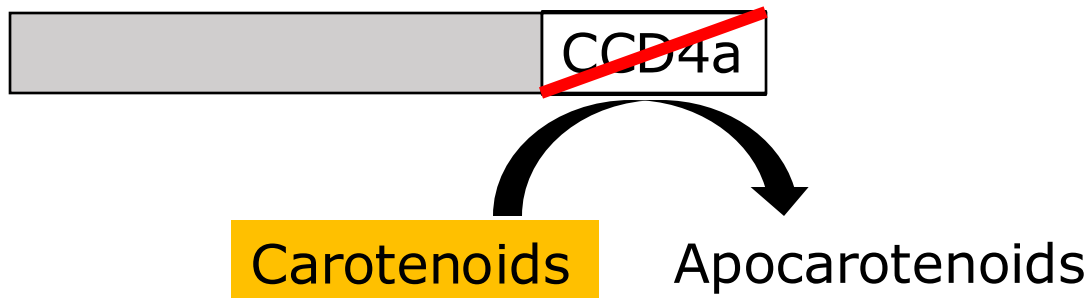
https://en.wikipedia.org/wiki/Genome-wide_association_study



Mutation

Causes variation

Change in DNA sequence



Mutations - causes

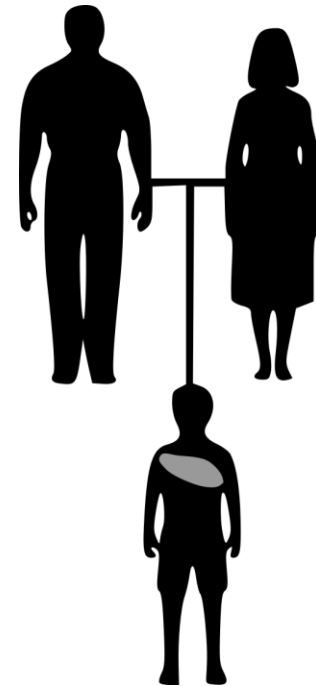
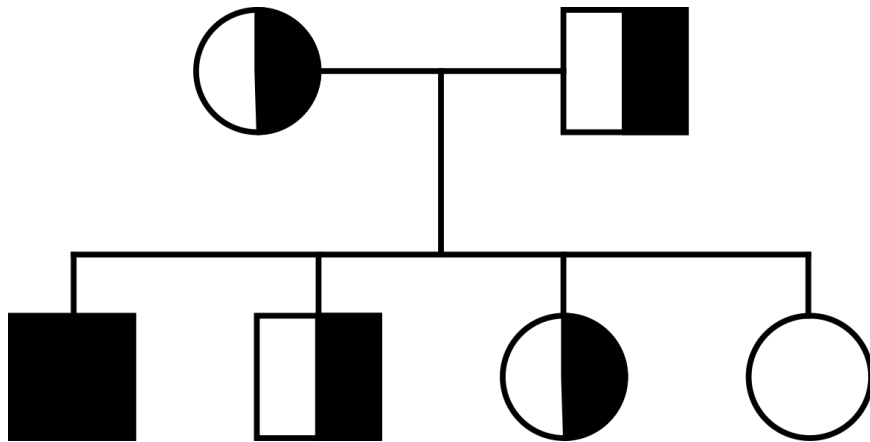
- Repair mistakes
- Unbalanced cell division
- Transposable elements



https://nl.wikipedia.org/wiki/Springend_gen

Mutations - types

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



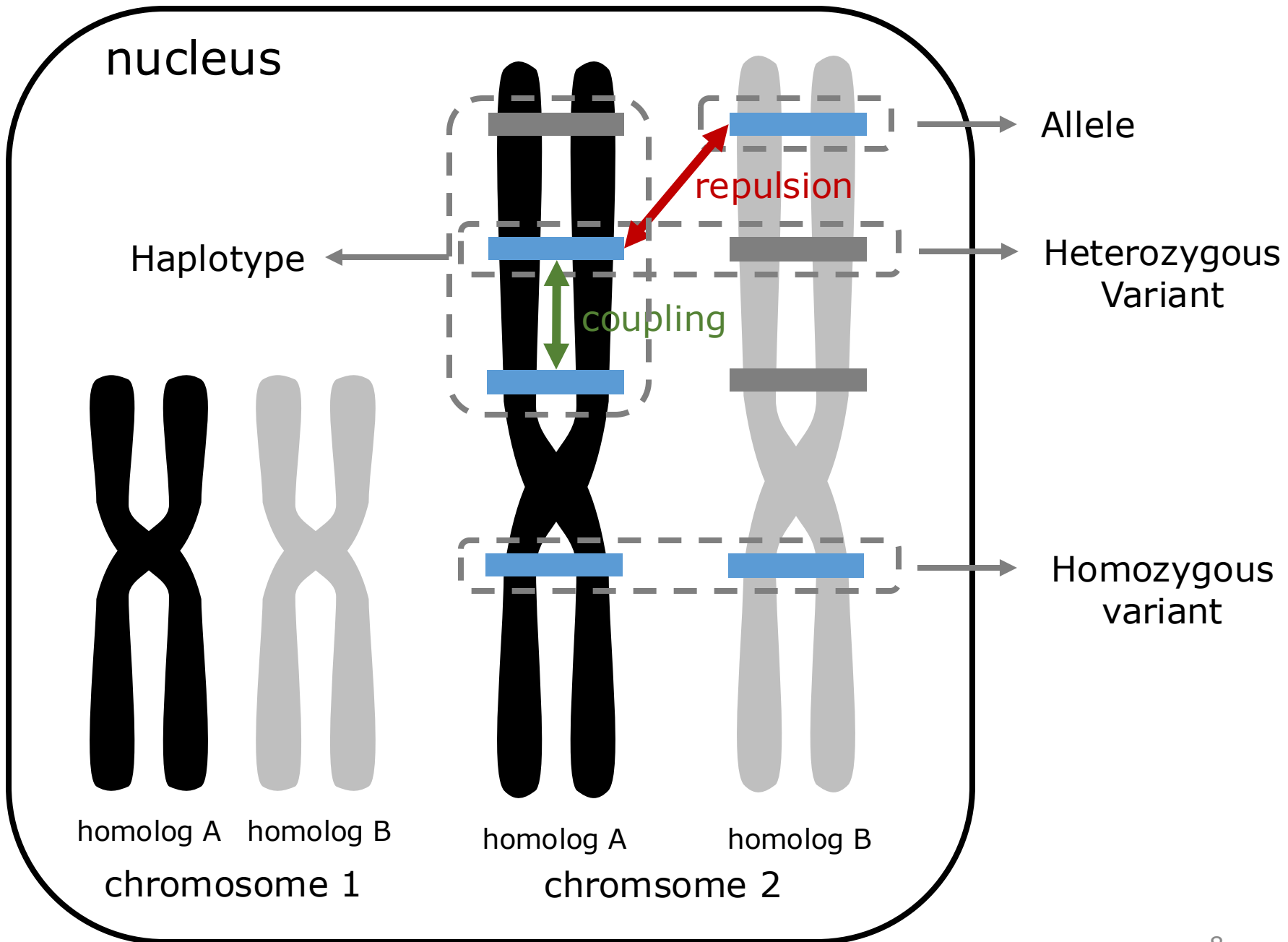
A cluster of chrysanthemum flowers. The flowers are in various stages of bloom, with some showing a mix of white and pink petals, and one prominent flower in the center with bright yellow petals. The background is a dark, out-of-focus green, suggesting foliage.

Question 4

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%)

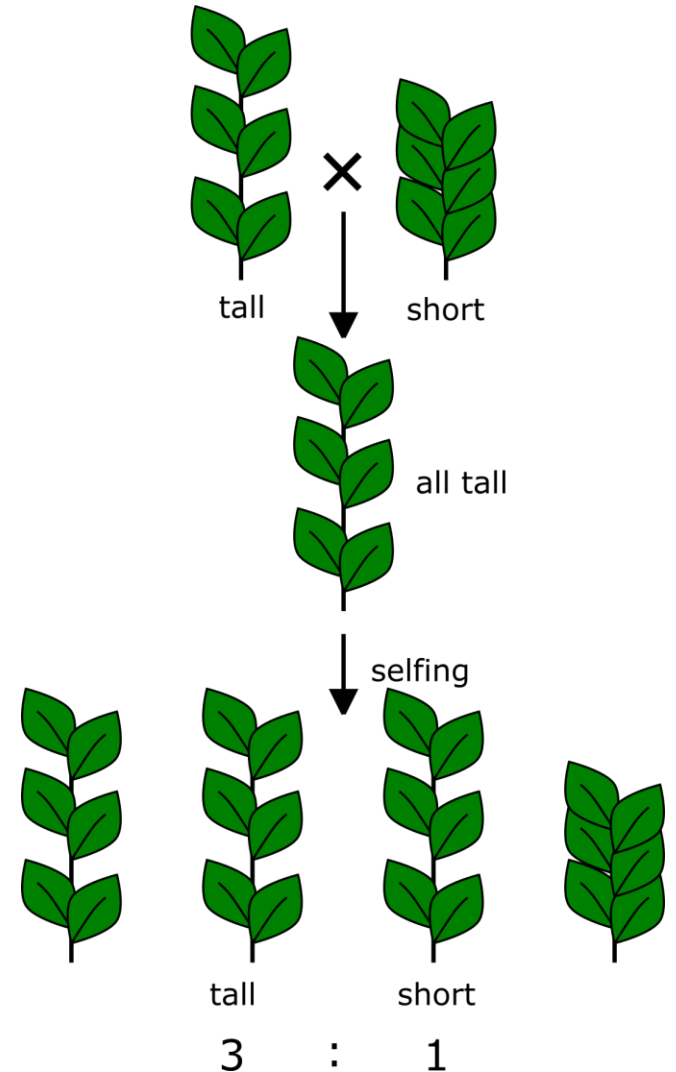
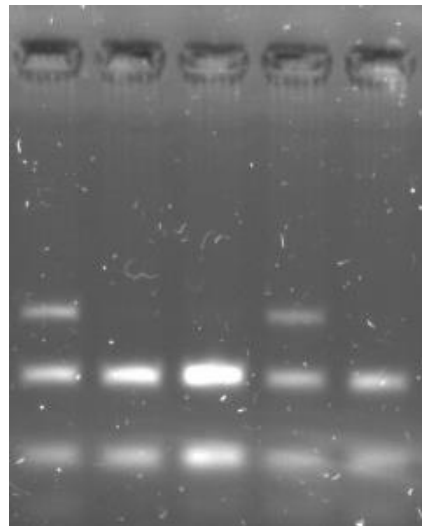
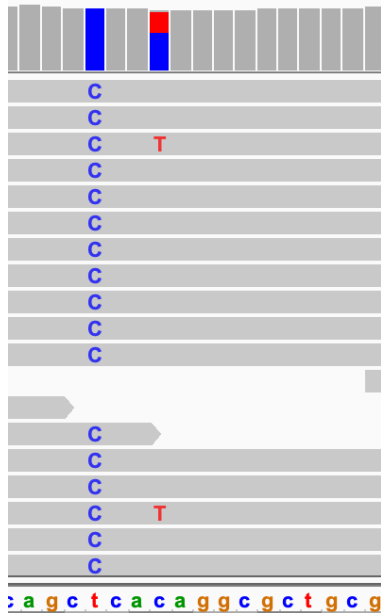
Variant vs polymorphism can be problematic: depends on the population



Question 5

Detecting variants

- Phenotypic analysis
- Molecular analysis
 - Sequencing



Small variants

- Single nucleotide variant (SNV)

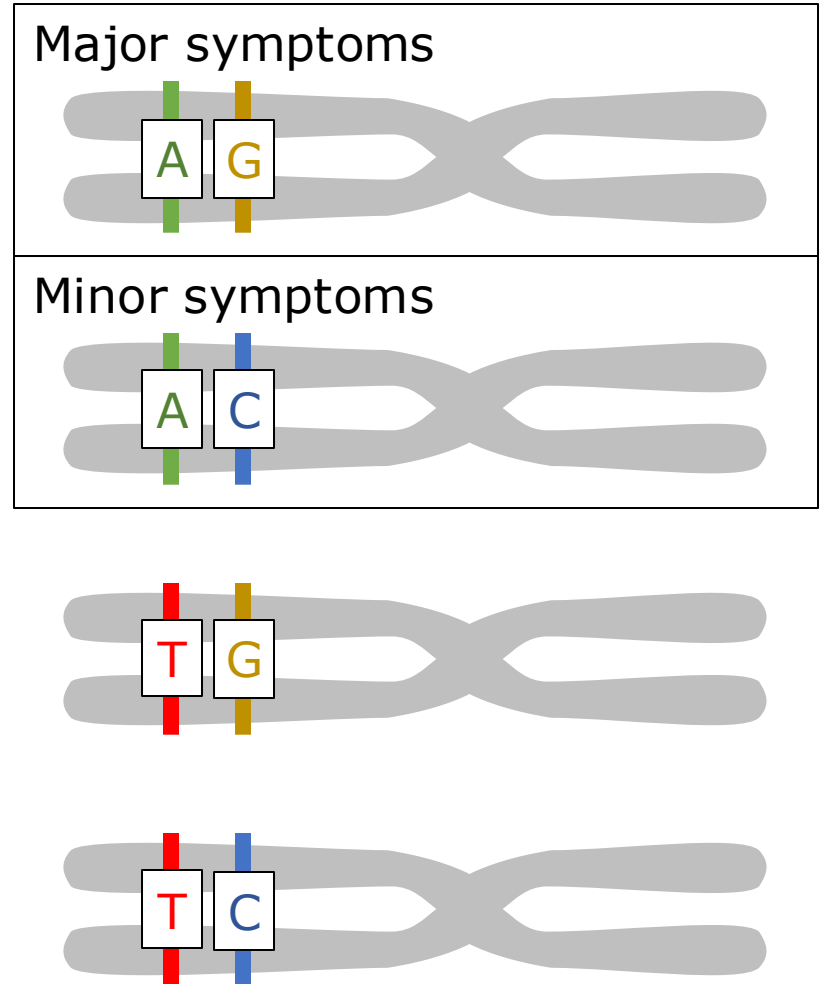
ATCATG**A**CCGTCA
ATCATG**T**CCGTCA

- Insertion/deletion (INDEL)

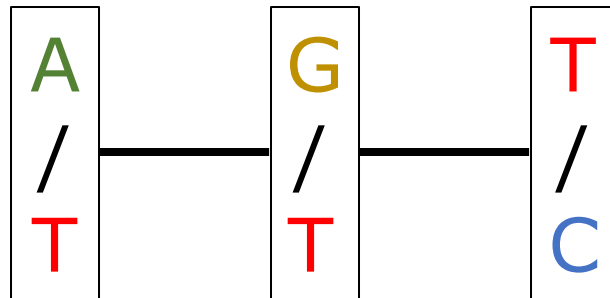
ATCATG**ACC**GTCA
ATCATG**- - -**GTCA

Haplotypes

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

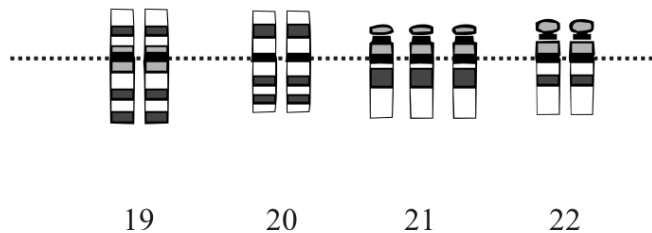


Question 6



Large variants

- Structural variation ($> 1,000$ 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

