*1 round of replication followed by 2 rounds of cell division*

4 Gamete (sperm or egg) cells are produced. These cells are haploid (1n)

**Mitosis:**

- **Interphase:** DNA replication
- **Prophase:** Chromosomes condense
- **Metaphase:** Chromosomes align at the cell's equator
- **Anaphase:** Sister chromatids separate
- **Telophase:** Chromosomes decondense

**Fertilization:**

- **Egg:** Haploid (1n), 1 copy of every chromosome
- **Sperm:** Haploid (1n), 1 copy of every chromosome
- **Zygote:** Diploid (2n), 1 copy of every chromosome from Mom + 1 copy of every chromosome from Dad = 2 total copies of every chromosome

Chromosomally typical humans have 23 unique chromosomes so $n=23$. $2n=46$ total chromosomes

**Euploidy (normal number of chromosomes):**

- $2n$: XX XX XX XX

**Atypical chromosome number:**

This can be a result of non-disjunction (incorrect chromosome splitting in meiosis):

- **Aberrant Euploidy:** Full extra or missing set of all chromosomes
  - $4n$: XX XX XX XX
  - **XX XX XX XX**

- **Aneuploidy:** one or a few extra or missing chromosomes
  - $2n+1$: XXX XX XX XX

**Karyotype:**

A visual representation of all chromosomes in an individual. *Typically shown directly following mitosis (cell division) and so it only has one copy of each chromosome from each parent.*
Each chromosome is comprised of two complementary strands of DNA running antiparallel to each other intertwined in a double helix.

SNP (Single nucleotide polymorphism): A change in DNA sequence where there is a change in one base for another base.

A different allele has a different (yet similar) nucleotide sequence to a wildtype allele. Small changes CAN code for a different protein and thus a different phenotype because it could be in a transcribed region of the DNA, the translated region of the mRNA transcript and could result in a codon that codes for a different amino acid.

*Hint: Only say something is a mutation if you are told it is. Many alleles in present day came from a mutation, but you would not tell that person they are a mutant.*

**Mutations:**

Haplosufficiency: This refers to a gene!

**Haplosufficient:** One wildtype allele is enough to produce the wildtype phenotype.

- The WT allele is dominant to the Mut allele.
- The mut allele is recessive.
- If a gene is haplosufficient, a heterozygous individual will have a wildtype phenotype.

**Haploinsufficient:** One wildtype allele is NOT enough to produce the wildtype phenotype.

- The mut allele is dominant to the WT allele.
- The WT allele is recessive.

**Silent mutation:** changes in nucleotide sequence does not result in a change in amino acid sequence and thus the same protein is made.

**Missense Mutation:** Changes in nucleotide sequence results in a change of one/a few amino acids. This can result in a small change in protein function (a leaky mutation).

**Nonsense mutation:** Changes in nucleotide sequence results in a large change in amino acid sequence and protein length due to a pre-mature stop codon. These result in null mutations which are characterized by the protein having a completely different function.

**Frameshift mutations** (from insertions and deletions) and changes to promoter and terminator regions often cause null mutations.

Each chromosome is comprised of two complementary strands of DNA running antiparallel to each other intertwined in a double helix.
A change in the DNA sequence COULD change the mRNA transcript.
A change in the mRNA transcript COULD change the amino acid sequence.
Mutations can sometimes (not always) result in a change in protein, protein function, and phenotype.

*DNA is read 3’ to 5’ to synthesize a daughter strand of DNA or transcribe a mRNA transcript that is 5’ to 3’.
mRNA is read 5’ to 3’ to translate an amino acid sequence N-terminus to C-terminus.
Leading strand: Continuous, made in the same direction as the fork opens.

Lagging strand: Made in small pieces (Okazaki fragments) because it is made in the opposite direction as the fork opens.

*Every new daughter strand of DNA has a leading and lagging strand*

---

**Transcription:**

**Eukaryotes**

- **Initiation:** TATA box binds near promoters.
- **Elongation:** Transcription factors bind to promoter, RNA polymerase II (RNAP II) is recruited.
- **Termination:** Specific sequence of termination is recognized by sigma factor.

**Prokaryotes**

- **Initiation:** Sigma factor recruits RNA polymerase to the promoter.
- **Elongation:** RNA polymerase synthesizes an mRNA transcript.
- **Termination:** Ribosome recognizes a sequence in the mRNA transcript.

---

**Translation:**

**Eukaryotes**

1. **Initiation:** Small ribosomal subunit (40S) and tRNA (already in P site) recognize S' GTP binds to the ribosome.
2. **Elongation:** The ribosome translates three nucleotides at a time (1 codon) in the A site for charged RNA to check if they are complementary. Complementary tRNA is allowed to stay, the amino acid sequence in the P site is attached to the new amino acid, and tRNA moves to the P site and the uncharged tRNA exits from the E site.
3. **Termination:** Release factor enters the A site when a stop codon is reached. Release factor promotes release of polypeptide, release mRNA transcript, and dissociation of the ribosomal subunits.

**Prokaryotes**

1. **Initiation:** Shine-Dalgarno sequence in mRNA.
2. **Elongation:** The ribosome translates three nucleotides at a time (1 codon) in the A site for charged RNA to check if they are complementary. Complementary tRNA is allowed to stay, the amino acid sequence in the P site is attached to the new amino acid, and tRNA moves to the P site and the uncharged tRNA exits from the E site.
3. **Termination:** Release factor enters the A site when a stop codon is reached. Release factor promotes release of polypeptide, release mRNA transcript, and dissociation of the ribosomal subunits.
### Dihybrid Cross

**Unlinked, un-interacting genes**

<table>
<thead>
<tr>
<th>Phenotypic Class</th>
<th>Complementation</th>
<th>Recessive Epistasis</th>
<th>Dominant Epistasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 phenotypic classes</td>
<td>2 phenotypic classes</td>
<td>3 phenotypic classes</td>
<td>3 phenotypic classes</td>
</tr>
</tbody>
</table>

#### Ratios:

**Parents: AaBb x AaBb**

* Take note of the collapsed phenotypic classes. *

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AaBb</td>
<td>9</td>
</tr>
<tr>
<td>Aabb</td>
<td>1</td>
</tr>
<tr>
<td>aaBb</td>
<td>1</td>
</tr>
<tr>
<td>aabb</td>
<td>1</td>
</tr>
</tbody>
</table>

**Parents: AaBb x aabb**

Dihybrid Test-Cross

Unlinked un-interacting genes

<table>
<thead>
<tr>
<th>Phenotypic Class</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 phenotypic classes</td>
<td></td>
</tr>
<tr>
<td>AaBb</td>
<td>1</td>
</tr>
<tr>
<td>Aabb</td>
<td>1</td>
</tr>
<tr>
<td>aaBb</td>
<td>1</td>
</tr>
<tr>
<td>aabb</td>
<td>1</td>
</tr>
</tbody>
</table>
Pedigrees & Modes of Inheritance:

*Assume that anyone mating into the family is homozygous wildtype. *

- Unaffected man (XY) □
- Affected man □
- Unaffected woman (XX) ○
- Affected woman ○

**Steps for determining mode of inheritance:**

1. Is the mode of inheritance mitochondrial?
   - All affected mothers always pass down the disorder to all offspring regardless of sex.
   - Only mothers can pass down the disorder.
   - No carriers or skipping of generations

2. Is there a sex-bias?
   - If yes, proceed to sex-linked.
   - If no, proceed to autosomal.

* You must state what type of autosomal or sex-linked mode of inheritance it is.
Simply stating “sex-linked” is not a full answer for a mode of inheritance. *

**Autosomal:**

- **Autosomal dominant:**
  - Many affected individuals.
  - No skipping of generations.
  - No carriers.

- **Autosomal recessive:**
  - Fewer affected individuals
  - Skipping of generations and carriers
  - Only homozygous recessive (homozygous mutant) individuals have a mutant phenotype

**Sex-linked:**

- **X-linked dominant:**
  - More females than males affected
  - No carriers or skipping of generations
  - Mothers with a mutant phenotype *COULD* pass the mutation to offspring of either sex
  - Fathers with a mutant phenotype *WILL ALWAYS* pass the mutation to all (and any) daughters.

- **X-linked recessive:**
  - More males than females affected.
  - Females need 2 mutant alleles to show the mutant phenotype.
  - Carriers and skipping of generations possible.
  - Mothers with a mutant phenotype *COULD* pass the mutation to offspring of either sex. Sons of mutant phenotypic mothers will always have a mutant phenotype.
  - Mothers with a mutant phenotype *WILL ALWAYS* pass a mutant allele to all (and any) daughters, but these daughters may have a wildtype allele from mom and be carriers.

- **Y-linked:**
  - Only males can have this disorder.
  - Dads with a mutant phenotype will always pass the disorder to all sons and all sons then will be affected.
  - No carriers or skipping of generations
All newly received DNA enters single stranded and must be incorporated into a plasmid or the chromosome and replicated in order for the recipient cell to keep it. Incorporation into a chromosome requires two recombination events.

**Toxins:**
- **R-Resistant** (Can live with the toxin)
- **S-Susceptible** (Dies in presence of toxin)

**Nutrients:**
- **+**: Functional gene can make nutrient and thus can live even if the nutrient is not available on the plate.
- **-**: Non-functional gene cannot make nutrient and thus needs it in the environment to survive

**Minimal media:** No nutrients or toxins on the plate.
**Full media:** All nutrients are supplied on the plate for the bacteria to use

A bacterium needs all amino acids in order to make proteins. If a bacterium does not have a functional copy of the gene to make each amino acid, it must have those nutrients it cannot make supplemented on the plate to survive. If a toxin/poison is in the environment, a bacteria must be resistant to it in order to survive.

**Steps to figure out if growth of colonies occurs:**
1. State which nutrients are on the plate.
2. Determine which nutrients are absent from the plate.
3. Understand genotypes. A bacteria will only survive if it can make those nutrients that are missing from the plate. (This means it must have a functional gene for these).
4. If there is a toxin/poison on the plate, the bacteria must have a resistance gene to that toxin in order to survive.
### Lac Operon:

<table>
<thead>
<tr>
<th>Regulator gene</th>
<th>Promoter</th>
<th>Operator</th>
<th>Structural Genes</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>P</td>
<td>O</td>
<td>Z Y a</td>
</tr>
<tr>
<td>Codes for repressor protein</td>
<td>RNA Polymerase binding spot</td>
<td>Repressor binding spot</td>
<td>Codes for lactose digesting enzyme</td>
</tr>
</tbody>
</table>

**Steps for Lactase Production Genotype Questions**

1. Check Promoter
   - P - (Non-functional): RNA polymerase can't bind and begin transcription on this strand regardless of the other genes.
2. Check Operator
   - Oc (Operator is constitutively on); Always make protein even with super repressor or absence of lactose as long as there are functional structural genes.
3. Check Repressor gene
   - If I+: No expression of the gene (unless there is an Oc)
   - If I-: Genes are always expressed

*Repressors are trans-acting. They can repress the strand that they are on or another strand*