Objectives

• Describe (in simple terms) Mendel’s basic research method, and discuss the results in the F₁ and F₂ generations.

• List Mendel’s laws and explain what they mean in plain English.

• Define gene, allele, genotype, phenotype, homozygosity, and heterozygosity.

• Explain how autosomal dominant, autosomal recessive, and X-linked recessive inheritance patterns work.

• Using Punnett squares, show the percentages of affected, unaffected, and carrier offspring for each of the above patterns.

• Know how each inheritance pattern appears on a pedigree (and be able to tell, if given a pedigree, which pattern of inheritance is present).
Mendelian Genetics

- Mendel, peas, and genes
- Walt, Teddy, and chromosomes
- Mendelian patterns of disease
Mendelian Genetics

• Mendel, peas, and genes
Gregor (Johann) Mendel
1822 – 1884
Augustinian Abbey of St. Thomas in Brno, Moravia, 1896.
The Abbey today.
In 1856, Mendel began investigating patterns of inheritance in garden peas.
First, he established pea lines with two different forms of a feature – like tall height and short height.
He grew each line for many generations until the line was pure-breeding.
Then, he bred the two lines with each other.

Result:

One form of a feature always concealed the other form.

He called the visible form a dominant trait, and the hidden form a recessive trait.
Then, he allowed the plants to self-fertilize.

Result:

The hidden form reappeared in a small number of plants – always in a 3:1 ratio!
He studied seven plant traits using this method.

<table>
<thead>
<tr>
<th>Flower color</th>
<th>Flower position</th>
<th>Seed color</th>
<th>Seed shape</th>
<th>Pod shape</th>
<th>Pod color</th>
<th>Stem length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purple</td>
<td>Axial</td>
<td>Yellow</td>
<td>Round</td>
<td>Inflated</td>
<td>Green</td>
<td>Tall</td>
</tr>
<tr>
<td>White</td>
<td>Terminal</td>
<td>Green</td>
<td>Wrinkled</td>
<td>Constricted</td>
<td>Yellow</td>
<td>Dwarf</td>
</tr>
</tbody>
</table>

The results were always the same:

\[ F_1 = 100\% \text{ dominant, } F_2 = 75\% \text{ dominant, } 25\% \text{ recessive} \]
In 1865, after experiments with almost 30,000 pea plants, Mendel presented his results to the Natural Science Society in Brno. They published his findings as a paper, “Experiments in Plant Hybridization,” in their Transactions of the Natural Science Society in Brno journal.
Mendel’s Model of Inheritance

1. Features like flower color are controlled by pairs of heritable factors that come in different versions.

   - **genes**: Segments of DNA that carry the information for specific features (like flower color).
   - **alleles**: Different versions of the same gene (one allele carries the info for white flowers, another allele carries the info for purple flowers).
1. Features like flower color are controlled by pairs of heritable factors that come in different versions.

2. One version (the dominant form) can mask the other (the recessive form).

That’s why this happens! Tall is dominant.
So far so good!

P

F₁

F₂

3 tall : 1 short
But what about this?
1. Features like flower color are controlled by pairs of heritable factors that came in different versions.

2. One version (the dominant form) can mask the other (the recessive form).

3. The two paired factors separate during gamete production, and one gamete randomly receives one factor.
Mendel’s Laws

Law of Segregation

When an organism makes gametes, each gamete randomly receives one of that organism’s two alleles.
Mendel’s Model of Inheritance

1. Features like flower color are controlled by pairs of heritable factors that come in different versions.

2. One version (the dominant form) can mask the other (the recessive form).

3. The two paired factors separate during gamete production, and one gamete randomly receives one factor.

4. Factors controlling different features are inherited independently of each other.
One feature (like seed color) did not affect the inheritance pattern of another feature (like seed shape).
Mendel’s Laws

Law of Independent Assortment

The alleles of two different genes get sorted into gametes independently of one another.
Q. Then what happened?
Q. Then what happened?
A. Nothing! Complete silence.
Q. Then what happened?
A. Nothing! Complete silence.

Q. WTF?! Why?
Q. Then what happened?
A. Nothing! Complete silence.

Q. WTF?! Why?
A. Because the “blending model” of inheritance was widely accepted. Also, ego.
<table>
<thead>
<tr>
<th>Blending Model Prediction</th>
<th>Mendel's Actual Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tall x Short</td>
<td>Tall x Short</td>
</tr>
<tr>
<td>All medium</td>
<td>All tall</td>
</tr>
<tr>
<td>self-fertilization</td>
<td>self-fertilization</td>
</tr>
<tr>
<td>All medium</td>
<td>3 tall : 1 short</td>
</tr>
</tbody>
</table>
Mendelian Genetics

- Mendel, peas, and genes
- Walt, Teddy, and chromosomes
Chromosome Theory of Inheritance

“Genes are found on chromosomes. Chromosomes come in pairs, one from mom and one from dad.”

“The way chromosomes behave during meiosis explains why genes are inherited according to Mendel’s laws.”

Walter Sutton
1902 paper

Theodor Boveri
1903 paper
Mendel said genes come in pairs – one from mom, one from dad.

Walt and Teddy said genes are located on chromosomes, which also come in pairs – one from mom, one from dad.
= chromosome from father

= chromosome from mother
Mendel’s law of segregation, explained!

Mendel: each gamete gets one allele.

Walt and Teddy: homologous chromosomes separate in meiosis, so each gamete gets one chromosome (and one allele).
Walt and Teddy: In meiosis, the members of different chromosome pairs are sorted into gametes independently of one another (and therefore, so are their different alleles).
Quick Summary of Mendelian Genetics

- Each trait is encoded by a single gene.
- Each trait has two forms, each encoded by a separate allele.
- One allele is always dominant, and the other is always recessive.
- The phenotypes are always predictable.
Quick Summary of Mendelian Genetics

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>(PP) (homozygous)</td>
<td>Purple</td>
</tr>
<tr>
<td>(Pp) (heterozygous)</td>
<td>Purple</td>
</tr>
<tr>
<td>(Pp) (heterozygous)</td>
<td>Purple</td>
</tr>
<tr>
<td>(pp) (homozygous)</td>
<td>White</td>
</tr>
</tbody>
</table>
Mendelian Genetics

• Mendel, peas, and genes
• Walt, Teddy, and chromosomes
• Mendelian patterns of disease
Many diseases show Mendelian inheritance. Let’s look at how this works with a pretend disease that makes your skin blue.

Assume that:

- The disease is caused by a single mutated gene.
- The mutated allele (B) is dominant, and the normal allele (b) is recessive.
Let’s say there’s a guy with the disease, and we know he’s heterozygous.

His wife doesn’t have the disease.

How many of their kids will have the disease?
According to Mendel’s laws, 50% of the children will inherit the dominant allele, and will have the disease.
Autosomal dominant inheritance
(same family as previous slide)
Pedigree

Autosomal dominant inheritance
(same family as previous slide)
Quick Review: How to Read a Pedigree

Founders = the first mother and father of the kindred

Kindred = the patient’s extended family

Proband = the patient (also called propositus, or index case)
Quick Review: How to Read a Pedigree

- Female
- Male
- Sex unspecified
- Affected
- Heterozygous
- Dead
- Aborted or stillborn

Siblings

Mating

Consanguineous mating

Divorced

Fraternal twins

Identical twins
## Mendelian Inheritance Patterns

<table>
<thead>
<tr>
<th></th>
<th>Dominant</th>
<th>Recessive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal</td>
<td>Autosomal dominant</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td>X-linked</td>
<td>X-linked dominant</td>
<td>X-linked recessive</td>
</tr>
</tbody>
</table>
Autosomal Dominant Inheritance Pattern

50% of children will be affected
Autosomal Dominant Inheritance Pattern

Affected person

Normal

allele

Disease

allele

Unaffected person
Autosomal Recessive Inheritance Pattern

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>b</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>BB</td>
<td>Bb</td>
</tr>
<tr>
<td>b</td>
<td>Bb</td>
<td>bb</td>
</tr>
</tbody>
</table>

**Mom (carrier)**

**Dad (carrier)**

Alleles:
- B = normal
- b = disease

25% of children will be affected
50% will be unaffected carriers
25% will be unaffected non-carriers
Autosomal Recessive Inheritance Pattern

- Affected person
- Unaffected person
- Carrier

Disease allele
Normal allele
X-linked Recessive Inheritance Pattern
Unaffected Dad, Carrier Mom

<table>
<thead>
<tr>
<th></th>
<th>X_1</th>
<th>X_2</th>
</tr>
</thead>
<tbody>
<tr>
<td>X_1</td>
<td>X_1X_1</td>
<td>X_1X_2</td>
</tr>
<tr>
<td>X_2</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

Dad: (unaffected)  
Mom: (carrier)  

Alleles:  
X_1 = normal  
X_2 = disease  

Daughters: 50% unaffected, 50% carriers  
Sons: 50% unaffected, 50% affected
X-linked Recessive Inheritance Pattern

Unaffected Dad, Carrier Mom

Affected person
Unaffected person
Carrier

Disease allele
Normal allele
Wait, why doesn’t a double dose of the X chromosome cause problems in women?

Or, put another way, why doesn’t it cause problems for men to just have one copy of the X chromosome?
Because X-inactivation!

In females, one X chromosome is inactivated (it gets crumpled up into a Barr body).

Early in embryonic development, each cell randomly inactivates one X.

All the cells descending from each of these early cells maintain the same pattern of X-inactivation.
X-inactivation is easy to see in tortoiseshell cats

Genotype

<table>
<thead>
<tr>
<th>Active chromosomes in somatic cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>$X^0Y$</td>
</tr>
<tr>
<td>$X^0Y$</td>
</tr>
<tr>
<td>$X^0X^0$</td>
</tr>
<tr>
<td>$X^0X^0$</td>
</tr>
<tr>
<td>$X^0X^0$</td>
</tr>
</tbody>
</table>

Phenotype

Males

Females

괄 = inactivated X chromosome (Barr body)
Can be used as a quick determination of sex
X-inactivation is often called “lyonization” in honor of Mary F. Lyon, the British geneticist who discovered the process in 1961.
X-linked Recessive Inheritance Pattern
Affected Dad, Unaffected Mom

Mom
(Unaffected)

<table>
<thead>
<tr>
<th></th>
<th>X₁</th>
<th>X₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>X₂</td>
<td>X₁X₂</td>
<td>X₁X₂</td>
</tr>
<tr>
<td>Y</td>
<td>X₁Y</td>
<td>X₁Y</td>
</tr>
</tbody>
</table>

Dad
(Affected)

Daughters: 100% carriers
Sons: 100% unaffected

Alleles: $X₁ = \text{normal}$
$X₂ = \text{disease}$
X-linked Recessive Inheritance Pattern

Affected Dad, Unaffected Mom

Affected person
Unaffected person
Carrier

Disease allele
Normal allele