HERITABLE VARIATION AND PATTERNS OF INHERITANCE

• **Heredity** is the transmission of traits from one generation to the next.

• **Genetics** is the scientific study of heredity

• Gregor Mendel
  – worked in the 1860s,
  – was the first person to analyze patterns of inheritance, and
  – deduced the **fundamental** principles of genetics.
Mendel studied garden peas because they
- were easy to grow,
- came in many readily distinguishable varieties,
- are easily manipulated, and
- can self-fertilize.

1. Removed stamens from purple flower.
2. Transferred pollen from stamens of white flower to carpel of purple flower.
3. Pollinated carpel matured into pod.
4. Planted seeds from pod.

Offspring (F₁)
A character is a heritable feature that varies among individuals.

A trait is a variant of a character.

Each of the characters Mendel studied occurred in two distinct traits.

Mendel

- created purebred varieties of plants and
- crossed two different purebred varieties.
In an Abbey Garden

• **Hybrids** are the offspring of two different purebred varieties.
  – The *parental* plants are the P generation.
  – Their *hybrid* offspring are the F\textsubscript{1} generation.
  – A cross of the F\textsubscript{1} plants forms the F\textsubscript{2} generation.
Mendel’s Law of Segregation

- Mendel tracked the inheritance of characters that occur **as two alternative traits**.
Monohybrid Crosses

- A **monohybrid cross** is a cross between **purebred parent plants** that differ in **only one character**.
P Generation (purebred parents)

Purple flowers × White flowers

F1 Generation

All plants have purple flowers

Fertilization among F1 plants (F1 × F1)

F2 Generation

\[ \frac{3}{4} \text{ of plants have purple flowers} \]
\[ \frac{1}{4} \text{ of plants have white flowers} \]
• Mendel developed four hypotheses from the monohybrid cross, listed here using modern terminology (including “gene” instead of “heritable factor”).

1. The alternative versions of genes are called alleles.

2. For each inherited character, an organism inherits two alleles, one from each parent.
   – An organism is homozygous for that gene if both alleles are identical.
   – An organism is heterozygous for that gene if the alleles are different.
3. If two alleles of an inherited pair differ,
   – then one **determines** the organism’s appearance and is called the **dominant allele** and
   – the other **has no noticeable effect on** the organism’s appearance and is called the **recessive allele**.

4. Gametes carry **only one allele** for each inherited character.
   – This statement is called the **law of segregation**.
Do Mendel’s hypotheses account for the 3:1 ratio he observed in the F₂ generation?

A Punnett square highlights the four possible combinations of gametes and the four possible offspring in the F₂ generation.
Monohybrid Crosses

- Geneticists distinguish between an organism’s **physical appearance** and its **genetic makeup**.
  - An organism’s **physical appearance** is its **phenotype**.
  - An organism’s **genetic makeup** is its **genotype**.

Genetic Alleles and Homologous Chromosomes

- A gene **locus** is a specific location of a gene in the chromosome.

- Homologous chromosomes have **alleles** (alternate versions) of a gene **at the same loci**.
Homologous chromosomes

Gene loci

Dominant allele

Recessive allele

Genotype:
- **PP**
  - Homozygous for the dominant allele
- **aa**
  - Homozygous for the recessive allele
- **Bb**
  - Heterozygous with one dominant and one recessive allele
Mendel’s Law of Independent Assortment

- A **dihybrid cross** is the mating of parental varieties differing in **two** characters.

- What would result from a dihybrid cross? Two hypotheses are possible:
  1. dependent assortment or
  2. independent assortment.
(a) Hypothesis: Dependent assortment

**P Generation**

- **RRYY** (Yellow round)
- **rryy** (Green wrinkled)

Gametes:

- **RY**
- **ry**

**F1 Generation**

- **RrYy**

**F2 Generation**

Predicted results (not actually seen)

(b) Hypothesis: Independent assortment

**F1 Generation**

- **RrYy**

**F2 Generation**

Actual results (support hypothesis)

- **RRYY** (Yellow round)
- **RrYY** (Green round)
- **rrYY** (Yellow wrinkled)
- **rryy** (Green wrinkled)
Mendel’s dihybrid cross supported the hypothesis that each pair of alleles segregates independently of the other pairs during gamete formation.

Thus, the inheritance of one character has no effect on the inheritance of another.

This is called Mendel’s law of independent assortment.
A Monohybrid Cross in Guinea Pigs
Using a Testcross to Determine an Unknown Genotype

• A **testcross** is a mating between
  
  – an individual of **dominant phenotype** (but **unknown genotype**) and
  
  – a **homozygous recessive** individual.
Figure 9.10

Two possible genotypes for the black dog:

Two possible genotypes for the black dog:

- **Genotypes**: $B_$ or $BB$
- **Gametes**: $B$ or $Bb$
- **Offspring**: All black

- **Genotypes**: $bb$
- **Gametes**: $b$
- **Offspring**: 1 black : 1 chocolate
The Rules of Probability

• Mendel’s strong background in mathematics helped him understand patterns of inheritance.

• The rule of multiplication states that the probability of a compound event is the product of the separate probabilities of the independent events.
Figure 9.11

**F₁ Genotypes**

\[ Bb \text{ female} \times Bb \text{ male} \]

**Formation of eggs**

**F₂ Genotypes**

**Male gametes**

\[
\begin{array}{c}
B \\
B \\
\end{array}
\]

\[
\frac{1}{2} \times \frac{1}{2} = \frac{1}{4}
\]

**Female gametes**

\[
\begin{array}{c}
B \\
\frac{1}{2} \\
\end{array}
\]

\[
\begin{array}{c}
b \\
\frac{1}{2} \\
\end{array}
\]

\[
\begin{array}{c}
B \\
\frac{1}{4} \\
\end{array}
\]

\[
\begin{array}{c}
b \\
\frac{1}{4} \\
\end{array}
\]

\[
\begin{array}{c}
B \\
\frac{1}{4} \\
\end{array}
\]

\[
\begin{array}{c}
b \\
\frac{1}{4} \\
\end{array}
\]

\[
\begin{array}{c}
b \\
\frac{1}{4} \\
\end{array}
\]

\[
\begin{array}{c}
b \\
\frac{1}{4} \\
\end{array}
\]

\[
\begin{array}{c}
b \\
\frac{1}{4} \\
\end{array}
\]

\[
\begin{array}{c}
b \\
\frac{1}{4} \\
\end{array}
\]
Figure 9.12

DOMINANT TRAITS

- Freckles
- Widow’s peak
- Free earlobe

RECESSIVE TRAITS

- No freckles
- Straight hairline
- Attached earlobe
Family Pedigrees

• **Dominant traits** are *not necessarily normal or more common.*

• **Wild-type traits** are
  – those seen most often in nature and
  – not necessarily specified by dominant alleles.

• A family **pedigree**
  – shows the **history of a trait** in a family and
  – allows geneticists to **analyze** human traits.
First generation (grandparents)

Second generation (parents, aunts, and uncles)

Third generation (brother and sister)

Female  Male  Attached  Female  Male  Free
Human Disorders Controlled by a Single Gene

• Many human traits
  – show simple inheritance patterns and
  – are controlled by single genes on autosomes.
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Major Symptoms</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recessive Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albinism</td>
<td>Lack of pigment in skin, hair, and eyes</td>
<td>$\frac{1}{22,000}$</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Excess mucus in lungs, digestive tract, liver; increased susceptibility to</td>
<td>$\frac{1}{1,800}$ European Americans</td>
</tr>
<tr>
<td></td>
<td>infections; death in early childhood unless treated</td>
<td></td>
</tr>
<tr>
<td>Phenylketonuria (PKU)</td>
<td>Accumulation of phenylalanine in blood; lack of normal skin pigment; mental</td>
<td>$\frac{1}{100,000}$ in U.S. and Europe</td>
</tr>
<tr>
<td></td>
<td>retardation unless treated</td>
<td></td>
</tr>
<tr>
<td>Sickle-cell disease</td>
<td>Sickled red blood cells; damage to many tissues</td>
<td>$\frac{1}{500}$ African Americans</td>
</tr>
<tr>
<td>Tay Sachs disease</td>
<td>Lipid accumulation in brain cells; mental deficiency; blindness; death in</td>
<td>$\frac{1}{3,500}$ European Jews</td>
</tr>
<tr>
<td></td>
<td>childhood</td>
<td></td>
</tr>
<tr>
<td><strong>Dominant Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Achondroplasia</td>
<td>Dwarfism</td>
<td>$\frac{1}{25,000}$</td>
</tr>
<tr>
<td>Alzheimer's disease (one type)</td>
<td>Mental deterioration; usually strikes late in life</td>
<td>Not known</td>
</tr>
<tr>
<td>Huntington's disease</td>
<td>Mental deterioration and uncontrollable movements; strikes in middle age</td>
<td>$\frac{1}{25,000}$</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>Excess cholesterol in blood; heart disease</td>
<td>$\frac{1}{500}$</td>
</tr>
</tbody>
</table>
Recessive Disorders

• **Most** human genetic disorders are **recessive**.

• Individuals who have the recessive allele but appear normal are **carriers** of the disorder.
Figure 9.14

Parents

Hearing

$Dd$  $Dd$

×

Offspring

Eggs

$D$  $d$

$D$  Hearing

$Dd$  Hearing (carrier)

$Dd$  Hearing (carrier)

$dd$  Deaf

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Cystic fibrosis is

– the most common lethal genetic disease in the United States and

– caused by a recessive allele carried by about one in 31 Americans.

Prolonged geographic isolation of certain populations can lead to inbreeding, the mating of close relatives.

Inbreeding increases the chance of offspring that are homozygous for a harmful recessive trait.
Dominant Disorders

- Some human genetic disorders are dominant.
  - **Achondroplasia** is a form of dwarfism.
    - The homozygous dominant genotype causes death of the embryo.
    - Thus, only heterozygotes have this disorder.
  - Huntington’s disease, which leads to degeneration of the nervous system, does not usually begin until middle age.
Figure 9.16

Parents

Normal (no achondroplasia)  \( dd \)  \( \times \)  Dwarf (achondroplasia)  \( Dd \)

<table>
<thead>
<tr>
<th>Eggs</th>
<th></th>
<th>Eggs</th>
</tr>
</thead>
<tbody>
<tr>
<td>( d )</td>
<td></td>
<td>( d )</td>
</tr>
<tr>
<td>( D )</td>
<td></td>
<td>( D )</td>
</tr>
<tr>
<td>Dwarf</td>
<td></td>
<td>Dwarf</td>
</tr>
<tr>
<td>( dd )</td>
<td></td>
<td>( dd )</td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td>Normal</td>
</tr>
</tbody>
</table>

Molly Jo  
Jeremy  
Jacob  
Zachary  
Matt  
Amy
Genetic Testing

- Today many tests can detect the presence of disease-causing alleles.

- Most genetic tests are performed during pregnancy.
  - Amniocentesis collects cells from amniotic fluid.
  - Chorionic villus sampling removes cells from placental tissue.

- Genetic counseling helps patients understand the results and implications of genetic testing.
VARIATIONS ON MENDEL’S LAWS

• Some patterns of genetic inheritance are not explained by Mendel’s laws

Incomplete Dominance in Plants and People

• In incomplete dominance, F₁ hybrids have an appearance between the phenotypes of the two parents.
Figure 9.18-3

P Generation

Red $RR$

White $rr$

Gametes $R$, $r$

F₁ Generation

Pink $Rr$

Gametes $\frac{1}{2}R$, $\frac{1}{2}r$

F₂ Generation

Sperm $\frac{1}{2}R$, $\frac{1}{2}r$

Eggs $\frac{1}{2}R$, $\frac{1}{2}r$

$RR$, $Rr$, $Rr$, $rr$
ABO Blood Groups: An Example of **Multiple Alleles** and **Codominance**

- The human blood type alleles $I^A$ and $I^B$ are **codominant**, meaning that both alleles are expressed in heterozygous individuals who have type AB blood.

<table>
<thead>
<tr>
<th>Blood Group (Phenotype)</th>
<th>Genotypes</th>
<th>Red Blood Cells</th>
<th>Antibodies Present in Blood</th>
<th>Reactions When Blood from Groups Below Is Mixed with Antibodies from Groups at Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>$I^A I^A$ or $I^A i$</td>
<td><img src="image" alt="Carbohydrate A" /></td>
<td>Anti-B</td>
<td><img src="image" alt="Reactions" /></td>
</tr>
<tr>
<td>B</td>
<td>$I^B iB$ or $I^B i$</td>
<td><img src="image" alt="Carbohydrate B" /></td>
<td>Anti-A</td>
<td><img src="image" alt="Reactions" /></td>
</tr>
<tr>
<td>AB</td>
<td>$I^A iB$</td>
<td><img src="image" alt="Carbohydrate A" /></td>
<td>—</td>
<td><img src="image" alt="Reactions" /></td>
</tr>
<tr>
<td>O</td>
<td>$ii$</td>
<td><img src="image" alt="Carbohydrate B" /></td>
<td>Anti-A Anti-B</td>
<td><img src="image" alt="Reactions" /></td>
</tr>
</tbody>
</table>
Pleiotropy and Sickle-Cell Disease

• Pleiotropy is when one gene influences several characters.

• Sickle-cell disease
  – exhibits pleiotropy,
  – results in abnormal hemoglobin proteins, and
  – causes disk-shaped red blood cells to deform into a sickle shape with jagged edges.
Individual homozygous for sickle-cell allele

Sickle-cell (abnormal) hemoglobin

Abnormal hemoglobin crystallizes into long flexible chains, causing red blood cells to become sickle-shaped.

Sickled cells can lead to a cascade of symptoms, such as weakness, pain, organ damage, and paralysis.
Sickle-cell disease, multiple effects of a single human gene

Individual homozygous for sickle-cell allele

Sickle-cell (abnormal) hemoglobin

Abnormal hemoglobin crystallizes, causing red blood cells to become sickle-shaped

Sickle cells

Breakdown of red blood cells

Physical weakness

Anemia

Heart failure

Pain and fever

Brain damage

Damage to other organs

Spleen damage

Impaired mental function

Paralysis

Pneumonia and other infections

Rheumatism

Kidney failure

Accumulation of sickled cells in spleen

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Polygenic Inheritance

Polygenic inheritance is the **additive effects** of two or more genes on a single phenotype.
The Role of Environment

• Many human characters result from a combination of heredity and environment.

• Only genetic influences are inherited.
Influence of the Environment on Hydrangea Flower Color
THE CHROMOSOMAL BASIS OF INHERITANCE

• The chromosome theory of inheritance states that
  – genes are located at specific positions (loci) on chromosomes and
  – the behavior of chromosomes during meiosis and fertilization accounts for inheritance patterns.

• It is chromosomes that
  – undergo segregation and independent assortment during meiosis and
  – account for Mendel’s laws.
Figure 9.24

P Generation

Round-yellow seeds (RRYY) × Wrinkled-green seeds (rryy)

Gametes

MEIOSIS

FERTILIZATION

F1 Generation

Law of Segregation: Follow the long chromosomes (carrying R and r) taking either the left or right branch.

MEIOSIS

Metaphase I (alternative arrangements)

Law of Independent Assortment: Follow both the long and the short chromosomes.

They are arranged in either of two equally likely ways at metaphase I.

Metaphase II

They sort independently, giving four gamete types.

Gametes

Fertilization recombines the r and R alleles at random.

FERTILIZATION AMONG THE F1 PLANTS

Fertilization results in the 9:3:3:1 phenotypic ratio in the F2 generation.

F2 Generation

9 : 3 : 3 : 1
Linked Genes

- **Linked genes**
  - are located close together on a chromosome and tend to be inherited together.

- **Thomas Hunt Morgan**
  - used the fruit fly *Drosophila melanogaster* and
  - determined that some genes were linked based on the inheritance patterns of their traits.
Dihybrid testcross

Gray body, long wings (wild-type)  
\( GgLl \)  
Female

Black body, short wings (mutant)  
\( ggll \)  
Male

\( GgLl \times ggll \)

Results

Offspring

Gray-long  
\( GgLl \)

Black-short  
\( ggll \)

Gray-short  
\( Ggll \)

Black-long  
\( ggLl \)

965  
944  
206  
185

Parental phenotypes 83%
Recombinant phenotypes 17%
Genetic Recombination: Crossing Over

- Crossing over can
  - separate linked genes,
  - produce gametes with recombinant chromosomes, and produce offspring with recombinant phenotypes. The percentage of recombinant offspring among the total is called the recombination frequency.
Figure 9.27

Parental gametes

Recombinant gametes

Parental (female)  GgLl

Recombinant (male) ggll

Eggs

Fertilization

Offspring

Parental

Recombinant
Linkage Maps

- Early studies of crossing over were performed using the fruit fly *Drosophila melanogaster*.
- Alfred H. Sturtevant, a student of Morgan, developed a method for mapping the relative gene locations, which resulted in the creation of linkage maps.
SEX CHROMOSOMES AND SEX-LINKED GENES

• Sex chromosomes influence the inheritance of certain traits. For example, humans that have a pair of sex chromosomes designated
  – X and Y are male or
  – X and X are female.
Figure 9.29

[Diagram showing the process of sexual reproduction, with labels for male and female gametes and somatic cells, and the resulting offspring with 22+X and 22+Y chromosomes for males and 22+X and 22+XX for females.]
Sex-Linked Genes

- Any gene located on a sex chromosome is called a **sex-linked gene**.
  - Most sex-linked genes are found on the X chromosome.
  - **Red-green colorblindness** is
    - a common human sex-linked disorder and
    - caused by a malfunction of light-sensitive cells in the eyes.
Figure 9.31

(a) Normal female × colorblind male
(b) Carrier female × normal male
(c) Carrier female × colorblind male

Key
- Unaffected individual
- Carrier
- Colorblind individual

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Hemophilia is a sex-linked recessive blood-clotting trait that may result in excessive bleeding and death after relatively minor cuts and bruises.
Figure 9.UN01

Meiosis

Haploid gametes
(allele pairs separate)

Diploid cell
(contains paired alleles, alternate forms of a gene)

Meiosis

Diploid zygote
(contains paired alleles)

Fertilization

Gamete from other parent

Haploid gametes
(allele pairs separate)
Phenotype

Genotype

Phenotype

Conclusion

- All dominant
- 1 dominant : 1 recessive

- Unknown parent is $PP$
- Unknown parent is $Pp$
Figure 9.UN03

Dominant phenotype
(RR)

×

Recessive phenotype
(rr)

Intermediate phenotype
(incomplete dominance)
(Rr)
Pleiotropy

Single gene

Multiple traits (e.g., sickle-cell disease)
Multiple genes

Polygenic inheritance

Single trait (e.g., height)
Figure 9.UN06

Male

44 + XY

Somatic cells

Female

44 + XX

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<table>
<thead>
<tr>
<th></th>
<th>Female: Two alleles</th>
<th>Male: One allele</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genotype</strong></td>
<td>$X^N X^N$</td>
<td>$X^N Y$</td>
</tr>
<tr>
<td><strong>Phenotype</strong></td>
<td>Normal female</td>
<td>Normal male</td>
</tr>
<tr>
<td></td>
<td>$X^N X^n$</td>
<td>$X^n Y$</td>
</tr>
<tr>
<td></td>
<td>Carrier female</td>
<td>Affected female (rare)</td>
</tr>
<tr>
<td></td>
<td>$X^n X^n$</td>
<td></td>
</tr>
</tbody>
</table>