Chapter 14
Mendel and the Gene Idea
Gregor Mendel

- Born and raised on a farm in the Czech Republic (Austria)
- 1840’s entered a monastic lifestyle and studied science
  - During this time many scientists were monks
- In 1857, Mendel began to perform experiments with garden peas to gain an understanding of inheritance
Why peas???

• Breeding could be strictly controlled
  – No random breeding
  – And no self-pollination, the male portions of the flowers were removed prior to maturity
  – Mendel performed cross-pollination
• Peas were removed from pods and Mendel could track the offspring from individual parents
• Lots of varieties of peas
Mendel kept records of:

– Heritable features; **characters**
  • Flower color is a character

– Variants for a character; **traits**
  • Purple flowers *or* white flowers are traits

• Mendel also made sure his projects began with pea varieties that were **true-breeding**
  – self-pollination only produces offspring that are the same variety
• In a typical breeding experiment, Mendel would cross-pollinate two contrasting, true-breeding pea varieties.

– Hybridization
  • Crossing of two true-breeding parents
    – P generation
  • Hybrid offspring represent the first filial generation
    – F₁ generation

– Mendel carried out most of his experiments at least to the F₂ generation
  • Produced by allowing the F₁ generation to self pollinate
• It was this second filial generation where Mendel noticed the fundamental principles of heredity
From these simple experiments Mendel derived:

- Law of segregation
- Law of independent assortment

- Now keep in mind, all of this occurred well before the technology to understand how meiosis worked had been developed!!!

- Some say Mendel got lucky!!!
- Some say Mendel cheated and fudged the data??
- Who knows??!!!
Mendel's model

• Let’s look at one of Mendel’s experiments
• What happened to the white flowers in $F_1$?
• If it were totally lost, then how could white flowers be present in the $F_2$?
• Mendel collected data on the number of offspring
  – $F_2$
    • 705 purple
    • 224 white
    • ~3:1
• Mendel described traits as
  – dominant
  – recessive
Mendel developed a hypothesis to explain the 3:1 inheritance ratios

- **Four concepts to Mendel’s model**
  
  1. Alternative versions of genes account for variations in inherited characters
     - These are called alleles; correspond to loci on chromosomes
  
  2. For each character, an organism inherits two alleles, one from each parent
  
  3. If the two alleles at a locus differ, the dominant allele determines the physical appearance; the recessive allele has no noticeable effect on appearance
  
  4. These alleles for an inherited character separate during gamete formation – **Law of Segregation**
Keep in mind..

• Mendel had no idea about
  – homologous chromosomes
  – where alleles were actually located at loci
Punnett Squares are useful to illustrate likely combinations of alleles.

Also, give insight to ratios and probabilities of offspring with a given

- Genotype – the genetic makeup
- Phenotype – physical appearance
• Phenotype
  – Ratio 3:1

• Genotype
  – **Homozygous**
    • Identical pair of alleles for a gene
    • Homozygous dominant or homozygous recessive
  – **Heterozygous**
    • Two unlike alleles for a gene
  – Ratio
    • 1:2:1
This same principle can also be used to determine if an organism which exhibits a dominant trait (phenotype) is homozygous or heterozygous (genotype) for a given trait.

- **Testcross** is used to make this determination

- **example**
  - We have a pea plant that has purple flowers
    - phenotype = purple
    - Genotype = PP *or* Pp
  - A testcross will be performed using a white flowered mate (white phenotype; must be homozygous recessive genotype, pp)
Dominant phenotype, unknown genotype: $PP$ or $Pp$?

Recessive phenotype, known genotype: $pp$

If $PP$, then all offspring purple:

If $Pp$, then $\frac{1}{2}$ offspring purple and $\frac{1}{2}$ offspring white:
• In these experiments where Mendel tracked a single character all of the $F_1$ offspring produced were hybrids of true-breeding parents for a single character
  – Monohybrids

• In his experiments Mendel tracked seven different characters
<table>
<thead>
<tr>
<th>Character</th>
<th>Dominant Trait</th>
<th>×</th>
<th>Recessive Trait</th>
<th>F₂ Generation</th>
<th>Dominant:Recessive</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flower color</td>
<td>Purple</td>
<td>×</td>
<td>White</td>
<td>705:224</td>
<td></td>
<td>3.15:1</td>
</tr>
<tr>
<td>Flower position</td>
<td>Axial</td>
<td>×</td>
<td>Terminal</td>
<td>651:207</td>
<td></td>
<td>3.14:1</td>
</tr>
<tr>
<td>Seed color</td>
<td>Yellow</td>
<td>×</td>
<td>Green</td>
<td>6022:2001</td>
<td></td>
<td>3.01:1</td>
</tr>
<tr>
<td>Seed shape</td>
<td>Round</td>
<td>×</td>
<td>Wrinkled</td>
<td>5474:1850</td>
<td></td>
<td>2.96:1</td>
</tr>
<tr>
<td>Pod shape</td>
<td>Inflated</td>
<td>×</td>
<td>Constricted</td>
<td>882:299</td>
<td></td>
<td>2.95:1</td>
</tr>
<tr>
<td>Pod color</td>
<td>Green</td>
<td>×</td>
<td>Yellow</td>
<td>428:152</td>
<td></td>
<td>2.82:1</td>
</tr>
<tr>
<td>Stem length</td>
<td>Tall</td>
<td>×</td>
<td>Dwarf</td>
<td>787:277</td>
<td></td>
<td>2.84:1</td>
</tr>
</tbody>
</table>
Law of Independent Assortment

• To derive his second law, Mendel had to track two characters at one time
• Used two true-breeding pea varieties
  • yellow round seeds (YYRR) x green wrinkled seeds (yyrr)
  • The F₁ offspring are known as dihybrids
    – YyRr genotype; yellow round seeds phenotypes
• When the dihybrid cross is performed, the phenotypical ratio of 3:1 is not seen
• This means that the alleles are segregated or separated at some point
• This illustrates the **law of independent assortment**
  – Each pair of alleles segregates independently of other pairs of alleles during gamete formation
P Generation

YYRR

Gametes

YR

×

yr

F₁ Generation

Hypothesis of dependent assortment

Hypothesis of independent assortment

YyRr

F₂ Generation (predicted offspring)

Eggs

1/2 YR

1/2 yr

1/4 YyRr

1/4 yyyrr

1/4 YyRr

1/4 yyrr

Phenotypic ratio 3:1

Sperm

1/4 YR

1/4 Yr

1/4 yR

1/4 yr

Eggs

YYRR

YYRr

YyRR

YyRr

YYrr

YyRr

Yyrr

Phenotypic ratio 9:3:3:1

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Mendel was lucky!!

• He chose – characters with alleles located on different chromosomes – not homologous chromosomes
  – Genes located near each other on the same chromosome tend to be inherited together and have more complex patterns of inheritance

• He chose – characters which exhibited complete dominance of one allele over another

• He chose characters controlled by only two alleles; no multiple alleles
Spectrum of dominance

• Complete dominance
  – The dominant allele determines phenotype over recessive allele
  – Ex: purple vs. white pea flowers
Spectrum of dominance

• Codominance
  – Both alleles affect the phenotype in separate distinguishable ways
  – EX: MN blood groups

  • Not blood type!!!!!!!
  – Codominant alleles for the synthesis of two specific glycoproteins
    – Individuals that are MM have RBC with M glycoproteins
    – Individuals that are NN have RBC with N glycoproteins
    – Individuals that are MN have RBC with both M and N glycoproteins
Spectrum of dominance

- Incomplete dominance
  - Alleles for some characters fall in the middle of the spectrum of dominance; phenotype represents a ‘blending’ of the two parental varieties
  - EX: snapdragon flower color
  - $F^2$ ratio 1:2:1
Multiple alleles

- More than two alleles control the phenotype

- **EX: Human blood type**
  - There are four possible phenotypes
    - A, B, AB, O
  - There are three alleles for the enzyme (I) that attaches the A or B carbohydrate to the RBC
    - $I^A$, $I^B$ or i (neither)
  - Matching blood type is essential!
    - If a person with type A blood receives blood from type B or AB their immune system attacks the cells with the B and can cause clumps/clots
    - AB – universal recipient
    - O – universal donor

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Phenotype (Blood Group)</th>
<th>Red Blood Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>$I^A I^A$ or $I^A i$</td>
<td>A</td>
<td><img src="https://via.placeholder.com/150" alt="A RBC" /></td>
</tr>
<tr>
<td>$I^B I^B$ or $I^B i$</td>
<td>B</td>
<td><img src="https://via.placeholder.com/150" alt="B RBC" /></td>
</tr>
<tr>
<td>$I^A I^B$</td>
<td>AB</td>
<td><img src="https://via.placeholder.com/150" alt="AB RBC" /></td>
</tr>
<tr>
<td>$i i$</td>
<td>O</td>
<td><img src="https://via.placeholder.com/150" alt="O RBC" /></td>
</tr>
</tbody>
</table>
So far we have treated inheritance as though each gene effects one character…

• This is not the norm.
• Most genes have multiple phenotypic effects
  – Pleiotropy

  – Pleiotropic alleles are responsible for multiple symptoms associated with some hereditary diseases
    • Cystic fibrosis
    • Sickle-cell disease (sickle-celled anemia)
Cystic fibrosis

- The most common lethal genetic disorder in the USA
- Most common in European lineages
- It is a recessively inherited disorder
  - Must be homozygous recessive)
- It is estimated that 1 in 25 Americans of European descent are **carriers** (heterozygotes) and have normal phenotypes
  - Normal allele codes for membrane protein that functions in chloride transport across mucous membranes
  - Homozygous recessive phenotypes exhibit multiple (pleiotropic) effects
    - Poor absorption of nutrients
    - Chronic bronchitis
    - Untreated is usually lethal before age 5 or 6
    - Aggressive treatment with antibiotics can allow for survival into early adult hood
Sickle-cell disease

• Most common in African lineages
  – Estimated that it affects 1 in 400 African Americans
• Recessively inherited disorder
• Homozygotes have malformed RBC due to slight change in hemoglobin protein
  – Poor oxygen transport
  – Irregular clotting/clumping of sickle shaped cells
  – Pleiotropic effects
  – Also exhibits incomplete dominance; heterozygotes (about 1 in 10 African Americans) may suffer some reduced symptoms
  – Why so common???
    • Possible link to malaria
      – Malarial parasite not able to infect sickle-shaped cells
Epistasis

• A gene at one locus alters the phenotypic expression of a gene at another locus
  – “Stop gene”
  – Example
    • Hair color in many mammals
      – Black (B) is dominant to brown (b)
        » So to have brown fur \( \rightarrow \) bb
      – A second gene determines if pigment will be deposited in the hair; dominant (C) is to have pigment deposition
      – If the mammal is homozygous recessive at the locus for the second gene (cc) then the coat is white regardless of what the first gene’s alleles say
• Note genotypes still 9:3:3:1

• But phenotypes are now 9:3:4!!!
### Sperm

- $1/4 \boxtimes BE$
- $1/4 \boxtimes bE$
- $1/4 \boxtimes Be$
- $1/4 \boxtimes be$

### Eggs

<table>
<thead>
<tr>
<th>Sperm Combination</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>$BBEE$</td>
<td>Golden</td>
</tr>
<tr>
<td>$BbEE$</td>
<td>Black</td>
</tr>
<tr>
<td>$BBee$</td>
<td>Black</td>
</tr>
<tr>
<td>$bbEE$</td>
<td>Black</td>
</tr>
<tr>
<td>$BbEe$</td>
<td>Chocolate</td>
</tr>
<tr>
<td>$bbee$</td>
<td>Yellow</td>
</tr>
<tr>
<td>$Bbee$</td>
<td>Black</td>
</tr>
<tr>
<td>$bbee$</td>
<td>Yellow</td>
</tr>
</tbody>
</table>

**Ratio:** 9 Black : 3 Chocolate : 4 Yellow
Polygenic inheritance

• Effect of two or more genes on a single phenotype
  – Opposite of pleiotropy

• Example
  – Skin pigmentation in humans
    • At least three separate genes
    • From gradations in phenotypic expression
Not all human genetic disorders are recessive

- **Achondroplasia** – form of dwarfism
  - 99.99% of population is homozygous recessive
  - About 1: 250,000 exhibit phenotype
    - (AA or Aa)

- **Huntington’s disease**
  - Degenerative disease of nervous system
  - Usually fatal by age 40
  - Approx 1 in 10,000 in USA
These and other genetic disorders have lead to many advances in genetic testing and counseling.

- **Amniocentesis** - testing of amniotic fluid
  - Can test fetal cells or presence of chemicals in fluid
• Chorionic villus sampling (CVS)
  – Tests a sample of tissue from placenta
  • Faster than amniocentesis
It is important to ponder…

• Are we who we are because of our genes?
  – nature

• Are we who we are because of our environment?
  – nurture
It is important to ponder...

• Nature vs. Nurture
• Even identical twins differ slightly (or markedly)
• Generally many factors (both genetic and environmental) affect phenotype – **multifactorial**