Extensions of Mendelian Genetics

(CHAPTER 4- Brooker Text)

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BIO 184
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Lethal Alleles

• **Essential genes** are those that are absolutely required for survival
  – The absence of their protein product leads to a lethal phenotype

• **Nonessential genes** are those not absolutely required for survival

• A **lethal allele** is one that has the potential to cause the death of an organism
  – These alleles are typically the result of mutations in essential genes
  – They are usually inherited in a recessive manner
Some lethal alleles exert their effect later in life

= Late age of onset

e.g. Huntington disease (progressive degeneration of the nervous system, dementia and early death; onset between 30-50 yrs old)

• **Conditional lethal alleles** may kill an organism only when certain environmental conditions prevail
  – **Temperature-sensitive (ts) lethals**
    • A developing *Drosophila* larva may be killed at 30 C
    • But it will survive if grown at 22 C

• **Semilethal alleles**
  – Kill some individuals in a population, not all of them
  – Environmental factors and other genes may help prevent the detrimental effects of semilethal genes

• In a simple dominant/recessive relationship, the recessive allele does not affect the phenotype of the heterozygote
  – So how can the wild-type phenotype of the heterozygote be explained?

• There are two possible explanations
  – 1. 50% of the normal protein is enough to accomplish the protein’s cellular function
  – 2. The heterozygote may actually produce more than 50% of the functional protein
    • The normal gene is “up-regulated” to compensate for the lack of function of the defective allele
Incomplete Dominance

- In **incomplete dominance** the heterozygote exhibits a phenotype that is intermediate between the corresponding homozygotes

- Example:
  - Flower color in the four o’clock plant
  - Two alleles
    - $C^R = \text{wild-type allele for red flower color}$
    - $C^W = \text{allele for white flower color}$

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<table>
<thead>
<tr>
<th>Genotype</th>
<th>$PP$</th>
<th>$Pp$</th>
<th>$pp$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount of functional protein $P$</td>
<td>100%</td>
<td>50%</td>
<td>0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Purple</th>
<th>Purple</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple dominant/ recessive relationship</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
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In this case, 50% of the $C^p$ protein is not sufficient to produce the red phenotype.

Example of Lethality and Incomplete Dominance

Creeper chicken = shortened legs and creep along
this is a incomplete dominant trait
heterozygotes are Creeper individuals
but homozygote condition is lethal

What are the phenotypic ratios of the following crosses?
Creeper x Normal  
Creeper x Creeper
Multiple Alleles (3 or more alleles)

- An interesting example is coat color in rabbits
  - Four different alleles
    - C (full coat color)
    - $c^{ch}$ (chinchilla pattern of coat color)
      - Partial defect in pigmentation
    - $c^h$ (himalayan pattern of coat color)
      - Pigmentation in only certain parts of the body
    - c (albino)
      - Lack of pigmentation
  - The dominance hierarchy is as follows:
    - $C > c^{ch} > c^h > c$
• The himalayan pattern of coat color is an example of a temperature-sensitive conditional allele

  – The enzyme encoded by this gene is functional only at low temperatures
    • Therefore, dark fur will only occur in cooler areas of the body
    • This is also the case in the Siamese pattern of coat color in cats
    • Refer to Figures 4.4c and 4.5

• The ABO blood group provides another example of multiple alleles

  • It is determined by the type of antigen present on the surface of red blood cells
    – Antigens are substances that are recognized by antibodies produced by the immune system

  • There are three different types of antigens found on red blood (Table 4.3)
    – Antigen A, which is controlled by allele \( I^A \)
    – Antigen B, which is controlled by allele \( I^B \)
    – Antigen O, which is controlled by allele \( i \)
Allele $i$ is recessive to both $I^A$ and $I^B$

Alleles $I^A$ and $I^B$ are codominant

- They are both expressed in a heterozygous individual

For safe blood transfusions to occur, the donor’s blood must be an appropriate match with the recipient’s blood

For example, if a type O individual received blood from a type A, type B or type AB blood

- Antibodies in the recipient blood will react with antigens in the donated blood cells (= agglutination and clogging)
Overdominance

- **Overdominance** is the phenomenon in which a heterozygote is more vigorous than both of the corresponding homozygotes
  - It is also called **heterozygote advantage**

- **Example = Sickle-cell anemia**
  - Autosomal recessive disorder
  - Affected individuals produce abnormal form of hemoglobin
  - Two alleles
    - \( Hb^A \) → Encodes the normal hemoglobin, hemoglobin A
    - \( Hb^S \) → Encodes the abnormal hemoglobin, hemoglobin S

- \( Hb^S Hb^S \) individuals have red blood cells that deform into a sickle shape under conditions of low oxygen tension
  - This has two major ramifications
    - 1. Sickling phenomenon greatly shortens the life span of the red blood cells
      - Anemia results
    - 2. Odd-shaped cells clump
      - Partial or complete blocks in capillary circulation

  - Thus, affected individuals tend to have a shorter life span than unaffected ones
• The sickle cell allele has been found at a fairly high frequency in parts of Africa where malaria is found
  – How come?

• Malaria is caused by a protozoan, *Plasmodium*
  – This parasite undergoes its life cycle in two main parts
    • One inside the *Anopheles* mosquito
    • The other inside red blood cells
  – Red blood cells of heterozygotes, are likely to rupture when infected by *Plasmodium sp.*
    • This prevents the propagation of the parasite

• Therefore, *Hb\(^A\)Hb\(^S\)* individuals are “better” than
  – *Hb\(^S\)Hb\(^S\)*, because they do not suffer from sickle cell anemia
  – *Hb\(^A\)Hb\(^A\)*, because they are more resistant to malaria