Chapter 15: The Chromosomal Basis of Inheritance

1. Sex Linkage
2. Linked Genes
3. Chromosome Abnormalities
1. Sex Linkage

Chapter Reading – pp. 294-298
Sex Determination

Sex determination in mammals involves the X and Y chromosomes:

\[ XX = \text{female} \]
\[ XY = \text{male} \]

(a) The X-Y system

(b) The X-0 system

(c) The Z-W system

(d) The haplo-diploid system

• other members of the animal kingdom use slightly different systems
Sex Linkage in Mammals

Sex linkage refers to inherited traits for which the inheritance pattern is different for males vs females.

Sex linkage involves genes on the X and Y chromosomes:

- **X-linked** genes are located on the X chromosome
- **Y-linked** genes are located on the Y chromosome

The vast majority of sex linked inheritance is due to X-linked genes since there are many more genes on the X chromosome (~1100) than the Y chromosome (~78)
In 1910, Thomas Hunt Morgan discovered a Drosophila mutant phenotype that appears only in males.

**EXPERIMENT**

<table>
<thead>
<tr>
<th>P Generation</th>
<th>F1 Generation</th>
<th>All offspring had red eyes.</th>
</tr>
</thead>
<tbody>
<tr>
<td>♀</td>
<td>♂</td>
<td></td>
</tr>
<tr>
<td>♀</td>
<td>♂</td>
<td></td>
</tr>
</tbody>
</table>

**RESULTS**

<table>
<thead>
<tr>
<th>F2 Generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>♀</td>
</tr>
</tbody>
</table>
Transmission of X-linked Traits

- females have 2 copies of each allele on the X chromosome and are homozygous or heterozygous
- males have 1 copy of each allele on the X chromosome and are hemizygous
An X-linked Human Trait

Genes on the X chromosome have a unique inheritance pattern in males:

- only 1 allele, so no masking of recessive alleles
- X-linked alleles are always inherited from the mother (carrier)

e.g., Hemophilia is caused by a recessive X-linked allele (h):
X Inactivation in Mammals

In females, the genes on only 1 X chromosome are expressed per cell, the other X chromosome is an inactive Barr body.

- during embryonic development, 1 X chromosome per cell is randomly inactivated
- all daughter cells inherit the same inactive chromosome
2. Linked Genes

Chapter Reading – pp. 292-294, 299-304
Yellow-round seeds (YYRR) × Green-wrinkled seeds (yyrr)

- All F₁ plants produce yellow-round seeds (YyRr).

Meiosis

- Law of Segregation: The two alleles for each gene separate during gamete formation.

- Law of Independent Assortment: Alleles of genes on nonhomologous chromosomes assort independently during gamete formation.

F₁ Generation

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

F₂ Generation

- An F₁ x F₁ cross-fertilization
- Fertilization recombines the R and r alleles at random.
- Fertilization results in the 9:3:3:1 phenotypic ratio in the F₂ generation.

• as we shall see, Mendel’s “Law of Independent Assortment” does not apply to genes on the same chromosome.
Linked Genes

Genes on the same chromosome are said to be linked.

- alleles for linked genes will be inherited together unless crossing over during Prophase I occurs between them.

Gene linkage is indicated when actual ratios of phenotypes deviate from expected ratios, and revealed by doing a test cross…
**Example of Linked Genes**

**EXPERIMENT**

P Generation (homozygous)

Wild type (gray body, normal wings)

\[ b^+ b^+ \text{vg}^+ \text{vg}^+ \]

\[ b^+ b^+ \text{vg}^+ \text{vg}^+ \]

F\textsubscript{1} dihybrid (wild type)

\[ b^+ b^+ \text{vg}^+ \text{vg}^+ \]

\[ b^+ b^+ \text{vg}^+ \text{vg}^+ \]

Testcross offspring

Eggs

\[ b^+ \text{vg}^+ \]

\[ b \text{vg} \]

\[ b^+ \text{vg} \]

\[ b \text{vg}^+ \]

Sperm

\[ b \text{vg} \]

\[ b^+ \text{vg}^+ \]

<table>
<thead>
<tr>
<th>Wild type (gray-normal)</th>
<th>Black-vestigial</th>
<th>Gray-vestigial</th>
<th>Black-normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ b^+ b^+ \text{vg}^+ \text{vg}^+ ]</td>
<td>[ b b \text{vg} \text{vg} ]</td>
<td>[ b^+ b^+ \text{vg}^+ \text{vg}^+ ]</td>
<td>[ b b \text{vg}^+ \text{vg} ]</td>
</tr>
</tbody>
</table>

**PREDICTED RATIOS**

If genes are located on different chromosomes:

1 : 1 : 1 : 1

If genes are located on the same chromosome and parental alleles are always inherited together:

1 : 1 : 0 : 0

**RESULTS**

965 : 944 : 206 : 185
Test Cross reveals Linkage...

Testcross parents

Gray body, normal wings (F₁ dihybrid)
- b⁺ vg⁺
- b⁺ vg
- b vg
- b vg⁺

Black body, vestigial wings (double mutant)
- b vg

Replication of chromosomes

Meiosis I

Meiosis II

Recombinant chromosomes

Eggs
- b⁺ vg⁺
- b vg

Sperm
- b vg

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...results of Test Cross

Testcross offspring

### Eggs
- **965 Wild type (gray-normal)**
- **944 Black-vestigial**
- **206 Gray-vestigial**
- **185 Black-normal**

#### Sperm
- **b vg**

#### Recombinant chromosomes

**Recombination frequency**

\[
\text{Recombination frequency} = \frac{391 \text{ recombinants}}{2,300 \text{ total offspring}} \times 100 = 17\%
\]
Using Recombination Frequencies to Map Genes

Frequency of recombinant chromosomes reflects the relative location of genes.

RESULTS

Recombination frequencies

9%  9.5%  17%

Chromosome

b  cn  vg
A Linkage Map in Drosophila

Mutant phenotypes

<table>
<thead>
<tr>
<th>Short aristae</th>
<th>Black body</th>
<th>Cinnabar eyes</th>
<th>Vestigial wings</th>
<th>Brown eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>48.5</td>
<td>57.5</td>
<td>67.0</td>
<td>104.5</td>
</tr>
</tbody>
</table>

Wild-type phenotypes

Long aristae (appendages on head)

Gray body | Red eyes | Normal wings | Red eyes

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3. Chromosome Abnormalities

Chapter Reading – pp. 304-309
Consequences of Nondisjunction

Meiosis I

Nondisjunction

Meiosis II

Non-disjunction

Gametes

Number of chromosomes

\( n + 1 \) \( n + 1 \) \( n - 1 \) \( n - 1 \)

\( n + 1 \) \( n - 1 \) \( n \) \( n \)

(a) Nondisjunction of homologous chromosomes in meiosis I

(b) Nondisjunction of sister chromatids in meiosis II
Down Syndrome

Trisomy 21

- example of aneuploidy
- due to nondisjunction
Other Chromosomal Aberrations

(a) Deletion

A deletion removes a chromosomal segment.

(b) Duplication

A duplication repeats a segment.

(c) Inversion

An inversion reverses a segment within a chromosome.

(d) Translocation

A translocation moves a segment from one chromosome to a nonhomologous chromosome.
Chromosome Translocation

Translocation is due to the exchange of chromosomal fragments between non-homologous chromosomes.

• when the fusion occurs within a gene involved in cell cycle regulation, the result can be an increased likelihood of cancer.
Genomic Imprinting

Genomic imprinting is when only one allele is expressed for certain autosomal genes while the other is inactive.

- occurs in <1% of mammalian genes
- inactive allele consistently comes from males or females, depending on the gene
- inactivation involves methylation of DNA in gene, modification of histones during gamete formation
(a) Homozygote

Paterna1 chromosome
Normal $Igf2$ allele is expressed.

Materna1 chromosome
Normal $Igf2$ allele is not expressed.

Normal-sized mouse (wild type)

Mutanta1 $Igf2$ allele
inherited from mother

Dwarf mouse (mutant)

Mutanta1 $Igf2$ allele
inherited from father

Normal-sized mouse (wild type)

Normal allele is expressed.

Mutant allele is expressed.

Normal allele is not expressed.

Mutant allele is not expressed.

(b) Heterozygotes

In this example, the paternal allele will always be expressed whereas the maternal will be inactive.

- mutant phenotype will only appear when inherited from the father
Mitochondrial Inheritance

Mitochondria contain their own small circular chromosome containing genes involving in mitochondrial gene expression, energy metabolism.

- human mitochondrial genome is only ~16,000 bp

Mitochondria are inherited almost exclusively from the mother.

- mutations in mitochondrial genes thus follow maternal inheritance and can affect energy metabolism
Key Terms for Chapter 15

- sex-linkage, X-linked, Y-linked, hemizygous
- X-inactivation, Barr body
- linked genes, linkage map
- nondisjunction, aneuploidy, polyploidy
- deletion, duplication, inversion, translocation
- genomic imprinting

Relevant Chapter Questions 1-9, 12