CHAPTER 15: The Chromosomal Basis of Inheritance:
Locating Genes Along Chromosomes
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CONCEPTS:

• 15.2 Sex-linked genes exhibit unique patterns of inheritance
• 15.3 Linked genes tend to be inherited together because they are located near each other on the same chromosome
• 15.4 Alterations of chromosome number or structure cause some genetic disorders
• 15.5 Some normal inheritance patterns are exceptions to the standard Mendelian inheritance
15.1 Mendel’s theories vindicated and accepted

- Mendel’s “hereditary factors” were purely abstract when first proposed
- Today we can show that the factors—genes—are located on chromosomes
- The location of a particular gene can be seen by tagging isolated chromosomes with a fluorescent dye that highlights the gene
15.1 Morgan showed that Mendelian inheritance has its physical basis in the behavior of chromosomes

- The first solid evidence associating a specific gene with a specific chromosome came in the early 20th century from the work of Thomas Hunt Morgan (1866 – 1945)
  - These early experiments provided convincing evidence that the chromosomes are the location of Mendel’s heritable factors
15.2 Sex-linked genes exhibit unique patterns of inheritance

- Morgan’s discovery of a trait that correlated with the gender of flies was *key to the development* of the chromosome theory of inheritance

- In *humans and some other animals*, there is a chromosomal basis of sex determination
15.2 The Chromosomal Basis of Sex

- In humans and other mammals, there are two varieties of sex chromosomes: a larger X chromosome and a smaller Y chromosome.

- A person with two X chromosomes develops as a female, while a male develops from a zygote with one X and one Y.
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- Other organisms have different methods of sex determination.
The SRY gene is on the Y chromosome

- Short segments at the ends of the Y chromosomes are homologous with the X, allowing the two to behave like homologues during meiosis in males

- A gene on the Y chromosome called SRY (sex-determining region on the Y) is responsible for development of the testes in an embryo

- In individuals lacking the SRY gene, the generic embryonic gonads develop into ovaries.
15.2 Inheritance of X-Linked Genes

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15.2 Inheritance of X-Linked Genes

- **X chromosomes** have genes for many *characters unrelated to sex*, whereas most **Y-linked genes** are related to sex determination.

- **X-linked genes** follow specific patterns of inheritance.
  - For a **recessive X-linked trait** to be expressed:
    - A **female** needs *two copies* of the allele (homozygous).
    - A **male** needs *only one* copy of the allele (hemizygous).

- **X-linked recessive disorders are much more common in males than in females.**

The transmission of X-linked recessive traits.
15.2 Inheritance of X-Linked Genes

- Example of disorders caused by recessive alleles on the X chromosome in humans:
  - Color blindness (mostly X-linked)
  - Duchenne muscular dystrophy
  - Hemophilia

- Males can only inherit X-linked traits from their mother
15.2 Although female mammals inherit two X chromosomes, only one X chromosome is active

X-Inactivation in Female Mammals

In mammalian females, one of the two X chromosomes in each cell is randomly inactivated during embryonic development.

- **Murray Barr** noticed that in the nucleus of females, but not males, a darkly staining body is visible.
- It was hypothesized that this was an inactivated X chromosome in females so that there would only be 1 functional copy of X genes – as in males.
- The inactivated X chromosome is called a Barr body:
  - Females with XXX genotype have 2 Barr bodies
  - XXY Males have one Barr body
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X-Inactivation in Female Mammals

In mammalian females, one of the two X chromosomes in each cell is randomly inactivated during embryonic development.

Barr bodies:

- If a female is heterozygous for a particular gene located on the X chromosome, she will be a mosaic for that character.
  - As a consequence, females consist of a mosaic of two types of cells, some with an active paternal X chromosome and others with an active maternal X chromosome.

  - If a female is heterozygous for a sex-linked trait, approximately half her cells will express one allele, and the other half will express the alternate allele.
15.2 Although female mammals inherit two X chromosomes, only one X chromosome is active

- **X inactivation** involves a set of genes that eventually cover one X chromosome with copies of RNA molecules.

- A particular region of each **X chromosome** contains several genes involved in the inactivation process.

- One of the genes called **XIST (X-inactive specific transcript)** is activated on the Barr-body chromosome.
  - Multiple copies of the **XIST RNA product** attach to the X chromosome on which they are made, almost covering it.
  - Interaction of this RNA with the chromosome initiates X inactivation.
15.3 Linked genes tend to be inherited together because they are located near each other on the same chromosome

- Each chromosome has hundreds or thousands of genes (except the Y chromosome)
- Genes located on the same chromosome that tend to be inherited together are called linked genes
  - Gene loci that are close together are more tightly linked
15.3 Linked genes tend to be inherited together because they are located near each other on the same chromosome

- Each chromosome has hundreds or thousands of genes (except the Y chromosome)
- Genes located on the same chromosome that tend to be inherited together are called linked genes
  - Gene loci that are close together are more tightly linked
  - This is because gene loci that are close to each other have less chance of having a cross-over event (during prophase) than those that are far apart

These loci are close together, leaving less chance of a cross-over event
The Chromosomal Basis for Inheritance:

Linked genes tend to be inherited together because they are located near each other on the same chromosome

15.3 Independent assortment of chromosomes produces genetic recombination of unlinked genes

- The genetic findings of Mendel and Morgan relate to the *chromosomal basis of recombination*

- Offspring with a phenotype matching one of the *parental phenotypes* are called *parental types*

- Offspring with nonparental phenotypes (new *combinations* of traits) are called *recombinant types*, or recombinants
The Chromosomal Basis for Inheritance:
Linked genes tend to be inherited together because they are located near each other on the same chromosome

15.3 Crossing over produces genetic recombination of linked genes

- Morgan discovered that genes can be linked, but the linkage was **incomplete**, because some recombinant phenotypes were observed.
- He proposed that **some process** must occasionally break the physical connection between genes on the same chromosome.
  - That mechanism was the **crossing over** of homologous chromosomes.
The Chromosomal Basis for Inheritance:

Linked genes tend to be inherited together because they are located near each other on the same chromosome

15.3 New combinations of alleles provide variation for natural selection

- Recombinant chromosomes bring alleles together in new combinations in gametes
- Random fertilization and Independent Assortment further increase the number of variant combinations that can be produced
- This abundance of genetic variation is the raw material upon which natural selection works
15.4 Alterations of chromosome number or structure cause some genetic disorders

- *Large-scale* chromosomal alterations in humans and other mammals often lead to spontaneous abortions (miscarriages) or cause a variety of developmental disorders

- *Plants* tolerate such genetic changes better than animals do
15.4 Nondisjunction leads to abnormal chromosome number

- In **nondisjunction**, pairs of homologous chromosomes *(or sister chromatids)* do *not separate* normally during meiosis.

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**The Chromosomal Basis for Inheritance:**

*Alterations of chromosome number or structure cause some genetic disorders*
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15.4 Nondisjunction leads to abnormal chromosome number

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[Diagram showing meiosis and nondisjunction]
15.4 Nondisjunction leads to abnormal chromosome number

- In **nondisjunction**, pairs of homologous chromosomes (or sister chromatids) do **not separate** normally during meiosis.

- As a result, **one gamete receives two** of the same type of chromosome, and another gamete receives no copy.
15.4 Nondisjunction leads to abnormal chromosome number

- **Aneuploidy** results from the fertilization of gametes in which nondisjunction occurred
- Offspring with this condition have an abnormal number of a particular chromosome
  - A **monosomic** zygote has only *one copy* of a particular chromosome
  - A **trisomic** zygote has *three copies* of a particular chromosome

✓ **Down Syndrome** results from trisomy of chromosome 21
The Chromosomal Basis for Inheritance:
Alterations of chromosome number or structure cause some genetic disorders

15.4 Human disorders are due to chromosome alterations

Down Syndrome (Trisomy 21)
- **Down syndrome** is an *aneuploid condition* that results from *three copies of chromosome 21*
  - It affects about one out of every 700 children born in the United States
  - The frequency of Down syndrome *increases with the age of the mother*, a correlation that has not been explained
The Chromosomal Basis for Inheritance:
Alterations of chromosome number or structure cause some genetic disorders

15.4 Human disorders are due to chromosome alterations

Klinefelter Syndrome (KS)

- Klinefelter Syndrome is an aneuploid condition that results from two copies of the X chromosome, and one copy of the Y chromosome.
  - The primary features are sterility and small testicles
The phenotypic effects of some mammalian genes depend on whether they are inherited from the mother or the father.

- There are two normal exceptions to Mendelian genetics:
  - One exception involves genes located in the nucleus.
  - The other exception involves genes located outside the nucleus.

- In both cases, the gender of the parent contributing an allele is a factor in the pattern of inheritance.
15.5 The phenotypic effects of some mammalian genes depend on whether they are inherited from the mother or the father

**Genomic Imprinting:**

- For a few mammalian traits, the *phenotype* depends on *which parent* passed along the alleles for those traits
- Such variation in phenotype is called **genomic imprinting**
  - Genomic imprinting involves the *silencing of certain genes* depending on which parent passes them on
  - Silenced (imprinted) genes are inactivated through **DNA methylation** during egg or sperm formation
  - In some cases, histones are methylated instead of DNA
- About 70 different instances of genomic imprinting have been identified in humans

**IGF2 gene** is located on chromosome 11p15.5, a region which contains numerous imprinted genes

**IGF2 inactivation may play a role in the development of Brown Fat**
15.5 The phenotypic effects of some mammalian genes depend on whether they are inherited from the mother or the father

**Genomic Imprinting:**
- For a few mammalian traits, the *phenotype* depends on *which parent* passed along the alleles for those traits
- Mammals should only have one copy of genes that are controlled by imprinting
  - The imprinted gene is generally only of either maternal or paternal origin – this prevents both copies from being inactivated

*IGF2* gene is located on chromosome 11p15.5, a region which contains numerous imprinted genes

*IGF2* inactivation may play a role in the development of Brown Fat
Extranuclear genes exhibit a non-Mendelian pattern of inheritance.

Inheritance of Organelle Genes:

- Extranuclear genes (or cytoplasmic genes) are found in organelles in the cytoplasm.
- **Mitochondria**, **chloroplasts**, and other plant **plastids** carry small circular DNA molecules.
- **Extranuclear genes** are inherited maternally because the *zygote’s cytoplasm comes from the egg*.
- In humans, the 16,569 base pairs of mitochondrial DNA encode **37 genes**.
The Chromosomal Basis for Inheritance:
Some inheritance patterns are exceptions to the standard Mendelian inheritance

15.5 Extranuclear genes exhibit a non-Mendelian pattern of inheritance.

- Some **defects in mitochondrial genes** prevent cells from making enough **ATP** and result in diseases that affect the muscular and nervous systems
- For example, **mitochondrial myopathy** and **Leber’s hereditary optic neuropathy**
The Chromosomal Basis for Inheritance:

Some inheritance patterns are exceptions to the standard Mendelian inheritance

15.5 Extranuclear genes exhibit a non-Mendelian pattern of inheritance.

Inheritance of Organelle Genes:

• Because mitochondrial DNA is always inherited from the mother, it is very useful in determining ancestral lineage