

Overview: Locating Genes Along Chromosomes

- Mendel's "hereditary factors" were genes
- Today we can show that 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

Concept 15.1: Mendelian inheritance has its physical basis in the behavior of chromosomes

- Mitosis and meiosis were first described in the late 1800s
- The **chromosome theory of inheritance** states:
 - Mendelian genes have specific loci (positions) on chromosomes
 - Chromosomes undergo segregation and independent assortment
- The behavior of chromosomes during meiosis can account for Mendel's laws of segregation and independent assortment

Morgan's Experimental Evidence: *Scientific Inquiry*

- The first solid evidence associating a specific gene with a specific chromosome came from Thomas Hunt Morgan, an embryologist
- Morgan's experiments with fruit flies provided convincing evidence that chromosomes are the location of Mendel's heritable factors

Morgan's Choice of Experimental Organism

- Several characteristics make fruit flies a convenient organism for genetic studies
 - They produce many offspring
 - A generation can be bred every two weeks
 - They have only four pairs of chromosomes
- Morgan noted **wild type**, or normal, phenotypes that were common in the fly populations
- Traits alternative to the wild type are called mutant phenotypes

Correlating Behavior of a Gene's Alleles with Behavior of a Chromosome Pair

- In one experiment, Morgan mated male flies with white eyes (mutant) with female flies with red eyes (wild type)
 - The F₁ generation all had red eyes
 - The F₂ generation showed the 3:1 red:white eye ratio, but only males had white eyes
- Morgan determined that the white-eyed mutant allele must be located on the X chromosome
- Morgan's finding supported the chromosome theory of inheritance

Concept 15.2: Sex-linked genes exhibit unique patterns of inheritance

- In humans and some other animals, there is a chromosomal basis of sex determination

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
- Only the ends of the Y chromosome have regions that are homologous with corresponding regions of the X chromosome
- The *SRY* gene on the Y chromosome codes for a protein that directs the development of male anatomical features
- Females are XX, and males are XY
- Each ovum contains an X chromosome, while a sperm may contain either an X or a Y chromosome
- Other animals have different methods of sex determination

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- A gene that is located on either sex chromosome is called a **sex-linked gene**
- Genes on the Y chromosome are called Y-linked genes; there are few of these
- Genes on the X chromosome are called **X-linked genes**

Inheritance of X-Linked Genes

- X chromosomes have genes for many characters unrelated to sex, whereas the Y chromosome mainly encodes genes 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
- Some disorders caused by recessive alleles on the X chromosome in humans
 - **Color blindness (mostly X-linked)**
 - **Duchenne muscular dystrophy**
 - **Hemophilia**

X Inactivation in Female Mammals

- In mammalian females, one of the two X chromosomes in each cell is randomly inactivated during embryonic development
- The inactive X condenses into a **Barr body**
- If a female is heterozygous for a particular gene located on the X chromosome, she will be a mosaic for that character

Concept 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**

How Linkage Affects Inheritance

- Morgan did other experiments with fruit flies to see how linkage affects inheritance of two characters
- Morgan crossed flies that differed in traits of body color and wing size
- Morgan found that body color and wing size are usually inherited together in specific combinations (parental phenotypes)
- He noted that these genes do not assort independently, and reasoned that they were on the same chromosome
- However, nonparental phenotypes were also produced
- Understanding this result involves exploring **genetic recombination**, the production of offspring with combinations of traits differing from either parent

Genetic Recombination and Linkage

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

Recombination of Unlinked Genes: Independent Assortment of Chromosomes

- Mendel observed that combinations of traits in some offspring differ from either parent
- 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**

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- A 50% frequency of recombination is observed for any two genes on different chromosomes

Recombination of Linked Genes: Crossing Over

- 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

New Combinations of Alleles: Variation for Normal Selection

- Recombinant chromosomes bring alleles together in new combinations in gametes
- Random fertilization increases even further the number of variant combinations that can be produced
- This abundance of genetic variation is the raw material upon which natural selection works

Mapping the Distance Between Genes Using Recombination Data: Scientific Inquiry

- Alfred Sturtevant, one of Morgan's students, constructed a **genetic map**, an ordered list of the genetic loci along a particular chromosome
- Sturtevant predicted that *the farther apart two genes are, the higher the probability that a crossover will occur between them and therefore the higher the recombination frequency*
- A **linkage map** is a genetic map of a chromosome based on recombination frequencies
- Distances between genes can be expressed as **map units**; one map unit, or centimorgan, represents a 1% recombination frequency
- Map units indicate relative distance and order, not precise locations of genes
- Genes that are far apart on the same chromosome can have a recombination frequency near 50%
- Such genes are physically linked, but genetically unlinked, and behave as if found on different chromosomes
- Sturtevant used recombination frequencies to make linkage maps of fruit fly genes
- Using methods like chromosomal banding, geneticists can develop cytogenetic maps of chromosomes
- **Cytogenetic maps** indicate the positions of genes with respect to chromosomal features

Concept 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

Abnormal Chromosome Number

- In **nondisjunction**, pairs of homologous chromosomes 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
- **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
- **Polyploidy** is a condition in which an organism has more than two complete sets of chromosomes

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- Triploidy ($3n$) is three sets of chromosomes
- Tetraploidy ($4n$) is four sets of chromosomes
- Polyploidy is common in plants, but not animals
- Polyploids are more normal in appearance than aneuploids

Alterations of Chromosome Structure

- Breakage of a chromosome can lead to four types of changes in chromosome structure
 - **Deletion** removes a chromosomal segment
 - **Duplication** repeats a segment
 - **Inversion** reverses orientation of a segment within a chromosome
 - **Translocation** moves a segment from one chromosome to another

Human Disorders Due to Chromosomal Alterations

- Alterations of chromosome number and structure are associated with some serious disorders
- Some types of aneuploidy appear to upset the genetic balance less than others, resulting in individuals surviving to birth and beyond
- These surviving individuals have a set of symptoms, or syndrome, characteristic of the type of aneuploidy

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

Aneuploidy of Sex Chromosomes

- Nondisjunction of sex chromosomes produces a variety of aneuploid conditions
- Klinefelter syndrome is the result of an extra chromosome in a male, producing XXY individuals
- Monosomy X, called *Turner syndrome*, produces X0 females, who are sterile; it is the only known viable monosomy in humans

Disorders Caused by Structurally Altered Chromosomes

- The syndrome *cri du chat* (“cry of the cat”), results from a specific deletion in chromosome 5
- A child born with this syndrome is mentally retarded and has a catlike cry; individuals usually die in infancy or early childhood
- Certain cancers, including *chronic myelogenous leukemia* (CML), are caused by translocations of chromosomes

Concept 15.5: Some inheritance patterns are exceptions to standard Mendelian inheritance

- There are two normal exceptions to Mendelian genetics
- One exception involves genes located in the nucleus, and the other exception involves genes located outside the nucleus
- In both cases, the sex of the parent contributing an allele is a factor in the pattern of inheritance

Genomic Imprinting

- For a few mammalian traits, the phenotype depends on which parent passed along the alleles for those traits

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- Such variation in phenotype is called **genomic imprinting**
- Genomic imprinting involves the silencing of certain genes that are “stamped” with an imprint during gamete production
- It appears that imprinting is the result of the methylation (addition of —CH₃) of cytosine nucleotides
- Genomic imprinting is thought to affect only a small fraction of mammalian genes
- Most imprinted genes are critical for embryonic development

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
- The first evidence of extranuclear genes came from studies on the inheritance of yellow or white patches on leaves of an otherwise green plant