13 | MODERN UNDERSTANDINGS OF INHERITANCE

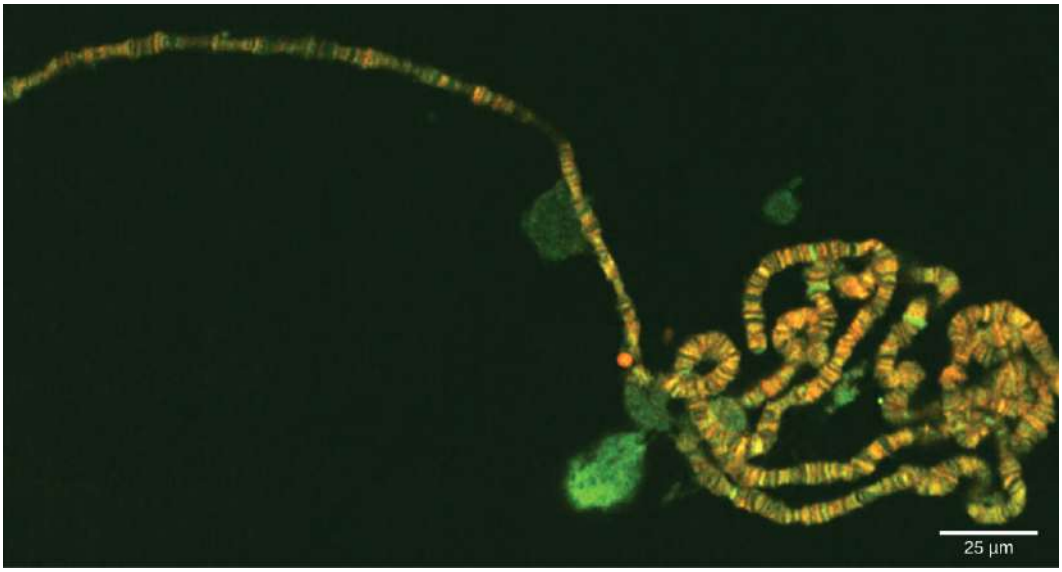


Figure 13.1 Chromosomes are threadlike nuclear structures consisting of DNA and proteins that serve as the repositories for genetic information. The chromosomes depicted here were isolated from a fruit fly's salivary gland, stained with dye, and visualized under a microscope. Akin to miniature bar codes, chromosomes absorb different dyes to produce characteristic banding patterns, which allows for their routine identification. (credit: modification of work by "LPLT"/Wikimedia Commons; scale-bar data from Matt Russell)

Chapter Outline

13.1: Chromosomal Theory and Genetic Linkages

13.2: Chromosomal Basis of Inherited Disorders

Introduction

According to the United Nations Office on Drugs and Crime, approximately 95% of those who commit homicide are men. While behavior is shaped by the environment one grows up and lives in, genetics also play a role. For example, scientists have discovered genes that appear to increase one's tendency to exhibit aggressive behavior. One of the genes, called MAOA, is located on the X chromosome. In one recent study involving a group of male prisoners in Finland, scientists found that the prisoners who inherited a variant of this gene were between 5% and 10% more likely to have committed a violent crime. Men only have one copy of the gene, since men only have one X chromosome. Women, however, have two copies of the X chromosome and therefore two copies of the gene. Therefore, women who inherit the variant allele will most likely also have a normal allele to counteract its effects. It is important to note that many men inherit the variant copy of MAOA and only some commit violent crimes. The environment seems to play a much more critical role. You can read more about nature/nurture roles in crime in this **article (http://openstaxcollege.org/l/32whysomany)** .

13.1 | Chromosomal Theory and Genetic Linkages

In this section, you will explore the following question:

- What is the relationship among genetic linkage, crossing over, and genetic variation?

Connection for AP® Courses

Proposed independently by Sutton and Boveri in the early 1900s, the Chromosomal Theory of Inheritance states that chromosomes are vehicles of genetic heredity. As we have discovered, patterns of inheritance are more complex than Mendel could have imagined. Mendel was investigating the behavior of genes. He was fortunate in choosing traits coded by genes that happened to be on different chromosomes or far apart on the same chromosome. When genes are linked or near each other on the same chromosome, patterns of segregation and independent assortment change. In 1913, Sturtevant devised a method to assess recombination frequency and infer the relative positions and distances of linked genes on a chromosome based on the average number of crossovers between them during meiosis.

The content presented in this section supports the Learning Objectives outlined in Big Idea 3 of the AP® Biology Curriculum Framework. The AP® Learning Objectives merge essential knowledge content with one or more of the seven Science Practices. These objectives provide a transparent foundation for the AP® Biology course, along with inquiry-based laboratory experiences, instructional activities, and AP® exam questions.

Big Idea 3	Living systems store, retrieve, transmit and respond to information essential to life processes.
Enduring Understanding 3.A	Heritable information provides for continuity of life.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**7.1** The student can connect phenomena and models across spatial and temporal scales.
Learning Objective	**3.10** The student is able to represent the connection between meiosis and increased genetic diversity necessary for evolution.
Essential Knowledge	**3.A.3** The chromosomal basis of inheritance provides an understanding of the pattern of passage (transmission) of genes from parent to offspring.
Science Practice	**1.1** The student can create representations and models of natural or man-made phenomena and systems in the domain.
Science Practice	**7.2** The student can connect concepts in and across domain(s) to generalize or extrapolate in and/or across enduring understandings and/or big ideas.
Learning Objective	**3.12** The student is able to construct a representation that connects the process of meiosis to the passage of traits from parent to offspring.

The Science Practice Challenge Questions contain additional test questions for this section that will help you prepare for the AP exam. These questions address the following standards:
[APLO 3.2][APLO 3.11][APLO 3.14][APLO 3.15][APLO 3.28][APLO 3.26][APLO 3.17][APLO 4.22]

Long before chromosomes were visualized under a microscope, the father of modern genetics, Gregor Mendel, began studying heredity in 1843. With the improvement of microscopic techniques during the late 1800s, cell biologists could stain and visualize subcellular structures with dyes and observe their actions during cell division and meiosis. With each mitotic division, chromosomes replicated, condensed from an amorphous (no constant shape) nuclear mass into distinct X-shaped bodies (pairs of identical sister chromatids), and migrated to separate cellular poles.

Chromosomal Theory of Inheritance

The speculation that chromosomes might be the key to understanding heredity led several scientists to examine Mendel's publications and re-evaluate his model in terms of the behavior of chromosomes during mitosis and meiosis. In 1902, Theodor Boveri observed that proper embryonic development of sea urchins does not occur unless chromosomes are present. That same year, Walter Sutton observed the separation of chromosomes into daughter cells during meiosis (**Figure 13.2**). Together, these observations led to the development of the **Chromosomal Theory of Inheritance**, which identified chromosomes as the genetic material responsible for Mendelian inheritance.

Figure 13.2 (a) Walter Sutton and (b) Theodor Boveri are credited with developing the Chromosomal Theory of Inheritance, which states that chromosomes carry the unit of heredity (genes).

The Chromosomal Theory of Inheritance was consistent with Mendel's laws and was supported by the following observations:

- During meiosis, homologous chromosome pairs migrate as discrete structures that are independent of other chromosome pairs.
- The sorting of chromosomes from each homologous pair into pre-gametes appears to be random.
- Each parent synthesizes gametes that contain only half of their chromosomal complement.
- Even though male and female gametes (sperm and egg) differ in size and morphology, they have the same number of chromosomes, suggesting equal genetic contributions from each parent.
- The gametic chromosomes combine during fertilization to produce offspring with the same chromosome number as their parents.

Despite compelling correlations between the behavior of chromosomes during meiosis and Mendel's abstract laws, the Chromosomal Theory of Inheritance was proposed long before there was any direct evidence that traits were carried on chromosomes. Critics pointed out that individuals had far more independently segregating traits than they had chromosomes. It was only after several years of carrying out crosses with the fruit fly, *Drosophila melanogaster*, that Thomas Hunt Morgan provided experimental evidence to support the Chromosomal Theory of Inheritance.

Genetic Linkage and Distances

Mendel's work suggested that traits are inherited independently of each other. Morgan identified a 1:1 correspondence between a segregating trait and the X chromosome, suggesting that the random segregation of chromosomes was the physical basis of Mendel's model. This also demonstrated that linked genes disrupt Mendel's predicted outcomes. The fact that each chromosome can carry many linked genes explains how individuals can have many more traits than they have chromosomes. However, observations by researchers in Morgan's laboratory suggested that alleles positioned on the same chromosome were not always inherited together. During meiosis, linked genes somehow became unlinked.

Homologous Recombination

In 1909, Frans Janssen observed chiasmata—the point at which chromatids are in contact with each other and may exchange segments—prior to the first division of meiosis. He suggested that alleles become unlinked and chromosomes physically exchange segments. As chromosomes condensed and paired with their homologs, they appeared to interact at distinct points. Janssen suggested that these points corresponded to regions in which chromosome segments were exchanged. It is now known that the pairing and interaction between homologous chromosomes, known as synapsis, does more than

simply organize the homologs for migration to separate daughter cells. When synapsed, homologous chromosomes undergo reciprocal physical exchanges at their arms in a process called **homologous recombination**, or more simply, "crossing over."

To better understand the type of experimental results that researchers were obtaining at this time, consider a heterozygous individual that inherited dominant maternal alleles for two genes on the same chromosome (such as *AB*) and two recessive paternal alleles for those same genes (such as *ab*). If the genes are linked, one would expect this individual to produce gametes that are either *AB* or *ab* with a 1:1 ratio. If the genes are unlinked, the individual should produce *AB*, *Ab*, *aB*, and *ab* gametes with equal frequencies, according to the Mendelian concept of independent assortment. Because they correspond to new allele combinations, the genotypes Ab and aB are **nonparental types** that result from homologous recombination during meiosis. **Parental types** are progeny that exhibit the same allelic combination as their parents. Morgan and his colleagues, however, found that when such heterozygous individuals were test crossed to a homozygous recessive parent (*AaBb* × *aabb*), both parental and nonparental cases occurred. For example, 950 offspring might be recovered that were either *AaBb* or *aabb*, but 50 offspring would also be obtained that were either *Aabb* or *aaBb*. These results suggested that linkage occurred most often, but a significant minority of offspring were the products of recombination.

visual CONNECTION

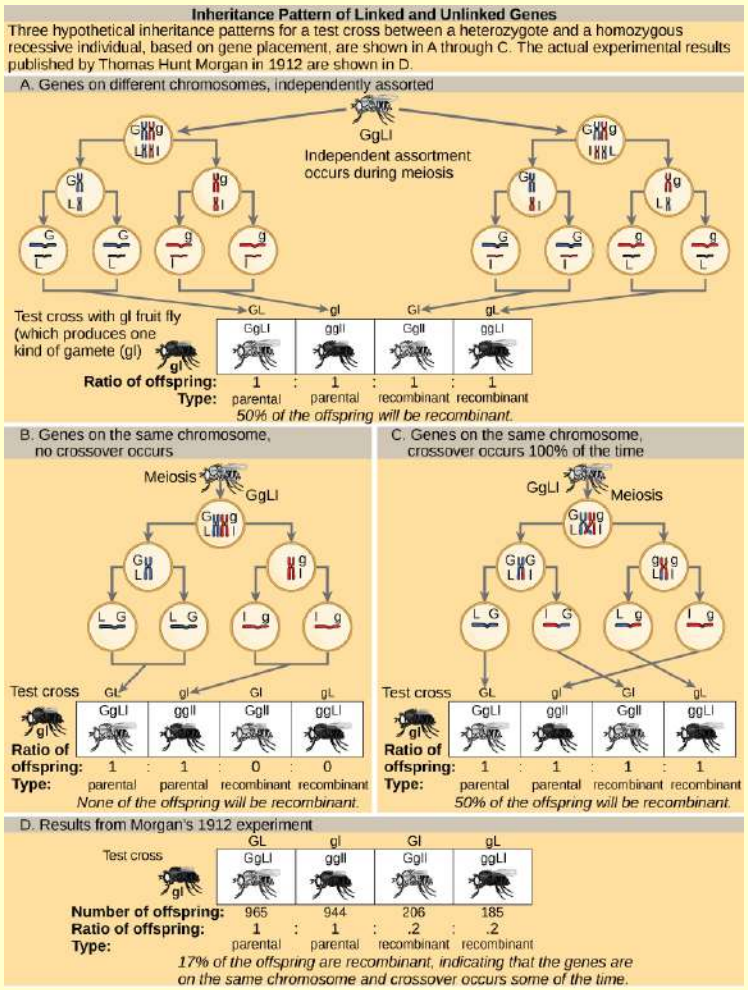


Figure 13.3 Inheritance patterns of unlinked and linked genes are shown. In (a), two genes are located on different chromosomes so independent assortment occurs during meiosis. The offspring have an equal chance of being the parental type (inheriting the same combination of traits as the parents) or a nonparental type (inheriting a different combination of traits than the parents). In (b), two genes are very close together on the same chromosome so that no crossing over occurs between them. The genes are therefore always inherited together and all of the offspring are the parental type. In (c), two genes are far apart on the chromosome such that crossing over occurs during every meiotic event. The recombination frequency will be the same as if the genes were on separate chromosomes. (d) The actual recombination frequency of fruit fly wing length and body color that Thomas Morgan observed in 1912 was 17 percent. A crossover frequency between 0 percent and 50 percent indicates that the genes are on the same chromosome and crossover occurs some of the time.

In a test cross for two characteristics such as the one shown here, can the predicted frequency of recombinant offspring be 60% ? Why or why not?

a. Yes, the predicted offspring frequencies range from 0% to 100%
b. No, the predicted offspring frequencies cannot be higher than 30%.
c. Yes, the predicted offspring frequencies range from 0% to 60%.
d. No, the predicted offspring frequencies range from 0% to 50%.

science practices CONNECTION for AP® Courses

Think About It

A test cross involving F_1 dihybrid flies produces more parental-type offspring than recombinant-type offspring. How can you explain these observed results?

everyday CONNECTION for AP® Courses

Genetic Markers for Cancers

Scientists have used genetic linkage to discover the location in the human genome of many genes that cause disease. They locate disease genes by tracking inheritance of traits through generations of families and creating linkage maps that measure recombination among groups of genetic "markers." The two BRCA genes, mutations which can lead to breast and ovarian cancers, were some of the first genes discovered by genetic mapping. Women who have family histories of these cancers can now be screened to determine if one or both of these genes carry a mutation. If so, they can opt to have their breasts and ovaries surgically removed. This decreases their chances of getting cancer later in life. The actress Angelia Jolie brought this to the public's attention when she opted for surgery in 2014 and again in 2015 after doctors found she carried a mutated BRCA1 gene.

Which of the following statements most accurately describes domestication syndrome?

a. Genes responsible for temperament are on the same chromosome as genes responsible for certain facial features.

b. A single gene codes for both temperament and certain facial features, such as jaw size.

c. Genes responsible for mild temperament are only expressed when genes encoding a cute face are also present.

d. The products of genes encoding temperament interact with the products of genes encoding facial features.

Genetic Maps

Janssen did not have the technology to demonstrate crossing over so it remained an abstract idea that was not widely accepted. Scientists thought chiasmata were a variation on synapsis and could not understand how chromosomes could break and rejoin. Yet, the data were clear that linkage did not always occur. Ultimately, it took a young undergraduate student and an "all-nighter" to mathematically elucidate the problem of linkage and recombination.

In 1913, Alfred Sturtevant, a student in Morgan's laboratory, gathered results from researchers in the laboratory, and took them home one night to mull them over. By the next morning, he had created the first "chromosome map," a linear representation of gene order and relative distance on a chromosome (**Figure 13.4**).

visual CONNECTION

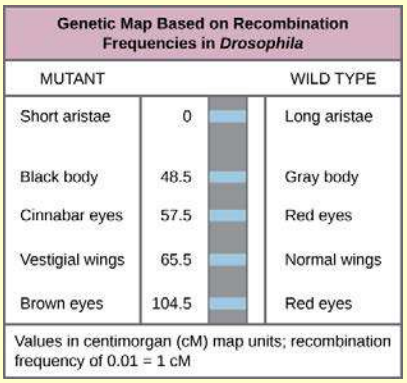


Figure 13.4 This genetic map orders *Drosophila* genes on the basis of recombination frequency.

Which of the following statements is true?

a. Recombination of the red/brown eye and long/short aristae alleles will occur more frequently than recombination of the alleles for wing length and body color.

b. Recombination of the body color and red/cinnabar eye alleles will occur more frequently than recombination of the alleles for wing length and aristae length.

c. Recombination of the body color and aristae length alleles will occur more frequently than recombination of red/brown eye alleles and the aristae length alleles.

d. Recombination of the gray/black body color and long/short aristae alleles will not occur.

As shown in **Figure 13.4**, by using recombination frequency to predict genetic distance, the relative order of genes on chromosome 2 could be inferred. The values shown represent map distances in centimorgans (cM), which correspond to recombination frequencies (in percent). Therefore, the genes for body color and wing size were 65.5 − 48.5 = 17 cM apart, indicating that the maternal and paternal alleles for these genes recombine in 17 percent of offspring, on average.

To construct a chromosome map, Sturtevant assumed that genes were ordered serially on threadlike chromosomes. He also assumed that the incidence of recombination between two homologous chromosomes could occur with equal likelihood anywhere along the length of the chromosome. Operating under these assumptions, Sturtevant postulated that alleles that were far apart on a chromosome were more likely to dissociate during meiosis simply because there was a larger region over which recombination could occur. Conversely, alleles that were close to each other on the chromosome were likely to be inherited together. The average number of crossovers between two alleles—that is, their **recombination frequency**—correlated with their genetic distance from each other, relative to the locations of other genes on that chromosome. Considering the example cross between *AaBb* and *aabb* above, the frequency of recombination could be calculated as 50/1000 = 0.05. That is, the likelihood of a crossover between genes *A/a* and *B/b* was 0.05, or 5 percent. Such a result would indicate that the genes were definitively linked, but that they were far enough apart for crossovers to occasionally occur. Sturtevant divided his genetic map into map units, or **centimorgans (cM)**, in which a recombination frequency of 0.01 corresponds to 1 cM.

By representing alleles in a linear map, Sturtevant suggested that genes can range from being perfectly linked (recombination frequency = 0) to being perfectly unlinked (recombination frequency = 0.5) when genes are on different chromosomes or genes are separated very far apart on the same chromosome. Perfectly unlinked genes correspond to the frequencies predicted by Mendel to assort independently in a dihybrid cross. A recombination frequency of 0.5 indicates that 50 percent of offspring are recombinants and the other 50 percent are parental types. That is, every type of allele combination is represented with equal frequency. This representation allowed Sturtevant to additively calculate distances between several genes on the same chromosome. However, as the genetic distances approached 0.50, his predictions became less accurate because it was not clear whether the genes were very far apart on the same chromosome or on different chromosomes.

In 1931, Barbara McClintock and Harriet Creighton demonstrated the crossover of homologous chromosomes in corn plants. Weeks later, homologous recombination in *Drosophila* was demonstrated microscopically by Curt Stern. Stern

observed several X-linked phenotypes that were associated with a structurally unusual and dissimilar X chromosome pair in which one X was missing a small terminal segment, and the other X was fused to a piece of the Y chromosome. By crossing flies, observing their offspring, and then visualizing the offspring's chromosomes, Stern demonstrated that every time the offspring allele combination deviated from either of the parental combinations, there was a corresponding exchange of an X chromosome segment. Using mutant flies with structurally distinct X chromosomes was the key to observing the products of recombination because DNA sequencing and other molecular tools were not yet available. It is now known that homologous chromosomes regularly exchange segments in meiosis by reciprocally breaking and rejoining their DNA at precise locations.

Review Sturtevant's process to create a genetic map on the basis of recombination frequencies **here (http://openstaxcollege.org/l/gene_crossover)** .

Genetic diversity is the total number of genetic characteristics in a species. Explain how chromosomal crossover contributes to genetic diversity.

a. Chromosomal crossover is a specific, non-random process during which chromosomes are linked together and exchange DNA, contributing to the genetic diversity.

b. Chromosomal crossover occurs during meiosis when chromosome pairs are linked and exchange DNA. Thus, crossover increases the variance of genetic combinations in the haploid gamete cell.

c. Chromosomal crossover results in the inheritance of genetic material by offspring and the recombination event is not variable in frequency or location.

d. Chromosomal crossover occurs during the mitotic process when chromosomes are linked together and recombination takes place, increasing the variance of genetic combinations in the haploid mitotic cells formed from mitosis.

Mendel's Mapped Traits

Homologous recombination is a common genetic process, yet Mendel never observed it. Had he investigated both linked and unlinked genes, it would have been much more difficult for him to create a unified model of his data on the basis of probabilistic calculations. Researchers who have since mapped the seven traits investigated by Mendel onto the seven chromosomes of the pea plant genome have confirmed that all of the genes he examined are either on separate chromosomes or are sufficiently far apart as to be statistically unlinked. Some have suggested that Mendel was enormously lucky to select only unlinked genes, whereas others question whether Mendel discarded any data suggesting linkage. In any case, Mendel consistently observed independent assortment because he examined genes that were effectively unlinked.

13.2 | Chromosomal Basis of Inherited Disorders

In this section, you will explore the following question:

- What are the genetic consequences that result from nondisjunction and errors in chromosome structure through inversions and translocations?

Connection for AP® Courses

The number, size, shape, and banding patterns of chromosomes make them easily identifiable in a karyogram and allows for the assessment of many chromosomal abnormalities. Although the cell cycle, mitosis, and meiosis are highly regulated to

prevent errors, the processes are not perfect. One example is the failure of homologous chromosomes or sister chromatids to separate properly during meiosis I or meiosis II (a phenomenon referred to as nondisjunction). This results in gametes with too many or too few chromosomes. Disorders in chromosome number (aneuploidy) are typically lethal to the embryo, although a few trisomic genotypes are viable (e.g., Down syndrome). Because of X inactivation, aberrations in sex chromosomes typically have milder phenotypic effects (e.g., Turner syndrome) than aneuploidy. Sometimes segments of chromosome are duplicated, deleted, or rearranged by inversion or translocation. These aberrations can result in problematic phenotypic effects. Diagnostic testing can detect many of these chromosomal disorders in individuals well before birth, resulting in medical, ethical, and civic issues, such as the right to privacy.

A condition in which an organism has more than the normal number of chromosome sets (two for diploid species) is called polyploidy. Polyploidy resulting in odd numbers of chromosomes is rare because it results in sterile organisms. One set of chromosomes has no pair so meiosis cannot proceed normally. In contrast, polyploidy resulting in even chromosome numbers is very common in the plant kingdom. Polyploid plants tend to be larger and more robust than individuals with the normal number of chromosomes.

Information presented and the examples highlighted in the section support concepts outlined in Big Idea 3 of the AP® Biology Curriculum Framework. The Learning Objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory experience, instructional activities, and AP® exam questions. A Learning Objective merges required content with one or more of the seven Science Practices.

Big Idea 3	Living systems store, retrieve, transmit and respond to information essential to life processes.
Enduring Understanding 3.A	Heritable information provides for continuity of life.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**6.2** The student can construct explanations of phenomena based on evidence produced through scientific practices.
Learning Objective	**3.9** The student is able to construct an explanation, using visual representations or narratives, as to how DNA in chromosomes is transmitted to the next generation via mitosis, or meiosis followed by fertilization.
Essential Knowledge	**3.A.3** The chromosomal basis of inheritance provides an understanding of the pattern of passage (transmission) of genes from parent to offspring.
Science Practice	**3.1** The student can pose scientific questions.
Learning Objective	**3.13** The student is able to pose questions about ethical, social or medical issues surrounding human genetic disorders.
Big Idea 3	Living systems store, retrieve, transmit and respond to information essential to life processes.
Enduring Understanding 3.C	The processing of genetic information is imperfect and is a source of genetic variation.
Essential Knowledge	**3.A.3** Changes in genotype can result in changes in phenotype.
Science Practice	**6.4** The student can make claims and predictions about natural phenomena based on scientific theories and models.
Science Practice	**7.2** The student can connect concepts in and across domain(s) to generalize or extrapolate in and/or across enduring understandings and/or big ideas.
Learning Objective	**3.24** The student is able to predict how a change in genotype, when expressed as a phenotype, provides a variation that can be subject to natural selection.

Inherited disorders can arise when chromosomes behave abnormally during meiosis. Chromosome disorders can be divided into two categories: abnormalities in chromosome number and chromosomal structural rearrangements. Because even small segments of chromosomes can span many genes, chromosomal disorders are characteristically dramatic and often fatal.

Identification of Chromosomes

The isolation and microscopic observation of chromosomes forms the basis of cytogenetics and is the primary method by which clinicians detect chromosomal abnormalities in humans. A **karyotype** is the number and appearance of chromosomes, and includes their length, banding pattern, and centromere position. To obtain a view of an individual's karyotype, cytologists photograph the chromosomes and then cut and paste each chromosome into a chart, or **karyogram**, also known as an ideogram (**Figure 13.5**).

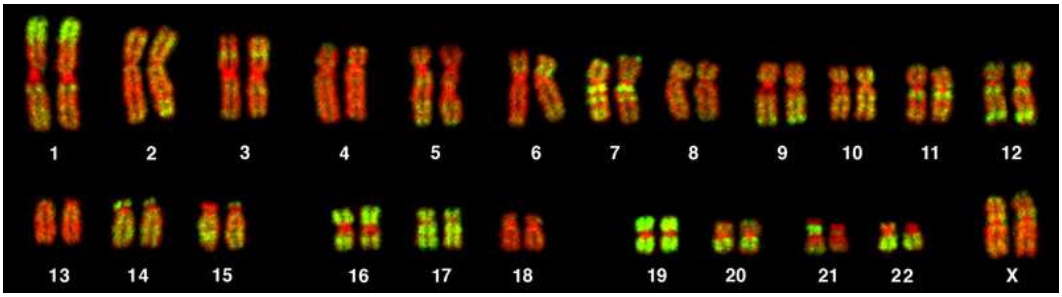


Figure 13.5 This karyotype is of a female human. Notice that homologous chromosomes are the same size, and have the same centromere positions and banding patterns. A human male would have an XY chromosome pair instead of the XX pair shown. (credit: Andreas Blozer et al)

In a given species, chromosomes can be identified by their number, size, centromere position, and banding pattern. In a human karyotype, **autosomes** or "body chromosomes" (all of the non–sex chromosomes) are generally organized in order of size from largest (chromosome 1) to smallest (chromosome 22). (The X and Y chromosomes, the 23rd pair, are not autosomes.) However, chromosome 21 is actually shorter than chromosome 22. This was discovered after the naming of Down syndrome as trisomy 21, reflecting how this disease results from possessing one extra chromosome 21 (three total). Not wanting to change the name of this disease, scientists retained the original numbering system. The chromosome "arms" projecting from either end of the centromere may be designated as short or long, depending on their relative lengths. The short arm is abbreviated *p* (for "petite"), whereas the long arm is abbreviated *q* (because it follows "p" alphabetically). Each arm is further subdivided and denoted by a number. For example, locus 3 on the short arm of chromosome 21 is denoted 21p3. Using this naming system, locations on chromosomes can be described consistently in the scientific literature.

career CONNECTION

Geneticists Use Karyograms to Identify Chromosomal Aberrations

Although Mendel is referred to as the "father of modern genetics," he performed his experiments with none of the tools that the geneticists of today routinely employ. One such powerful cytological technique is karyotyping, a method in which traits characterized by chromosomal abnormalities can be identified from a single cell. To observe an individual's karyotype, a person's cells (like white blood cells) are first collected from a blood sample or other tissue. In the laboratory, the isolated cells are stimulated to begin actively dividing. A chemical called colchicine is then applied to cells to arrest condensed chromosomes in metaphase. Cells are then made to swell using a hypotonic solution so the chromosomes spread apart. Finally, the sample is preserved in a fixative and applied to a slide.

The geneticist then stains chromosomes with one of several dyes to better visualize the distinct and reproducible banding patterns of each chromosome pair. Following staining, the chromosomes are viewed using bright-field microscopy. A common stain choice is the Giemsa stain. Giemsa staining results in approximately 400–800 bands (of tightly coiled DNA and condensed proteins) arranged along all of the 23 chromosome pairs; an experienced geneticist can identify each band. In addition to the banding patterns, chromosomes are further identified on the basis of size and centromere location. To obtain the classic depiction of the karyotype in which homologous pairs of chromosomes are aligned in numerical order from longest to shortest, the geneticist obtains a digital image, identifies each chromosome, and manually arranges the chromosomes into this pattern (**Figure 13.5**).

At its most basic, the karyogram may reveal genetic abnormalities in which an individual has too many or too few chromosomes per cell. Examples of this are Down Syndrome, which is identified by a third copy of chromosome 21, and Turner Syndrome, which is characterized by the presence of only one X chromosome in women instead of the normal two. Geneticists can also identify large deletions or insertions of DNA. For instance, Jacobsen Syndrome—which involves distinctive facial features as well as heart and bleeding defects—is identified by a deletion on chromosome 11. Finally, the karyotype can pinpoint **translocations**, which occur when a segment of genetic material breaks from one chromosome and reattaches to another chromosome or to a different part of the same chromosome.

During Mendel's lifetime, inheritance was an abstract concept that could only be inferred by performing crosses and observing the traits expressed by offspring. By observing a karyogram, today's geneticists can actually visualize the chromosomal composition of an individual to confirm or predict genetic abnormalities in offspring, even before birth.

Disorders in Chromosome Number

Of all of the chromosomal disorders, abnormalities in chromosome number are the most obviously identifiable from a karyogram. Disorders of chromosome number include the duplication or loss of entire chromosomes, as well as changes in the number of complete sets of chromosomes. They are caused by **nondisjunction**, which occurs when pairs of homologous chromosomes or sister chromatids fail to separate during meiosis. Misaligned or incomplete synapsis, or a dysfunction of the spindle apparatus that facilitates chromosome migration, can cause nondisjunction. The risk of nondisjunction occurring increases with the age of the parents.

Nondisjunction can occur during either meiosis I or II, with differing results (**Figure 13.6**). If homologous chromosomes fail to separate during meiosis I, the result is two gametes that lack that particular chromosome and two gametes with two copies of the chromosome. If sister chromatids fail to separate during meiosis II, the result is one gamete that lacks that chromosome, two normal gametes with one copy of the chromosome, and one gamete with two copies of the chromosome.

visual CONNECTION

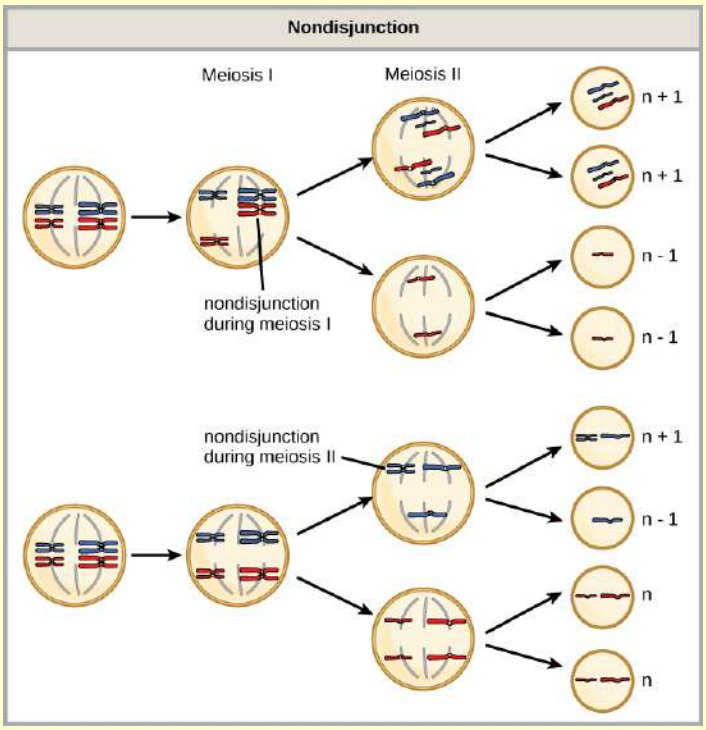


Figure 13.6 Nondisjunction occurs when homologous chromosomes or sister chromatids fail to separate during meiosis, resulting in an abnormal chromosome number. Nondisjunction may occur during meiosis I or meiosis II.

Which of the following statements about nondisjunction is true?

a. Nondisjunction only results in gametes with n+1 or n-1 chromosomes.

b. Nondisjunction occurring during meiosis II results in 50% normal gametes.

c. Nondisjunction during meiosis I results in 50% normal gametes.

d. Nondisjunction always results in four different kinds of gametes.

Aneuploidy

An individual with the appropriate number of chromosomes for their species is called **euploid**; in humans, euploidy corresponds to 22 pairs of autosomes and one pair of sex chromosomes. An individual with an error in chromosome number is described as **aneuploid**, a term that includes **monosomy** (loss of one chromosome) or **trisomy** (gain of an extraneous chromosome). Monosomic human zygotes missing any one copy of an autosome invariably fail to develop to birth because they lack essential genes. This underscores the importance of "gene dosage" in humans. Most autosomal trisomies also fail to develop to birth; however, duplications of some of the smaller chromosomes (13, 15, 18, 21, or 22) can result in offspring that survive for several weeks to many years. Trisomic individuals suffer from a different type of genetic imbalance: an excess in gene dose. Individuals with an extra chromosome may synthesize an abundance of the gene products encoded by that chromosome. This extra dose (150 percent) of specific genes can lead to a number of functional challenges and often precludes development. The most common trisomy among viable births is that of chromosome 21, which corresponds to Down Syndrome. Individuals with this inherited disorder are characterized by short stature and stunted digits, facial distinctions that include a broad skull and large tongue, and significant developmental delays. The incidence of Down syndrome is correlated with maternal age; older women are more likely to become pregnant with fetuses carrying the trisomy 21 genotype (**Figure 13.7**).

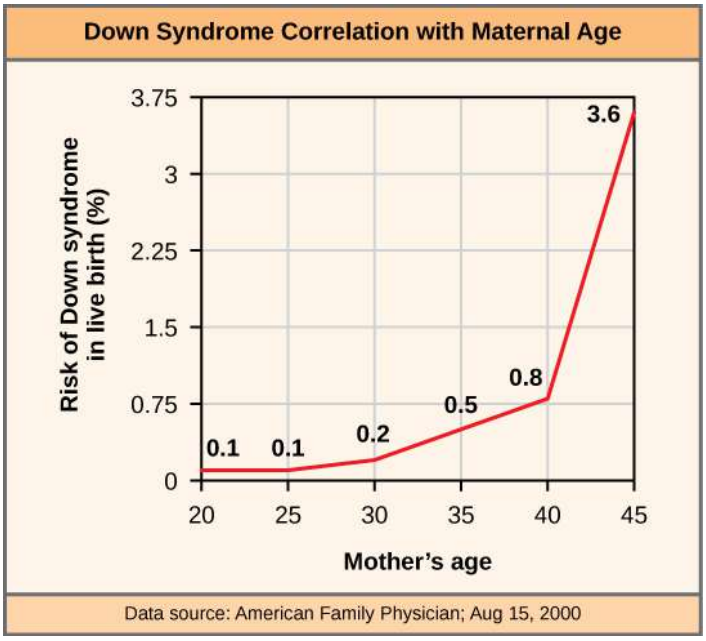


Figure 13.7 The incidence of having a fetus with trisomy 21 increases dramatically with maternal age.

LINK TO LEARNING

Visualize the addition of a chromosome that leads to Down syndrome in this **video simulation (http://openstaxcollege.org/l/down_syndrome)** .

With increasing age, women are at increased risk of having a baby with a chromosomal abnormality such as Down syndrome. Why is age a risk factor?

a. Cells are more likely to make mistakes as we age due to an increase in the nondisjunction of cells during cell division, which is the reason for the occurrence of Down syndrome.

b. The chance of this disorder increases with age due to increased mistakes in the mitotic cells with age.

c. There are increased risks of translocation mutations with age, even though other mutation rates are constant, and this increases the risk.

d. The risk of having a child with Down syndrome is associated primarily with lifestyle factors that change with age.

Polyploidy

An individual with more than the correct number of chromosome sets (two for diploid species) is called **polyploid**. For instance, fertilization of an abnormal diploid egg with a normal haploid sperm would yield a triploid zygote. Polyploid animals are extremely rare, with only a few examples among the flatworms, crustaceans, amphibians, fish, and lizards. Polyploid animals are sterile because meiosis cannot proceed normally and instead produces mostly aneuploid daughter cells that cannot yield viable zygotes. Rarely, polyploid animals can reproduce asexually by haplodiploidy, in which an unfertilized egg divides mitotically to produce offspring. In contrast, polyploidy is very common in the plant kingdom, and polyploid plants tend to be larger and more robust than euploids of their species (**Figure 13.8**).

Figure 13.8 As with many polyploid plants, this triploid orange daylily (*Hemerocallis fulva*) is particularly large and robust, and grows flowers with triple the number of petals of its diploid counterparts. (credit: Steve Karg)

Sex Chromosome Nondisjunction in Humans

Humans display dramatic deleterious effects with autosomal trisomies and monosomies. Therefore, it may seem counterintuitive that human females and males can function normally, despite carrying different numbers of the X chromosome. Rather than a gain or loss of autosomes, variations in the number of sex chromosomes are associated with relatively mild effects. In part, this occurs because of a molecular process called **X inactivation**. Early in development, when female mammalian embryos consist of just a few thousand cells (relative to trillions in the newborn), one X chromosome in each cell inactivates by tightly condensing into a quiescent (dormant) structure called a Barr body. The chance that an X chromosome (maternally or paternally derived) is inactivated in each cell is random, but once the inactivation occurs, all cells derived from that one will have the same inactive X chromosome or Barr body. By this process, females compensate for their double genetic dose of X chromosome. In so-called "tortoiseshell" cats, embryonic X inactivation is observed as color variegation (**Figure 13.9**). Females that are heterozygous for an X-linked coat color gene will express one of two different coat colors over different regions of their body, corresponding to whichever X chromosome is inactivated in the embryonic cell progenitor of that region.

Figure 13.9 In cats, the gene for coat color is located on the X chromosome. In the embryonic development of female cats, one of the two X chromosomes is randomly inactivated in each cell, resulting in a tortoiseshell pattern if the cat has two different alleles for coat color. Male cats, having only one X chromosome, never exhibit a tortoiseshell coat color. (credit: Michael Bodega)

An individual carrying an abnormal number of X chromosomes will inactivate all but one X chromosome in each of her cells. However, even inactivated X chromosomes continue to express a few genes, and X chromosomes must reactivate for the proper maturation of female ovaries. As a result, X-chromosomal abnormalities are typically associated with mild mental and physical defects, as well as sterility. If the X chromosome is absent altogether, the individual will not develop in

utero.

Several errors in sex chromosome number have been characterized. Individuals with three X chromosomes, called triplo-X, are phenotypically female but express developmental delays and reduced fertility. The XXY genotype, corresponding to one type of Klinefelter syndrome, corresponds to phenotypically male individuals with small testes, enlarged breasts, and reduced body hair. More complex types of Klinefelter syndrome exist in which the individual has as many as five X chromosomes. In all types, every X chromosome except one undergoes inactivation to compensate for the excess genetic dosage. This can be seen as several Barr bodies in each cell nucleus. Turner syndrome, characterized as an X0 genotype (i.e., only a single sex chromosome), corresponds to a phenotypically female individual with short stature, webbed skin in the neck region, hearing and cardiac impairments, and sterility.

Duplications and Deletions

In addition to the loss or gain of an entire chromosome, a chromosomal segment may be duplicated or lost. Duplications and deletions often produce offspring that survive but exhibit physical and mental abnormalities. Duplicated chromosomal segments may fuse to existing chromosomes or may be free in the nucleus. Cri-du-chat (from the French for “cry of the cat”) is a syndrome associated with nervous system abnormalities and identifiable physical features that result from a deletion of most of 5p (the small arm of chromosome 5) (**Figure 13.10**). Infants with this genotype emit a characteristic high-pitched cry on which the disorder’s name is based.

Figure 13.10 This individual with cri-du-chat syndrome is shown at two, four, nine, and 12 years of age. (credit: Paola Cerruti Mainardi)

Chromosomal Structural Rearrangements

Cytologists have characterized numerous structural rearrangements in chromosomes, but chromosome inversions and translocations are the most common. Both are identified during meiosis by the adaptive pairing of rearranged chromosomes with their former homologs to maintain appropriate gene alignment. If the genes carried on two homologs are not oriented correctly, a recombination event could result in the loss of genes from one chromosome and the gain of genes on the other. This would produce aneuploid gametes.

Chromosome Inversions

A **chromosome inversion** is the detachment, 180° rotation, and reinsertion of part of a chromosome. Inversions may occur

in nature as a result of mechanical shear, or from the action of transposable elements (special DNA sequences capable of facilitating the rearrangement of chromosome segments with the help of enzymes that cut and paste DNA sequences). Unless they disrupt a gene sequence, inversions only change the orientation of genes and are likely to have more mild effects than aneuploid errors. However, altered gene orientation can result in functional changes because regulators of gene expression could be moved out of position with respect to their targets, causing aberrant levels of gene products.

An inversion can be **pericentric** and include the centromere, or **paracentric** and occur outside of the centromere (**Figure 13.11**). A pericentric inversion that is asymmetric about the centromere can change the relative lengths of the chromosome arms, making these inversions easily identifiable.

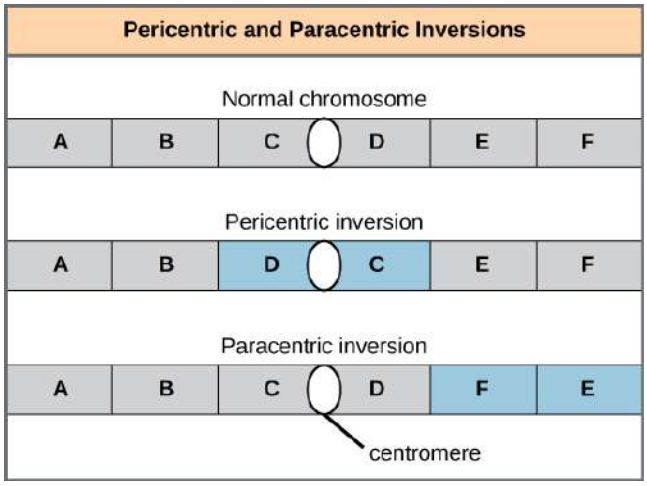


Figure 13.11 Pericentric inversions include the centromere, and paracentric inversions do not. A pericentric inversion can change the relative lengths of the chromosome arms; a paracentric inversion cannot.

When one homologous chromosome undergoes an inversion but the other does not, the individual is described as an inversion heterozygote. To maintain point-for-point synapsis during meiosis, one homolog must form a loop, and the other homolog must mold around it. Although this topology can ensure that the genes are correctly aligned, it also forces the homologs to stretch and can be associated with regions of imprecise synapsis (**Figure 13.12**).

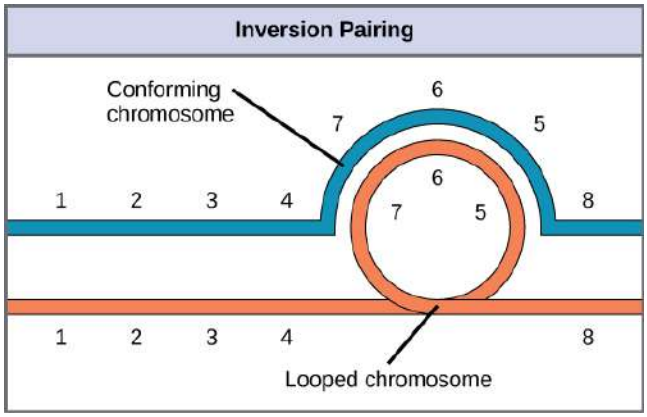


Figure 13.12 When one chromosome undergoes an inversion but the other does not, one chromosome must form an inverted loop to retain point-for-point interaction during synapsis. This inversion pairing is essential to maintaining gene alignment during meiosis and to allow for recombination.

evolution CONNECTION

The Chromosome 18 Inversion

Not all structural rearrangements of chromosomes produce nonviable, impaired, or infertile individuals. In rare instances, such a change can result in the evolution of a new species. In fact, a pericentric inversion in chromosome 18 appears to have contributed to the evolution of humans. This inversion is not present in our closest genetic relatives, the chimpanzees. Humans and chimpanzees differ cytogenetically by pericentric inversions on several chromosomes and by the fusion of two separate chromosomes in chimpanzees that correspond to chromosome two in humans.

The pericentric chromosome 18 inversion is believed to have occurred in early humans following their divergence from a common ancestor with chimpanzees approximately five million years ago. Researchers characterizing this inversion have suggested that approximately 19,000 nucleotide bases were duplicated on 18p, and the duplicated region inverted and reinserted on chromosome 18 of an ancestral human.

A comparison of human and chimpanzee genes in the region of this inversion indicates that two genes—*ROCK1* and *USP14*—that are adjacent on chimpanzee chromosome 17 (which corresponds to human chromosome 18) are more distantly positioned on human chromosome 18. This suggests that one of the inversion breakpoints occurred between these two genes. Interestingly, humans and chimpanzees express *USP14* at distinct levels in specific cell types, including cortical cells and fibroblasts. Perhaps the chromosome 18 inversion in an ancestral human repositioned specific genes and reset their expression levels in a useful way. Because both *ROCK1* and *USP14* encode cellular enzymes, a change in their expression could alter cellular function. It is not known how this inversion contributed to hominid evolution, but it appears to be a significant factor in the divergence of humans from other primates.[1]

According to the passage, which of the following events are believed to have occurred after humans diverged from their common ancestor with chimpanzees?

a. Paracentric inversions occurred at several chromosomes, including human chromosome 18.

b. Two separate chromosomes underwent a pericentric inversion, then fused to form chromosome 2 in humans.

c. $19,000$ nucleotide bases were duplicated, inverted, and reinserted at human chromosome 18.

d. The ROCK1 and USP14 genes were duplicated in early humans, which increased expression of these genes.

Translocations

A **translocation** occurs when a segment of a chromosome dissociates and reattaches to a different, nonhomologous chromosome. Translocations can be benign or have devastating effects depending on how the positions of genes are altered with respect to regulatory sequences. Reciprocal translocations result from the exchange of chromosome segments between two nonhomologous chromosomes such that there is no gain or loss of genetic information (**Figure 13.13**).

1.
Violaine Goidts et al., "Segmental duplication associated with the human-specific inversion of chromosome 18: a further example of the impact of segmental duplications on karyotype and genome evolution in primates," *Human Genetics*. 115 (2004):116-122

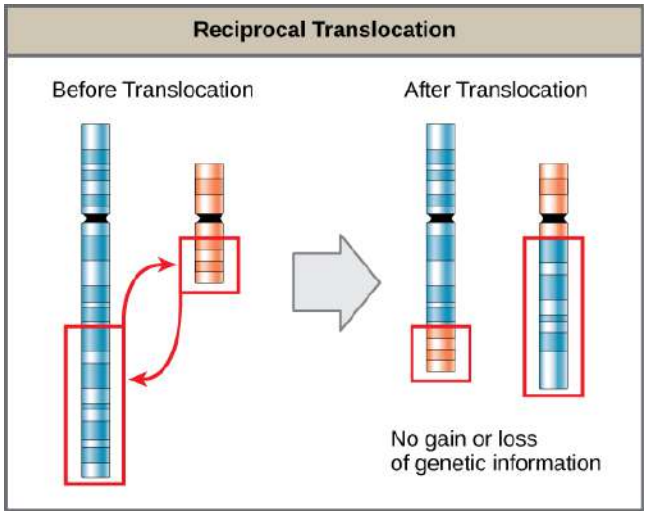


Figure 13.13 A reciprocal translocation occurs when a segment of DNA is transferred from one chromosome to another, nonhomologous chromosome. (credit: modification of work by National Human Genome Research/USA)

science practices CONNECTION for AP® Courses

Activity

A Day in the Life. Compose a short story, PowerPoint presentation, video, poem, or significant piece of art to describe a day in the life of a teenager afflicted with a single gene disorder or chromosomal abnormality. You need to include the causes and effects of the disorder and pose a question about a social, medical, or ethical issue(s) associated with human genetic disorders.

Think About It

Create a series of representations to show how nondisjunction can result in a trisomic zygote from a cell with $2n = 4$.

KEY TERMS

aneuploid individual with an error in chromosome number; includes deletions and duplications of chromosome segments

autosome any of the non-sex chromosomes

centimorgan (cM) (also, map unit) relative distance that corresponds to a recombination frequency of 0.01

Chromosomal Theory of Inheritance theory proposing that chromosomes are the vehicles of genes and that their behavior during meiosis is the physical basis of the inheritance patterns that Mendel observed

chromosome inversion detachment, 180° rotation, and reinsertion of a chromosome arm

euploid individual with the appropriate number of chromosomes for their species

homologous recombination process by which homologous chromosomes undergo reciprocal physical exchanges at their arms, also known as crossing over

karyogram photographic image of a karyotype

karyotype number and appearance of an individuals chromosomes; includes the size, banding patterns, and centromere position

monosomy otherwise diploid genotype in which one chromosome is missing

nondisjunction failure of synapsed homologs to completely separate and migrate to separate poles during the first cell division of meiosis

nonparental (recombinant) type progeny resulting from homologous recombination that exhibits a different allele combination compared with its parents

paracentric inversion that occurs outside of the centromere

parental types progeny that exhibits the same allelic combination as its parents

pericentric inversion that involves the centromere

polyploid individual with an incorrect number of chromosome sets

recombination frequency average number of crossovers between two alleles; observed as the number of nonparental types in a population of progeny

translocation process by which one segment of a chromosome dissociates and reattaches to a different, nonhomologous chromosome

trisomy otherwise diploid genotype in which one entire chromosome is duplicated

X inactivation condensation of X chromosomes into Barr bodies during embryonic development in females to compensate for the double genetic dose

CHAPTER SUMMARY

13.1 Chromosomal Theory and Genetic Linkages

The Chromosomal Theory of inheritance, proposed by Sutton and Boveri, states that chromosomes are the vehicles of genetic heredity. Neither Mendelian genetics nor gene linkage is perfectly accurate; instead, chromosome behavior involves segregation, independent assortment, and occasionally, linkage. Sturtevant devised a method to assess recombination frequency and infer the relative positions and distances of linked genes on a chromosome on the basis of the average number of crossovers in the intervening region between the genes. Sturtevant correctly presumed that genes are arranged in serial order on chromosomes and that recombination between homologs can occur anywhere on a chromosome with equal likelihood. Whereas linkage causes alleles on the same chromosome to be inherited together, homologous recombination biases alleles toward an inheritance pattern of independent assortment.

13.2 Chromosomal Basis of Inherited Disorders

The number, size, shape, and banding pattern of chromosomes make them easily identifiable in a karyogram and allows for the assessment of many chromosomal abnormalities. Disorders in chromosome number, or aneuploidies, are typically lethal to the embryo, although a few trisomic genotypes are viable. Because of X inactivation, aberrations in sex chromosomes typically have milder phenotypic effects. Aneuploidies also include instances in which segments of a chromosome are duplicated or deleted. Chromosome structures may also be rearranged, for example by inversion or translocation. Both of these aberrations can result in problematic phenotypic effects. Because they force chromosomes to assume unnatural topologies during meiosis, inversions and translocations are often associated with reduced fertility because of the likelihood of nondisjunction.

REVIEW QUESTIONS

1. When comparing humans (or in *Drosophila*), are X-linked recessive traits observed more frequently in males, in similar numbers between males and females, more frequently in females, or is the frequency different depending on the trait? Why?

a. in more males than females

b. in more females than males

c. in males and females equally

d. in different distributions depending on the trait

2. Which recombination frequency corresponds to perfect linkage and violates the law of independent assortment?

a. 0

b. 0.25

c. 0.5

d. 0.75

3. Which recombination frequency corresponds to independent assortment and the absence of linkage?

a. 0

b. 0.25

c. 0.5

d. 0.75

4.

Genetic Map Based on Recombination Frequencies in *Drosophila*

MUTANT		WILD TYPE
Short aristae	0	Long aristae
Black body	48.5	Gray body
Cinnabar eyes	57.5	Red eyes
Vestigial wings	65.5	Normal wings
Brown eyes	104.5	Red eyes

Values in centimorgan (cM) map units; recombination frequency of 0.01 = 1 cM

Based on the diagram, which of the following statements is true?

a. Recombination of the body color and red/ cinnabar eye alleles will occur more frequently than recombination of the alleles for wing length and aristae length.

b. Recombination of the body color and aristae length alleles will occur more frequently than recombination of red/ brown eye alleles and the aristae length alleles.

c. Recombination of the gray/black body color and long/short aristae alleles will not occur.

d. Recombination of the red/brown eye and long/ short aristae alleles will occur more frequently than recombination of the alleles for wing length and body color.

5. Which of the following codes describes position 12 on the long arm of chromosome 13?

a. 13p12
b. 13q12
c. 12p13
d. 12q13

6. Assume a pericentric inversion occurred in one of two homologs prior to meiosis. The other homolog remains normal. During meiosis, what structure, if any, would these homologs assume in order to pair accurately along their lengths?

a. V formation
b. cruciform
c. a loop
d. pairing would not be possible

CRITICAL THINKING QUESTIONS

7. Which best describes the Chromosomal Theory of Inheritance?

a. The theory was proposed by Charles Darwin. It describes the units of inheritance between parents and offspring as well as the processes by which those units control offspring development.
b. The theory was proposed by Boveri-Sutton. It describes linkage, recombination, and crossing over and states that Mendelian genes have specific loci on chromosomes, which undergo segregation and independent assortment.
c. The theory was proposed by Charles Darwin. It states the Mendelian genes have two alternate forms and undergo independent assortment. It helped increase understanding of linkage and recombination.
d. The theory was proposed by Boveri-Sutton. It describes the units of inheritance between parents and offspring as well as the processes by which those units control development in offspring.

8. In a test cross for two characteristics (dihybrid cross), can the predicted frequency of recombinant offspring be 60%? Why or why not?

a. No. The predicted frequency of recombinant offspring ranges from 0% (for linked traits) to 50% (for unlinked traits) because of both parental and nonparental cases.
b. Yes. The predicted frequency of recombinant offspring can be 60% if genes are located very far from each other.
c. Yes. The predicted frequency can be 60% if crossing over occurs during every meiotic event.
d. No. The predicted frequency can never be 60% due to the presence of mutations such as deletions.

9. Choose the statement that best describes how nondisjunction (see **Figure 13.6**) can result in an aneuploid zygote.

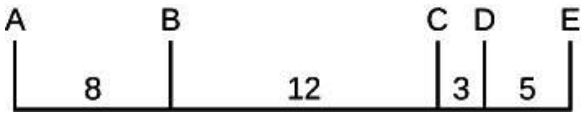
a. Nondisjunction only occurs when homologous chromosomes do not separate during meiosis I, resulting in the formation of gametes containing n+1 and n-1 chromosomes.
b. Nondisjunction only occurs when sister chromatids do not separate in meiosis II, resulting in the formation of gametes containing n+1 and n-1 chromosomes.
c. Nondisjunction is the failure of homologous chromosomes to separate during meiosis I or the failure of sister chromatids to separate during meiosis II, leading to the formation of n+1/n-1/n chromosomes.
d. Nondisjunction occurs when the sister chromatids fail to separate during mitosis II, resulting in the formation of gametes containing n+1 and n-1/n chromosomes.

10. Select the answer that correctly identifies the various chromosomal aberrations and their respective genetic consequence.

a. nondisjunction - aneuploid gametes; duplication - physical and mental abnormalities; deletion - lethal to a diploid organism; inversion - chromosomal breaks in gene; translocations - effects depend on how positions of genes are altered
b. nondisjunction - physical and mental abnormalities; inversion - genetic imbalance; duplication - aneuploid gametes; translocations - chromosomal breaks in the gene; deletion - effects depend on how positions of genes are altered
c. deletion -aneuploid gametes; translocations - physical and mental abnormalities; duplication - effects depend on positions of genes; nondisjunction - causes genetic imbalance lethal to a diploid organism; aneuploidy - leads to various syndromes
d. nondisjunction - chromosomal breaks in gene; duplication - physical and mental abnormalities; deletion - genetic imbalance lethal to a diploid organism; inversion - aneuploid gametes; translocations - effects depend on positions of genes

TEST PREP FOR AP® COURSES

11.



The figure represents a Drosophila linkage map for genes A-E. The numbers between the gene loci are the relative map units between each gene. Based on the linkage map, which two genes are most likely to segregate together?

a. A and B
b. B and C
c. C and D
d. D and E

12. A test cross was made between true-breeding EEWW flies and eeww flies. The resulting F_1 generation was then crossed with eeww flies. 100 offspring in the F_2 generation were examined, and it was discovered that the E and W genes were not linked. Which is the correct genotype of the F_2 offspring if the genes were linked and if the genes were not linked?

a. Linked: 50% EeWw and 50% eeww; not linked: 25% EeWw, 25%, Eeww 25% eeWw, and 25% eeww
b. Linked: 25% Eeww, 50% eeWw; not linked: parental genotypes EeWw and eeww.
c. Linked genotypes (EeWw and eeww) and recombinant genotypes (Eeww and eeWw) in the F2 generation are nearly the same irrespective of their linkage.
d. Linked: mostly with parental genotypes, Eeww and eeWw; unlinked: 25% EeWw and eeww with 75% Eeww and eeWw.

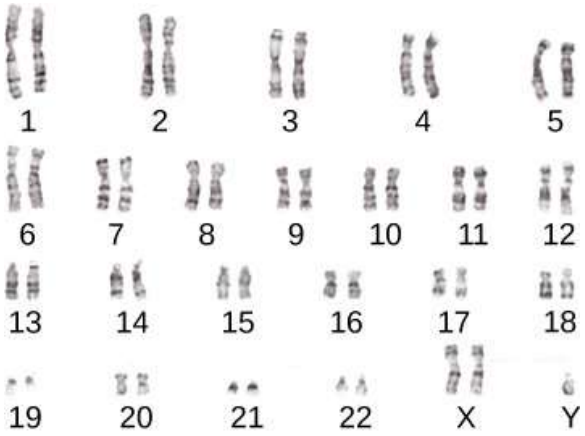
13.

	Number Observed			
F_2 Genotype	A	B	C	D
AaBb	46	4	25	50
Aabb	4	46	25	0
aaBb	4	46	25	0
Aabb	46	4	25	50

A cross was made with true-breeding AABB flies and true-breeding aabb flies. The resulting F_1 generation was then crossed with true-breeding aabb flies. Based on the linkage map, which of the following F_2 generation genotype ratios is most likely to be observed?

a. Number Observed: AaBb (46), Aabb (4), aaBb (4), Aabb (46)
b. Number Observed: AaBb (4), Aabb (46), aaBb (46), Aabb (4)
c. Number Observed: AaBb (25), Aabb (25), aaBb (25), Aabb (25)
d. Number Observed: AaBb (50), Aabb (0), aaBb (0), Aabb (50)

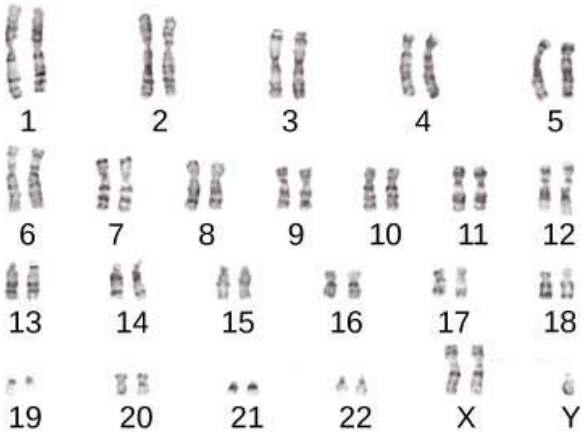
14.



Which of the following symptoms is most likely associated with the disorder shown in the karyotype?

a. lethality
b. infertility
c. heart and bleeding defects
d. short stature and stunted growth

15.



Choose the correct option amongst the following that describes the disorder shown in the karyotype and the social, ethical or medical issue related to the disorder.

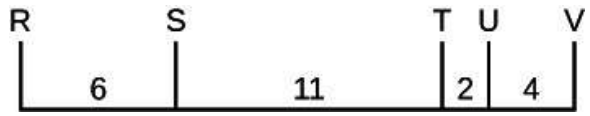
a. Down syndrome (47 XY +21) causes intellectual disability, vision problems, congenital heart disease, and susceptibility to cancer. Healthcare providers often do not discuss the positive aspects of raising a child with Down syndrome and often provide out of date information.

b. Klinefelter syndrome (47 XY +21) causes intellectual disability, vision problems, congenital heart disease, and susceptibility to cancer. Arguments are often made against abortion of an affected fetus.

c. Klinefelter syndrome (47 XXY) causes sterility and reduced testosterone production. Arguments are often made against informing insurance companies about a diagnosis of this disease.

d. Down syndrome (47 XXY) causes sterility and lower testosterone production. Arguments are often made against informing insurance companies about a diagnosis of this disease.

16.



Which of the following gene orders is the most likely outcome of an inversion mutation in the chromosome shown?

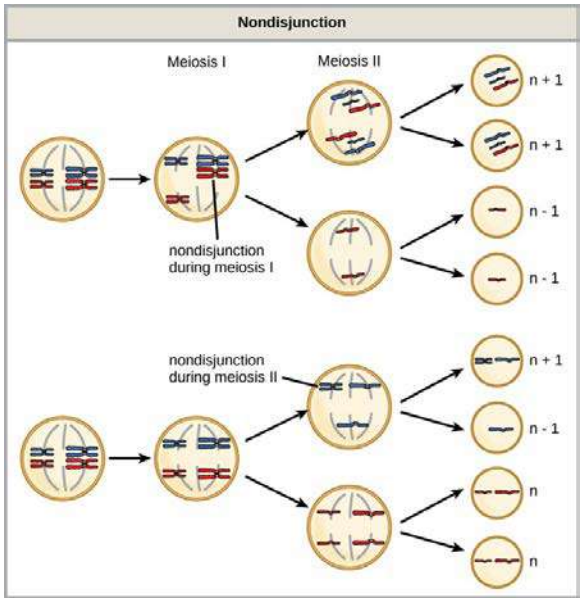
a. RSTUV

b. RRSTUV

c. RSUV

d. RTSUV

17.



With the help the diagram given, choose the most appropriate statement describing nondisjunction and its genetic consequences.

a. Nondisjunction occurs when a homologous pair is unable to separate during meiosis I, resulting in the formation of gametes containing n+1 and n-1 chromosomes. This is called aneuploidy.

b. Nondisjunction occurs due to the inability of sister chromatids to separate during meiosis II, resulting in the formation of gametes containing n+1 and n-1 chromosomes. This results in heart and bleeding defects.

c. Nondisjunction is the failure of homologous chromosomes to separate during meiosis I or failure of sister chromatids to separate during meiosis II. This results in aneuploid gametes.

d. Nondisjunction occurs when a pair of homologous chromosomes fails to segregate during meiosis II resulting in the formation of gametes containing n+1, n-1, or n numbers of chromosomes. This results in abnormal growth patterns.

18. If the effects of Klinefelter syndrome are compared to the effects of Down Syndrome, this disorder is _____.

a. more severe than Down syndrome, due to gene deletions in this syndrome

b. more severe than Down syndrome, due to trisomy in Klinefelter syndrome

c. less severe than Down syndrome, due to monosomy in Down Syndrome

d. less severe than Down syndrome, due to X-inactivation in this disorder

SCIENCE PRACTICE CHALLENGE QUESTIONS

19. *Drosophila* that are true breeding for the traits straight wings (S) and red eyes (R) are crossed with flies that are true breeding for curved wings (s) and brown eyes (r). A test cross is then made between the offspring and the true-breeding ssrr flies.

A. Use the symbols S, s, R, and r to **construct a representation** of the parental genotypes in the test cross.

B. If these genes are located on different chromosomes, use a Punnett square to **construct a representation** of the offspring of the test cross.

C. **Predict** the distribution of genotypes and phenotypes resulting from the test cross.

D. As it happens, these genes are both on chromosome II as shown below. Use the symbols S, s, R, and r to **construct a representation** of the parental and recombinant genotypes in the test cross.

E. Suppose that 500 flies are produced in the test cross. **Apply mathematical methods** to calculate the expected number of recombinant offspring using the linear map units (LMU) shown in the diagram below.

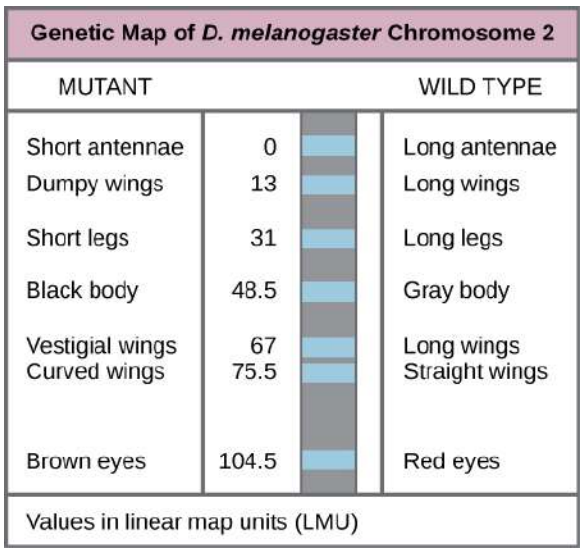


Figure 13.14

20. Studies like the one described in question AP12.1 were carried out by Morgan and Sturtevant beginning in 1911. The discovery of linkage was made by Bateson and Punnett in 1900. They crossed a true-breeding purple (P) plant with long seeds (L) with a true-breeding red (r) plant with round seeds (l). They then performed a self-cross between the F_1 generations. They obtained the F_2 data shown below.

Phenotype	Genotype(s)	Observed	Expected
purple, long		4831	
purple, round		390	
red, long		393	
red, round		1338	
total		6952	

Table 13.1

A. Use the symbols P, p, L, and l to **construct a representation** of the F_2 genotypes and complete the second column in the table.

B. Complete the fourth column of the table above by recording the values of the **predicted** numbers of plants with each genotype.

C. Apply a c^2 test at the 95% confidence level to **evaluate the claim** that these data confirm linkage. The definition of the statistic $\chi^2 = \sum \frac{(o-e)^2}{e}$ and this table are provided in the AP Biology Exam.

D. At first, Bateson and Punnett did not see that these genes are located on the same chromosome and proceeded to measure the linkage distance between them, taking the first step toward creating a gene map. **Justify** the selection of data and the procedure from which data could be collected that would have provided the necessary evidence to confirm linkage and recombination.

21. Review the observations that provided researchers with evidence in support of the Chromosomal Theory of Inheritance.

A. **Evaluate** the dependence of these observations on improvements in a critical technology during the period from 1850 to 1940. **Identify** this technology and **describe** how this technology allowed scientists to make the connection between chromosomes and genes. (As a hint, the name “chromosome” is taken from the Greek word *chroma*, which means colored or stained.)

B. Mendel’s laws of inheritance are explained by the chromosomal theory. Use these observations to **justify**:

- the law of segregation
- the law of independent assortment

22. Errors in the transmission of genetic information to future generations are essential. Otherwise, organisms could not evolve over time. Some errors in the synthesis of

new DNA during S phase in either meiosis or mitosis are not repaired. These errors usually involve single nucleotides. Errors that occur during prophase I of meiosis that are not corrected can involve the exchange of sequences between homologous chromosomes (duplications) or even nonhomologous chromosomes (translocations). Duplications are usually retained, and the organism remains viable without a change in phenotype. Translocations are usually lethal or significantly alter phenotype. In eukaryotes, duplications and the shuffling of parental genes through recombination are important sources of variation.

Construct an explanation of the role of duplication as a source of raw material for future mutations and selection and contrast this type of variation with recombination.

23. Bacteria and Archaea reproduce asexually, and genetic material is in a closed loop. In both domains, genetic material is transferred horizontally, and polyploidy is common. Polypoidy is common in plants and occurs in invertebrate animals but is less common in vertebrates. In all domains, multiple copies of genes (gene duplication) are common.

Based on this information, **compare and contrast** the mechanisms that provide genetic variation in the three domains: Bacteria, Archaea, and Eukarya.