UNIT 2 - MOLECULAR GENETICS REVIEW

Precision Healthcare: Genomics-Informed Nursing by Andrea Gretchev

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Unit 2 Contents

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2.1 UNIT OVERVIEW

Learning Objectives

- Review DNA structure and function.
- Describe the process of cellular reproduction.
- Explain the central dogma and how DNA encodes protein.
- Identify factors that influence gene expression.
- Explain inheritance at the cellular level.
- Calculate expected outcomes for monohybrid crosses involving different patterns of inheritance.

*In most chapters of this textbook, the learning outcomes are listed solely in the chapter overview. This chapter is longer than the others to provide a comprehensive review of foundational biology concepts that students will need to progress in this course. As such, learning objectives will be provided at the beginning of each chapter in this unit as an exception.

Note: this chapter is intended to provide a review of these concepts, which would have been covered in previous biology courses. Many of these principles and core concepts are presented here as an overview but will be revisited in greater detail in subsequent units. Cancer is covered briefly in this unit from a cellular perspective for a complete understanding of replication and division. Cancer genomics will be reviewed in greater detail in unit 12.

Students who are well-versed in this content can move through this chapter quickly. For students who need a deeper review, additional learning resources will be recommended in the chapter summary. It is recommended to start with the final summary and the review questions at the end of each chapter to identify learning needs.

Outline

Topics covered in this chapter include:

- DNA structure and function
- The genome and the life cycle
- Cancer and the cell cycle
- The cellular basis of inheritance
- Patterns of inheritance

Competencies Nurses will Develop in this Chapter

NHS, 2023:

Demonstrate a knowledge and understanding of genomics in human development, variation and health to underpin effective practice.

- underpinned by core genomic concepts that form a sufficient knowledge base for understanding the implications of different conditions and clinical situations that may be encountered.

Key terminology

*This unit will summarize additional key terminology at the end of each chapter.

Adenine

Adenine (A) is one of the four nucleotide bases in DNA, with the other three being cytosine (C), guanine (G) and thymine (T). Within a double-stranded DNA molecule, adenine bases on one strand pair with thymine bases on the opposite strand. The sequence of the four nucleotide bases encodes DNA's information.

Allele

An allele is one of two or more versions of DNA sequence (a single base or a segment of bases) at a given genomic location. An individual inherits two alleles, one from each parent, for any given genomic location where such variation exists. If the two alleles are the same, the individual is homozygous for

that allele. If the alleles are different, the individual is heterozygous.

Amino Acid

An amino acid is the fundamental molecule that is the building block for proteins. There are 20 different amino acids. A protein consists of one or more chains of amino acids (called polypeptides) whose sequence is encoded in a gene. Some amino acids can be synthesized in the body, but others (essential amino acids) cannot and must be obtained from a person's diet.

Aneuploidy

Aneuploidy is an abnormality in the number of chromosomes in a cell due to loss or duplication. Aneuploidy would be any number of chromosomes other than the usual 46 in humans.

Autosomal Dominant Disorder

Autosomal dominant is a pattern of inheritance characteristic of some genetic disorders. "Autosomal" means that the gene in question is located on one of the numbered, or non-sex, chromosomes. "Dominant" means that a single copy of the gene variant (from one parent) is enough to cause the disorder. A child of a person affected by an autosomal dominant condition has a 50% chance of being affected by that condition via inheritance of a dominant allele. By contrast, an autosomal recessive disorder requires two copies of the gene variant (one from each parent) to cause the disorder. Huntington's disease is an example of an autosomal dominant genetic disorder.

Autosomal Recessive Disorder

Autosomal recessive is a pattern of inheritance characteristic of some genetic disorders. "Autosomal" means that the gene in question is located on one of the numbered, or non-sex, chromosomes. "Recessive" means that two copies of the gene variant (one from each parent) are required to cause the disorder. In a family where both parents are carriers and do not have the disease, roughly a quarter of their children will inherit two disease-causing alleles and have the disease. By contrast, an autosomal dominant disorder requires only a single copy of the gene variant from one parent to cause the disorder. Sickle cell anemia is an example of an autosomal recessive genetic disorder.

Autosome

An autosome is one of the numbered chromosomes, as opposed to the sex chromosomes. Humans have 22 pairs of autosomes and one pair of sex chromosomes (XX or XY). Autosomes are numbered

roughly in relation to their sizes. The largest autosome — chromosome 1 — has approximately 2,800 genes; the smallest autosome — chromosome 22 — has approximately 750 genes.

Base Pair

A base pair consists of two complementary DNA nucleotide bases that pair together to form a "rung of the DNA ladder." DNA is made of two linked strands that wind around each other to resemble a twisted ladder — a shape known as a double helix. Each strand has a backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases: adenine (A), cytosine (C), guanine (G) or thymine (T). The two strands are held together by hydrogen bonds between pairs of bases: adenine pairs with thymine, and cytosine pairs with guanine.

Cancer

Cancer is a disease in which some of the body's cells grow uncontrollably. There are many different types of cancer, and each begins when a single cell acquires a genomic change (or mutation) that allows the cell to divide and multiply unchecked. Additional variants can cause the cancer to spread to other sites. Such variants can be caused by errors during DNA replication or result from DNA damage due to environmental exposures (such as tobacco smoke or the sun's ultraviolet rays). In certain cases, variants in cancer genes are inherited, which increases a person's risk of developing cancer.

Carrier

A carrier, as related to genetics, is an individual who "carries" and can pass on to its offspring a genomic variant (allele) associated with a disease (or trait) that is inherited in an autosomal recessive or sex-linked manner, and who does not show symptoms of that disease (or features of that trait). The carrier has inherited the variant allele from one parent and a normal allele from the other parent. Any offspring of carriers is at risk of inheriting a variant allele from their parents, which would result in that child having the disease (or trait).

Central Dogma

The central dogma of molecular biology is a theory first proposed by Francis Crick in 1958. It states that genetic information flows only in one direction, from DNA to RNA to protein. Scientists have since discovered several exceptions to the theory.

Chromosome

Chromosomes are threadlike structures made of protein and a single molecule of DNA that serve to carry the genomic information from cell to cell. In plants and animals (including humans), chromosomes reside in the nucleus of cells. Humans have 22 pairs of numbered chromosomes (autosomes) and one pair of sex chromosomes (XX or XY), for a total of 46. Each pair contains two chromosomes, one coming from each parent, which means that children inherit half of their chromosomes from their mother and half from their father. Chromosomes can be seen through a microscope when the nucleus dissolves during cell division.

Codon

A codon is a DNA or RNA sequence of three nucleotides (a trinucleotide) that forms a unit of genomic information encoding a particular amino acid or signaling the termination of protein synthesis (stop signals). There are 64 different codons: 61 specify amino acids and 3 are used as stop signals.

Codominance

Codominance, as it relates to genetics, refers to a type of inheritance in which two versions (alleles) of the same gene are expressed separately to yield different traits in an individual. That is, instead of one trait being dominant over the other, both traits appear, such as in a plant or animal that has more than one pigment color.

Learn more about Codominance (https://www.genome.gov/genetics-glossary/Codominance)

Cytosine

Cytosine (C) is one of the four nucleotide bases in DNA, with the other three being adenine (A), guanine (G) and thymine (T). Within a double-stranded DNA molecule, cytosine bases on one strand pair with guanine bases on the opposite strand. The sequence of the four nucleotide bases encodes DNA's information.

Deoxyribonucleic Acid (DNA)

Deoxyribonucleic acid (abbreviated DNA) is the molecule that carries genetic information for the development and functioning of an organism. DNA is made of two linked strands that wind around each other to resemble a twisted ladder — a shape known as a double helix. Each strand has a

backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases: adenine (A), cytosine (C), guanine (G) or thymine (T). The two strands are connected by chemical bonds between the bases: adenine bonds with thymine, and cytosine bonds with guanine. The sequence of the bases along DNA's backbone encodes biological information, such as the instructions for making a protein or RNA molecule.

Diploid

Diploid is a term that refers to the presence of two complete sets of chromosomes in an organism's cells, with each parent contributing a chromosome to each pair. Humans are diploid, and most of the body's cells contain 23 chromosomes pairs. Human gametes (egg and sperm cells), however, contain a single set of chromosomes and are said to be haploid.

DNA Replication

DNA replication is the process by which the genome's DNA is copied in cells. Before a cell divides, it must first copy (or replicate) its entire genome so that each resulting daughter cell ends up with its own complete genome.

Dominant Traits and Alleles

Dominant, as related to genetics, refers to the relationship between an observed trait and the two inherited versions of a gene related to that trait. Individuals inherit two versions of each gene, known as alleles, from each parent. In the case of a dominant trait, only one copy of the dominant allele is required to express the trait. The effect of the other allele (the recessive allele) is masked by the dominant allele. Typically, an individual who carries two copies of a dominant allele exhibits the same trait as those who carry only one copy. This contrasts to a recessive trait, which requires that both alleles be present to express the trait.

Epistasis

Epistasis is a circumstance where the expression of one gene is modified (e.g., masked, inhibited or suppressed) by the expression of one or more other genes.

Exome

An exome is the sequence of all the exons in a genome, reflecting the protein-coding portion of a genome. In humans, the exome is about 1.5% of the genome.

Exon

An exon is a region of the genome that ends up within an mRNA molecule. Some exons are coding, in that they contain information for making a protein, whereas others are non-coding. Genes in the genome consist of exons and introns.

Gamete

A gamete is a reproductive cell of an animal or plant. In animals, female gametes are called ova or egg cells, and male gametes are called sperm. Ova and sperm are haploid cells, with each cell carrying only one copy of each chromosome. During fertilization, a sperm and ovum unite to form a new diploid organism.

Genetic code

Genetic code refers to the instructions contained in a gene that tell a cell how to make a specific protein. Each gene's code uses the four nucleotide bases of DNA: adenine (A), cytosine (C), guanine (G) and thymine (T) — in various ways to spell out three-letter "codons" that specify which amino acid is needed at each position within a protein.

Gene Regulation

Gene regulation is the process used to control the timing, location and amount in which genes are expressed. The process can be complicated and is carried out by a variety of mechanisms, including through regulatory proteins and chemical modification of DNA. Gene regulation is key to the ability of an organism to respond to environmental changes.

Genomic Variation

Genomic variation refers to DNA sequence differences among individuals or populations. A variant is a change in the DNA sequence of an organism. Some variants influence biological function (such as a mutation that causes a genetic disease), while others have no biological effects. Variants can result from errors in DNA replication during cell division, exposure to mutagens or a viral infection. Germline variants (that occur in eggs and sperm) can be passed on to offspring, while somatic variants (that occur in body cells) are not passed on.

Genotype

A genotype is a scoring of the type of variant present at a given location (i.e., a locus) in the genome. It can be represented by symbols. For example, BB, Bb, bb could be used to represent a given variant in a gene. Genotypes can also be represented by the actual DNA sequence at a specific location, such as CC, CT, TT. DNA sequencing and other methods can be used to determine the genotypes at millions of locations in a genome in a single experiment. Some genotypes contribute to an individual's observable traits, called the phenotype.

Germ Line

Germ line refers to the sex cells (eggs and sperm) that sexually reproducing organisms use to pass on their genomes from one generation to the next (parents to offspring). Egg and sperm cells are called germ cells, in contrast to the other cells of the body, which are called somatic cells.

Guanine

Guanine (G) is one of the four nucleotide bases in DNA, with the other three being adenine (A), cytosine (C) and thymine (T). Within a double-stranded DNA molecule, guanine bases on one strand pair with cytosine bases on the opposite strand. The sequence of the four nucleotide bases encodes DNA's information.

Haploid

Haploid refers to the presence of a single set of chromosomes in an organism's cells. Sexually reproducing organisms are diploid (having two sets of chromosomes, one from each parent). In humans, only the egg and sperm cells are haploid.

Heterozygous

Heterozygous, as related to genetics, refers to having inherited different versions (alleles) of a genomic marker from each biological parent. Thus, an individual who is heterozygous for a genomic marker has two different versions of that marker. By contrast, an individual who is homozygous for a marker has identical versions of that marker.

Histone

A histone is a protein that provides structural support for a chromosome. Each chromosome contains a long molecule of DNA, which must fit into the cell nucleus. To do that, the DNA wraps around complexes of histone proteins, giving the chromosome a more compact shape. Histones also play a role in the regulation of gene expression.

Homologous Recombination

Homologous recombination is a type of genetic recombination in which nucleotide sequences are exchanged between two similar or identical molecules of DNA. During the formation of egg and sperm cells (meiosis), paired chromosomes from the male and female parents align so that similar DNA sequences can cross over, or be exchanged, from one chromosome to the other. This exchanging of DNA is an important source of the genomic variation seen among offspring.

Homozygous

Homozygous, as related to genetics, refers to having inherited the same versions (alleles) of a genomic marker from each biological parent. Thus, an individual who is homozygous for a genomic marker has two identical versions of that marker. By contrast, an individual who is heterozygous for a marker has two different versions of that marker.

Inherited

Inherited, as related to genetics, refers to a trait or variants encoded in DNA and passed from parent to offspring during reproduction. Inheritance is determined by the rules of Mendelian genetics.

Intron

An intron is a region that resides within a gene but does not remain in the final mature mRNA molecule following transcription of that gene and does not code for amino acids that make up the protein encoded by that gene. Most protein-coding genes in the human genome consist of exons and introns.

Linkage

Linkage, as related to genetics and genomics, refers to the closeness of genes or other DNA sequences

to one another on the same chromosome. The closer two genes or sequences are to each other on a chromosome, the greater the probability that they will be inherited together.

Locus

A locus, as related to genomics, is a physical site or location within a genome (such as a gene or another DNA segment of interest), somewhat like a street address. The plural of locus is loci.

Lyonization

Lyonization (also called X-inactivation) refers to the normal phenomenon in which one of the two X chromosomes in every cell of a female individual is inactivated during embryonic development. This inactivation prevents females from having twice as many X chromosome gene products as males, who possess only a single copy of the X chromosome. Lyonization is named after Mary F. Lyon, the British geneticist who discovered the phenomenon.

Meiosis

Meiosis is a type of cell division in sexually reproducing organisms that reduces the number of chromosomes in gametes (the sex cells, or egg and sperm). In humans, body (or somatic) cells are diploid, containing two sets of chromosomes (one from each parent). To maintain this state, the egg and sperm that unite during fertilization must be haploid, with a single set of chromosomes. During meiosis, each diploid cell undergoes two rounds of division to yield four haploid daughter cells — the gametes.""Mendel, Johann (Gregor)""Gregor Mendel was an Austrian monk in the 19th century who worked out the basic laws of inheritance through experiments with pea plants. In his monastery garden, Mendel performed thousands of crosses with pea plants, discovering how characteristics are passed down from one generation to the next — namely, dominant and recessive traits. Mendel's early experiments provided the basis of modern genetics.

Mendelian Inheritance

Mendelian inheritance refers to certain patterns of how traits are passed from parents to offspring. These general patterns were established by the Austrian monk Gregor Mendel, who performed thousands of experiments with pea plants in the 19th century. Mendel's discoveries of how traits (such as color and shape) are passed down from one generation to the next introduced the concept of dominant and recessive modes of inheritance.

Messenger RNA (mRNA)

Messenger RNA (abbreviated mRNA) is a type of single-stranded RNA involved in protein synthesis. mRNA is made from a DNA template during the process of transcription. The role of mRNA is to carry protein information from the DNA in a cell's nucleus to the cell's cytoplasm (watery interior), where the protein-making machinery reads the mRNA sequence and translates each three-base codon into its corresponding amino acid in a growing protein chain.

Mitosis

Mitosis is the process by which a cell replicates its chromosomes and then segregates them, producing two identical nuclei in preparation for cell division. Mitosis is generally followed by equal division of the cell's content into two daughter cells that have identical genomes.

Mutagen

A mutagen is a chemical or physical agent capable of inducing changes in DNA, formerly called mutations, now termed variants. Examples of mutagens include tobacco products, radioactive substances, x-rays, ultraviolet radiation and a wide variety of chemicals. Exposure to a mutagen can produce DNA changes that cause or contribute to certain diseases.

Non-Coding DNA

Non-coding DNA corresponds to the portions of an organism's genome that do not code for amino acids, the building blocks of proteins. Some non-coding DNA sequences are known to serve functional roles, such as in the regulation of gene expression, while other areas of non-coding DNA have no known function.

Nucleic Acids

Nucleic acids are large biomolecules that play essential roles in all cells and viruses. A major function of nucleic acids involves the storage and expression of genomic information. Deoxyribonucleic acid, or DNA, encodes the information cells need to make proteins. A related type of nucleic acid, called ribonucleic acid (RNA), comes in different molecular forms that play multiple cellular roles, including protein synthesis.

Nucleosome

A nucleosome is the basic repeating subunit of chromatin packaged inside the cell's nucleus. In humans, about six feet of DNA must be packaged into a nucleus with a diameter less than a human hair, and nucleosomes play a key role in that process. A single nucleosome consists of about 150 base pairs of DNA sequence wrapped around a core of histone proteins. In forming a chromosome, the nucleosomes repeatedly fold in on themselves to tighten and condense the packaged DNA.

Oncogene

An oncogene is a gene variant that has the potential to cause cancer. Before an oncogene becomes altered, it is called a proto-oncogene, and it plays a role in regulating normal cell division. Cancer can arise when a proto-oncogene is altered, changing it into an oncogene and causing the cell to divide and multiply uncontrollably. Some oncogenes work like an accelerator pedal in a car, pushing a cell to divide again and again. Others work like a faulty brake in a car parked on a hill, also causing the cell to divide unchecked.

Phenotype

Phenotype refers to an individual's observable traits, such as height, eye color and blood type. A person's phenotype is determined by both their genomic makeup (genotype) and environmental factors.

Proto-oncogene:

A normal gene that controls cell division by regulating the cell cycle that becomes an oncogene if it is altered.

Ribonucleic Acid (RNA)

Ribonucleic acid (abbreviated RNA) is a nucleic acid present in all living cells that has structural similarities to DNA. Unlike DNA, however, RNA is most often single-stranded. An RNA molecule has a backbone made of alternating phosphate groups and the sugar ribose, rather than the deoxyribose found in DNA. Attached to each sugar is one of four bases: adenine (A), uracil (U), cytosine (C) or guanine (G). Different types of RNA exist in cells: messenger RNA (mRNA), ribosomal RNA (rRNA) and transfer RNA (tRNA). In addition, some RNAs are involved in regulating gene expression. Certain viruses use RNA as their genomic material.

Sex Chromosome

A sex chromosome is a type of chromosome involved in sex determination. Humans and most other mammals have two sex chromosomes, X and Y, that in combination determine the sex of an individual. Females have two X chromosomes in their cells, while males have one X and one Y.

Somatic Cells

Somatic cells are the cells in the body other than sperm and egg cells (which are called germ cells). In humans, somatic cells are diploid, meaning they contain two sets of chromosomes, one inherited from each parent. DNA mutations in somatic cells can affect an individual, but they cannot be passed on to their offspring.

Stop Codon

A stop codon is a sequence of three nucleotides (a trinucleotide) in DNA or messenger RNA (mRNA) that signals a halt to protein synthesis in the cell. There are 64 different trinucleotide codons: 61 specify amino acids and 3 are stop codons (i.e., UAA, UAG and UGA).

Trait

A trait, as related to genetics, is a specific characteristic of an individual. Traits can be determined by genes, environmental factors or by a combination of both. Traits can be qualitative (such as eye color) or quantitative (such as height or blood pressure). A given trait is part of an individual's overall phenotype.

Telomere

A telomere is a region of repetitive DNA sequences at the end of a chromosome. Telomeres protect the ends of chromosomes from becoming frayed or tangled. Each time a cell divides, the telomeres become slightly shorter. Eventually, they become so short that the cell can no longer divide successfully, and the cell dies.

Thymine

Thymine (T) is one of the four nucleotide bases in DNA, with the other three being adenine (A), cytosine (C) and guanine (G). Within a double-stranded DNA molecule, thymine bases on one strand

pair with adenine bases on the opposite strand. The sequence of the four nucleotide bases encodes DNA's information.

Transcription

Transcription is the process of making an RNA copy of a gene sequence. This copy, called a messenger RNA (mRNA) molecule, leaves the cell nucleus and enters the cytoplasm, where it directs the synthesis of the protein, which it encodes.

Translation

Translation is the process of translating the sequence of a messenger RNA (mRNA) molecule to a sequence of amino acids during protein synthesis. The genetic code describes the relationship between the sequence of base pairs in a gene and the corresponding amino acid sequence that it encodes. In the cell cytoplasm, the ribosome reads the sequence of the mRNA in groups of three bases to assemble the protein

Tumor Suppressor Gene

A tumor suppressor gene encodes a protein that acts to regulate cell division, keeping it in check. When a tumor suppressor gene is inactivated by a variant, the protein it encodes is not produced or does not function properly, and as a result, uncontrolled cell division may occur. Such variants may contribute to the development of a cancer.

Uracil

Uracil (U) is one of the four nucleotide bases in RNA, with the other three being adenine (A), cytosine (C) and guanine (G). In RNA, uracil pairs with adenine. In a DNA molecule, the nucleotide thymine (T) is used in place of uracil.

X Chromosome

The X chromosome is one of the two sex chromosomes that are involved in sex determination. Humans and most other mammals have two sex chromosomes (X and Y) that in combination determine the sex of an individual. Females have two X chromosomes in their cells, while males have one X and one Y.

Y Chromosome

The Y chromosome is one of the two sex chromosomes that are involved in sex determination. Humans and most other mammals have two sex chromosomes (X and Y) that in combination determine the sex of an individual. Females have two X chromosomes in their cells, while males have one X and one Y.

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References

National Health Service (NHS). (2023). *The 2023 genomic competency framework for UK nurses*. https://www.genomicseducation.hee.nhs.uk/wp-content/uploads/2023/12/2023-Genomic-Competency-Framework-for-UK-Nurses.pdf

2.2 DNA STRUCTURE AND FUNCTION

Learning Objectives

- Describe the structure of DNA.
- Explain the process of DNA replication.
- Describe mechanisms of DNA repair.
- Explain the central dogma.
- Explain the main steps of transcription.
- Discuss why every cell does not express all of its genes.
- Identify how eukaryotic gene expression occurs at the epigenetic, transcriptional, post-transcriptional, translational, and post-translational levels.
- Describe the different steps in protein synthesis.
- Describe the genetic code and how the nucleotide sequence determines the amino acid and the protein sequence.

Let's begin with a review the structure of the two types of nucleic acids, **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA).** The building blocks of DNA are **nucleotides**, which are made up of three parts: a **deoxyribose** (5-carbon sugar), a phosphate group, and a **nitrogenous base** (Figure 2.1). There are four types of nitrogenous bases in DNA. **Adenine (A)** and **guanine (G)** are **double-ringed purines**, and **cytosine (C)** and **thymine (T)** are smaller, single-ringed pyrimidines. The nucleotide is named according to the nitrogenous base it contains.

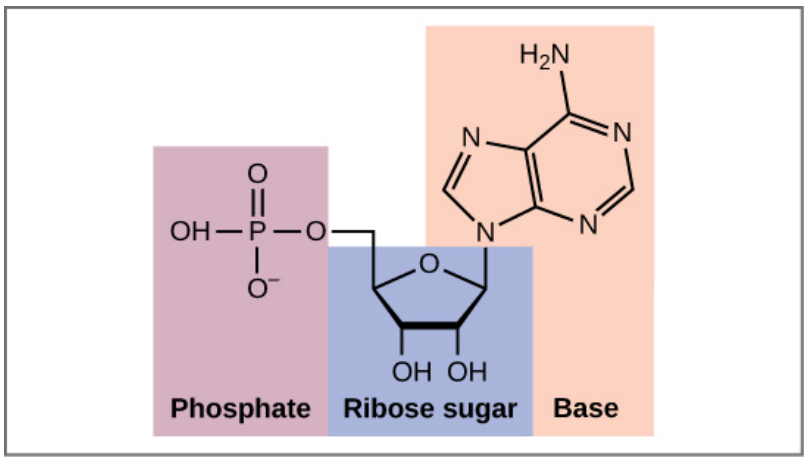


Figure 2.1 Each DNA nucleotide is made up of a sugar, a phosphate group, and a base. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0).

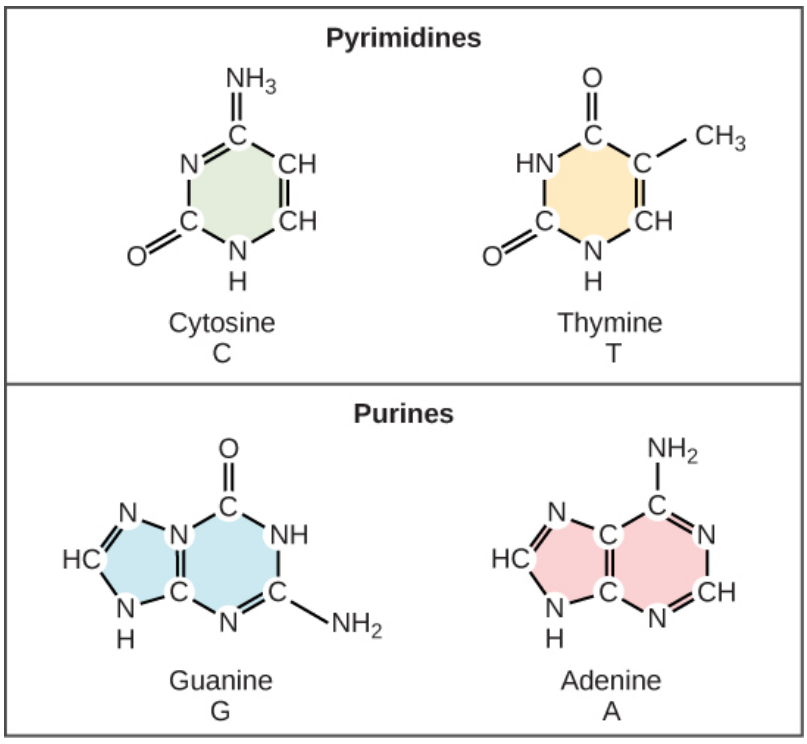


Figure 2.2 Cytosine and thymine are pyrimidines. Guanine and adenine are purines. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0).

The phosphate group of one nucleotide bonds covalently with the sugar molecule of the next nucleotide, and so on, forming a long polymer of nucleotide monomers. The sugar–phosphate groups line up in a "backbone" for each single strand of DNA, and the nucleotide bases stick out from this backbone. The carbon atoms of the five-carbon sugar are numbered clockwise from the oxygen as 1′, 2′, 3′, 4′, and 5′ (1′ is

read as "one prime"). The phosphate group is attached to the 5′ carbon of one nucleotide and the 3′ carbon of the next nucleotide. In its natural state, each DNA molecule is actually composed of two single strands held together along their length with hydrogen bonds between the bases.

DNA is made up of two strands that are twisted around each other to form a right-handed helix, called a **double helix**. Base pairing occurs between a purine and pyrimidine: A pairs with T, and G pairs with C. In other words, adenine and thymine are complementary base pairs, and cytosine and guanine are complementary base pairs. This is the basis for Chargaff's rule; because of their complementarity, there is as much adenine as thymine in a DNA molecule and as much guanine as cytosine. Two hydrogen bonds, connect adenine and thymine and cytosine and guanine are connected by three hydrogen bonds. The two strands are anti-parallel; one strand will have the 3′ carbon of the sugar in the "upward" position, whereas the other strand will have the 5′ carbon in the upward position. The diameter of the DNA double helix is uniform throughout because a purine (two rings) always pairs with a pyrimidine (one ring), and their combined lengths are always equal. (Figure 2.3).

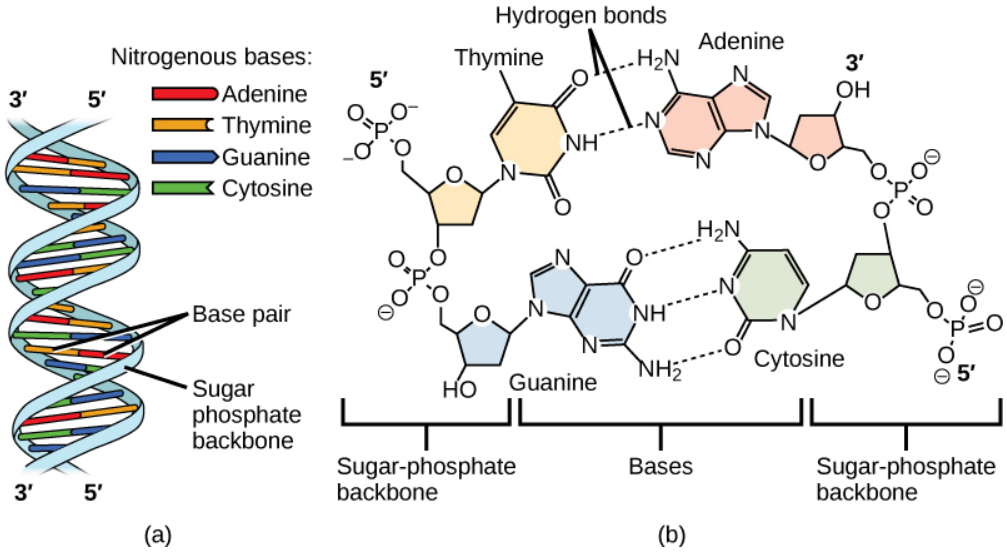


Figure 2.3 DNA (a) forms a double-stranded helix, and (b) adenine pairs with thymine and cytosine with guanine. **Source:** modification of work by Jerome Walker, Dennis Myts, *Concepts of Biology* (OpenStax), CC BY 4.0)

The Structure of RNA

A second nucleic acid in all cells is called **ribonucleic acid, or RNA**. Like DNA, RNA is a polymer of nucleotides. Each of the nucleotides in RNA is made up of a nitrogenous base, a five-carbon sugar, and a phosphate group. In the case of RNA, the **five-carbon sugar is ribose, not deoxyribose**. Ribose has a hydroxyl group at the 2′ carbon, unlike deoxyribose, which has only a hydrogen atom (Figure 2.4).

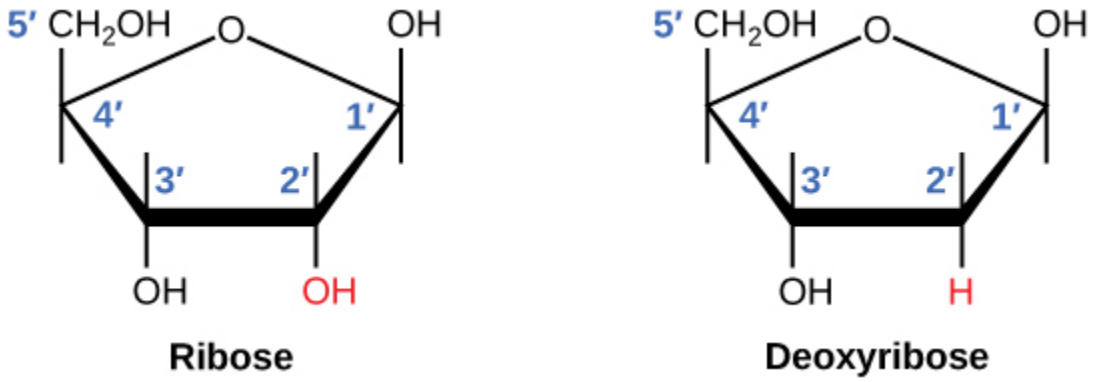


Figure 2.4 The difference between the ribose found in RNA and the deoxyribose found in DNA is that ribose has a hydroxyl group at the 2' carbon. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0).

RNA nucleotides contain the nitrogenous bases adenine, cytosine, and guanine. However, they d**o not contain thymine, which is replaced by uracil,** symbolized by a "U." RNA exists as a single-stranded molecule rather than a double-stranded helix. Molecular biologists have named several kinds of RNA based on their function. These include messenger RNA (mRNA), transfer RNA (**tRNA**), and ribosomal RNA (**rRNA**)—molecules that are involved in the production of proteins from the DNA code.

How DNA Is Arranged in the Cell

DNA is a working molecule; it must be replicated when a cell is ready to divide, and it must be "read" to produce the molecules, such as proteins, to carry out the functions of the cell. For this reason, the DNA is protected and packaged in particular ways. In addition, DNA molecules can be very long. Stretched end-to-end, the DNA molecules in a single human cell would come to a length of about 2 meters. Thus, the DNA for a cell must be packaged in a very ordered way to fit and function within a structure (the cell) that is not visible to the naked eye.

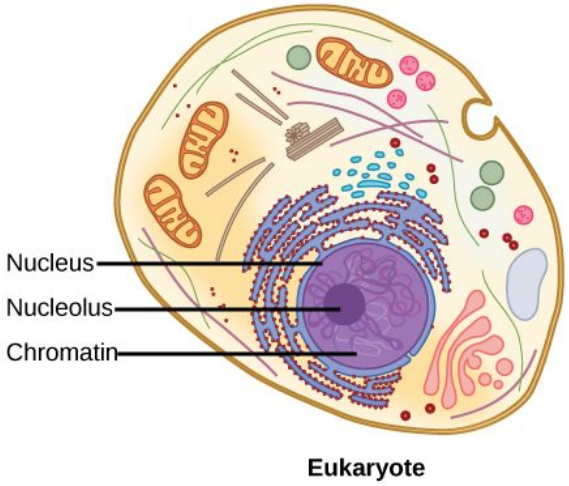


Figure 2.5 A eukaryotic cell**. Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Eukaryotes, whose chromosomes each consist of a linear DNA molecule, have a specific packing strategy to fit their DNA inside the nucleus. At the most basic level, DNA is wrapped around proteins known as histones to form structures called nucleosomes. The DNA is wrapped tightly around the histone core. This nucleosome is linked to the next one by a short strand of DNA that is free of histones. This is also known as the "beads on a string" structure; the nucleosomes are the "beads," and the short lengths of DNA between them are the "string." With their DNA coiled around them, the nucleosomes stack compactly onto each other to form a 30-nm–wide fiber. This fibre is further coiled into a thicker and more compact structure. At the metaphase stage of mitosis, when the chromosomes are lined up in the center of the cell, the chromosomes are at their most compacted. They are approximately 700 nm in width, and are associated with scaffold proteins.

In interphase, the phase of the cell cycle between mitoses at which the chromosomes are decondensed, eukaryotic chromosomes have two distinct regions that can be distinguished by staining. There is a tightly packaged region that stains darkly and a less dense region. The darkly staining regions usually contain genes that are not active and are found in the centromere and telomere regions. The lightly staining regions usually contain active genes, with DNA packaged around nucleosomes but not further compacted.

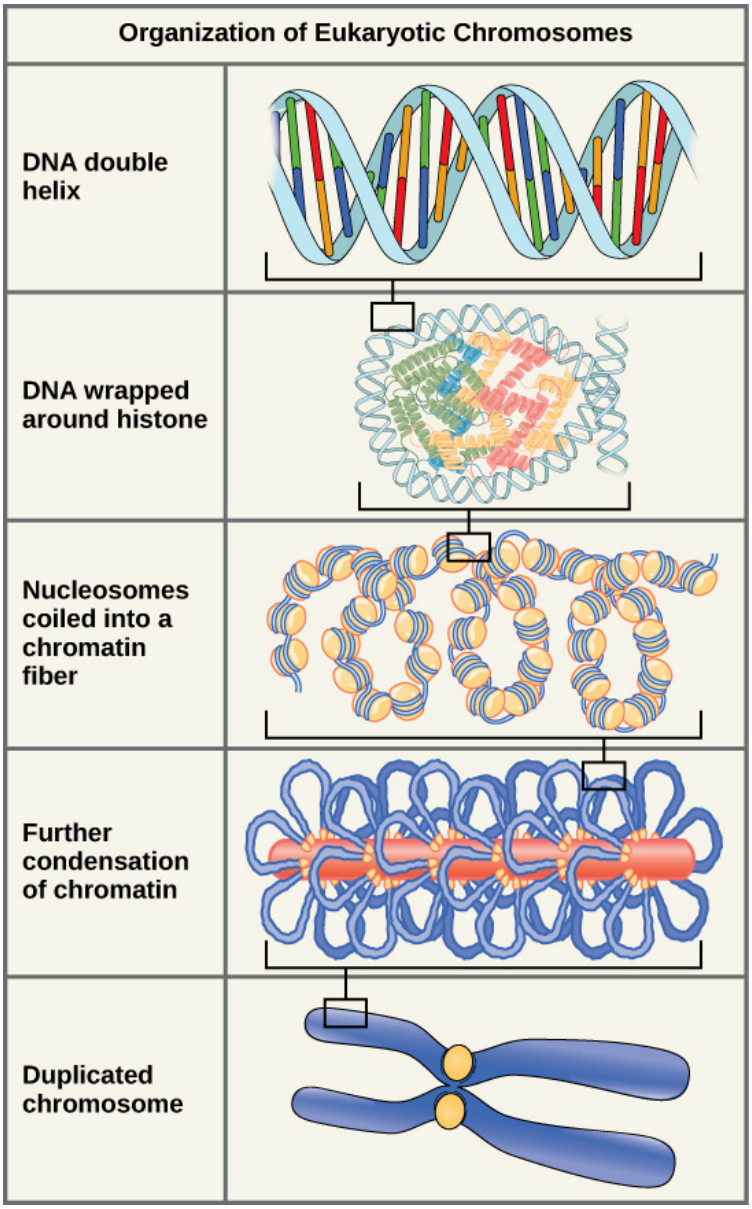


Figure 2.6 These figures illustrate the compaction of the eukaryotic chromosome. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Concept in Action – DNA

Use the interactive slideshow to review this concept in action, or access the videos and questions using the text version.

Concept in Action – DNA (text version)

Watch How DNA is Packaged (Advanced) (2 mins) on YouTube (https://youtu.be/gbSIBhFwQ4s)

Watch the video DNA is the Genetic Material (4 mins) on BCCampus (https://media.bccampus.ca/media/DNA+as+Genetic+Material/0_ajd2anyl) and try the following knowledge check:

Pause the video at 1:55 and match the terms to the correct blanks for this statement:

Terms: copied, changes, encode

Genetic material must be able to [Blank A] information. Genetic material must be [Blank B] when cells divide. Mutations are [Blank C] to a DNA sequence.

Check your answer in footnote[1]

Activity source: Concept in Action – DNA by Andrea Gretchev is licensed under CC BY-NC 4.0, except where otherwise noted.

When a cell divides, each daughter cell must receive an identical copy of the DNA. The process of DNA replication accomplishes this. DNA replication occurs during the synthesis phase, or S phase, of the cell cycle before the cell enters mitosis or meiosis.

The elucidation of the structure of the double helix provided a hint as to how DNA is copied. Recall that adenine nucleotides pair with thymine nucleotides and cytosine with guanine. This means that the two strands are complementary to each other. For example, a strand of DNA with a nucleotide sequence of AGTCATGA will have a complementary strand with the sequence TCAGTACT (Figure 2.7).

1. A – encode, B – copied, C – changes

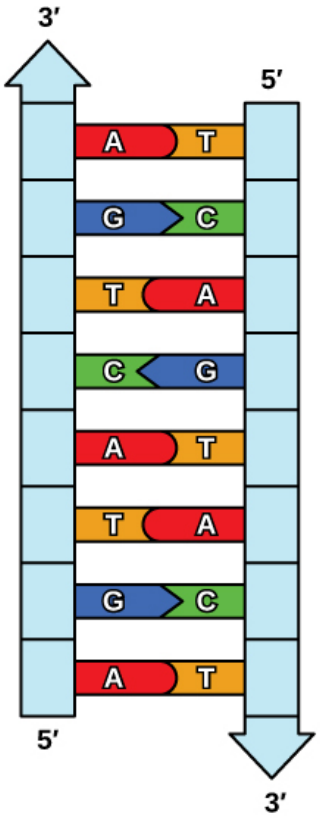


Figure 2.7 The two strands of DNA are complementary, meaning the sequence of bases in one strand can be used to create the correct sequence of bases in the other strand.
Source: *Concepts of Biology* (OpenStax), CC BY 4.0.

Because of the complementarity of the two strands, having one strand makes it possible to recreate the other strand. This model for replication suggests that the two strands of the double helix separate during replication, and each strand serves as a template from which the new complementary strand is copied (Figure 2.8).

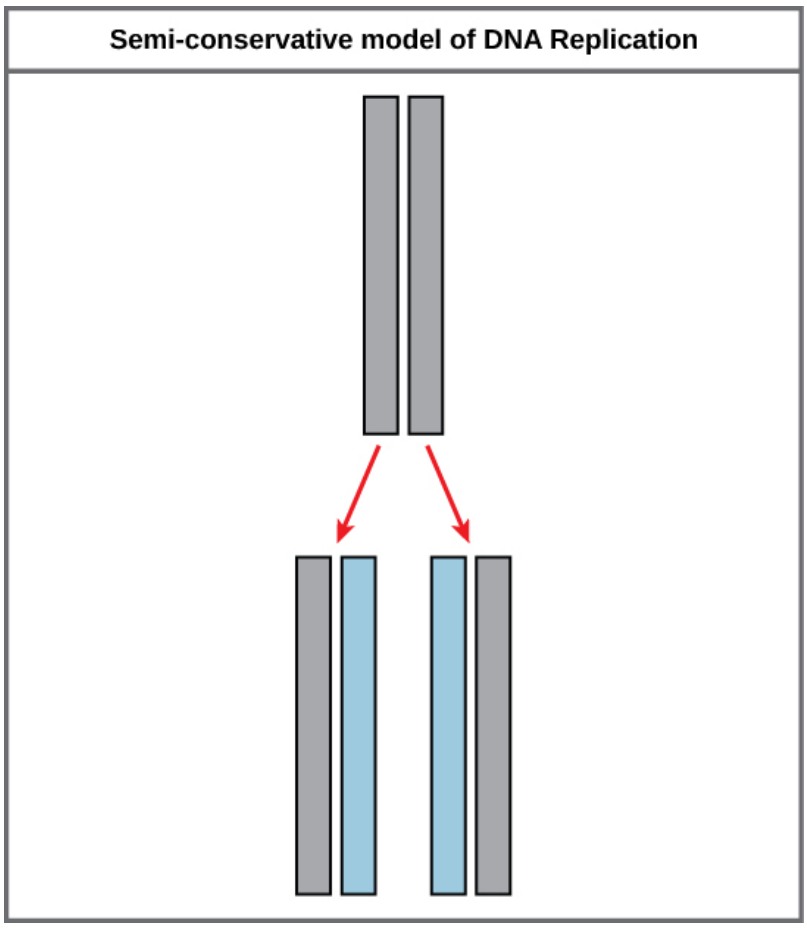


Figure 2.8 The semiconservative model of DNA replication is shown. Gray indicates the original DNA strands, and blue indicates newly synthesized DNA**. Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

During DNA replication, each of the two strands that make up the double helix serves as a **template** from which new strands are copied. The new strand will be **complementary** to the parental or "old" strand. Each new double strand consists of one parental strand and one new daughter strand. This is known as **semiconservative replication**. When two DNA copies are formed, they have an identical sequence of nucleotide bases and are divided equally into two daughter cells.

DNA Replication in Eukaryotes

Because eukaryotic genomes are very complex, DNA replication is a very complicated process that involves several enzymes and other proteins. It occurs in three main stages: **i**nitiation, elongation, and termination.

Recall that eukaryotic DNA is bound to proteins known as histones to form structures called nucleosomes. During **initiation**, the DNA is made accessible to the proteins and enzymes involved in the replication process. How does the replication machinery know where on the DNA double helix to begin? It

turns out that there are specific nucleotide sequences called **origins of replication** at which replication begins. Certain proteins bind to the origin of replication while an enzyme called **helicase** unwinds and opens up the DNA helix. As the DNA opens up, Y-shaped structures called **replication forks** are formed (Figure 2.9). Two replication forks are formed at the origin of replication, which are extended in both directions as replication proceeds. There are multiple origins of replication on the eukaryotic chromosome, such that replication can occur simultaneously from several places in the genome.

During elongation, an enzyme called **DNA polymerase** adds DNA nucleotides to the 3′ end of the template. Because DNA polymerase can only add new nucleotides at the end of a backbone, a primer sequence, which provides this starting point, is added with complementary RNA nucleotides. This primer is removed later, and the nucleotides are replaced with DNA nucleotides. One strand, which is complementary to the parental DNA strand, is synthesized continuously toward the replication fork so the polymerase can add nucleotides in this direction. This continuously synthesized strand is known as the **leading strand**. Because DNA polymerase can only synthesize DNA in a 5′ to 3′ direction, the other new strand is put together in short pieces called Okazaki fragments. The Okazaki fragments each require a primer made of RNA to start the synthesis. The strand with the Okazaki fragments is known as the **lagging strand**. As synthesis proceeds, an enzyme removes the RNA primer, which is then replaced with DNA nucleotides, and the gaps between fragments are sealed by an enzyme called **DNA ligase**.

The process of DNA replication can be summarized as follows:

1. DNA unwinds at the origin of replication.
2. New bases are added to the complementary parental strands. One new strand is made continuously, while the other strand is made in pieces.
3. Primers are removed, new DNA nucleotides are put in place of the primers and the backbone is sealed by DNA ligase.

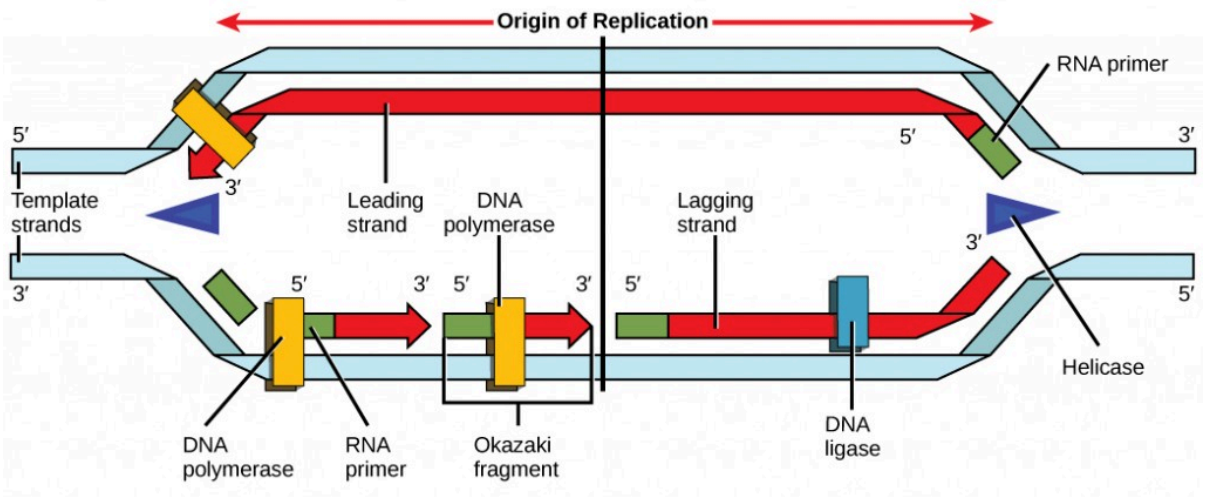


Figure 2.9 A replication fork is formed by the opening of the origin of replication, and helicase separates the DNA strands. An RNA primer is synthesized and is elongated by the DNA polymerase. DNA is synthesized continuously on the leading strand, whereas on the lagging strand, DNA is synthesized in short stretches. The DNA fragments are joined by DNA ligase (not shown)**. Source:** *Concepts of Biology* (OpenStax), CC BY 4.0).

Telomere Replication

Because eukaryotic chromosomes are linear, DNA replication comes to the end of a line in eukaryotic chromosomes. As you have learned, the DNA polymerase enzyme can add nucleotides in only one direction. In the leading strand, synthesis continues until the end of the chromosome is reached; however, on the lagging strand, there is no place for a primer to be made for the DNA fragment to be copied at the end of the chromosome. This presents a problem for the cell because the ends remain unpaired; over time, these ends get progressively shorter as cells continue to divide. The ends of the linear chromosomes are known as **telomeres**, which have **repetitive sequences** that do not code for a particular gene. As a consequence, it is telomeres that are shortened with each round of DNA replication instead of genes. For example, in humans, a six base-pair sequence, TTAGGG, is repeated 100 to 1000 times. The discovery of the enzyme **telomerase** (Figure 2.10) helped in the understanding of how chromosome ends are maintained. The telomerase attaches to the end of the chromosome, and complementary bases to the RNA template are added on the end of the DNA strand. Once the lagging strand template is sufficiently elongated, DNA polymerase can add nucleotides complementary to the ends of the chromosomes. Thus, the ends of the chromosomes are replicated.

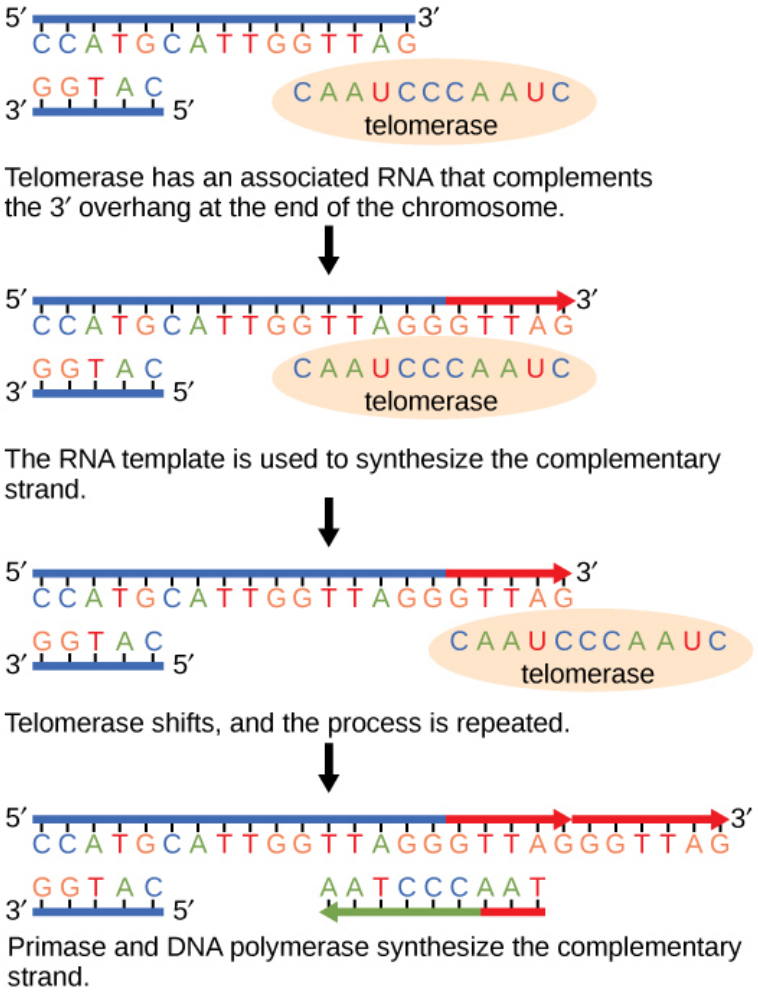


Figure 2.10 The ends of linear chromosomes are maintained by the action of the telomerase enzyme. **Source**: *Biology (OpenStax)*, CC BY 4.0.

Telomerase is typically found to be active in germ cells, adult stem cells, and some cancer cells. Elizabeth Blackburn (Figure 2.11) received the Nobel Prize for Medicine and Physiology in 2009 for her discovery of telomerase and its action.

Figure 2.11 Elizabeth Blackburn, 2009 Nobel Laureate, was the scientist who discovered how telomerase works. **Source:** Image by U.S. Embassy, Stockholm, Sweden, CC BY 2.0.

Telomerase is not active in adult somatic cells. Adult somatic cells that undergo cell division continue to have their telomeres shortened. This essentially means that telomere shortening is associated with aging. In 2010, scientists found that telomerase can reverse some age-related conditions in mice, which may have potential in regenerative medicine.[2] Telomerase-deficient mice were used in these studies; these mice have tissue atrophy, stem-cell depletion, organ system failure, and impaired tissue injury responses. Telomerase reactivation in these mice caused extension of telomeres, reduced DNA damage, reversed neurodegeneration, and improved functioning of the testes, spleen, and intestines. Thus, telomere reactivation may have the potential to treat age-related diseases in humans.

Concept in Action – DNA Replication

Watch DNA replication animation by interact Medical (1 min) on YouTube (https://youtu.be/zdDkiRw1PdU)

2. Mariella Jaskelioff, et al., "Telomerase reactivation reverses tissue degeneration in aged telomerase-deficient mice," *Nature, 469* (2011):102–

DNA Repair

DNA polymerase can make mistakes while adding nucleotides. It edits the DNA by **proofreading** every newly added base. Incorrect bases are removed and replaced by the correct base, then polymerization continues (Figure 2.12 **a**). Most mistakes are corrected during replication, although the mismatch repair mechanism is employed when this does not happen. **Mismatch repair** enzymes recognize the wrongly incorporated base and excise it from the DNA, replacing it with the correct base (Figure 2.12 b). In yet another type of repair, **nucleotide excision repair**, the DNA double-strand is unwound and separated, the incorrect bases are removed along with a few bases on the 5′ and 3′ end, and these are replaced by copying the template with the help of DNA polymerase (Figure 2.12 c). Nucleotide excision repair is particularly important in correcting thymine dimers, which are primarily caused by ultraviolet light. In a thymine dimer, two thymine nucleotides adjacent to each other on one strand are covalently bonded to each other rather than their complementary bases. If the dimer is not removed and repaired, it will become a variant. Individuals with flaws in their nucleotide excision repair genes show extreme sensitivity to sunlight and develop skin cancers early in life.

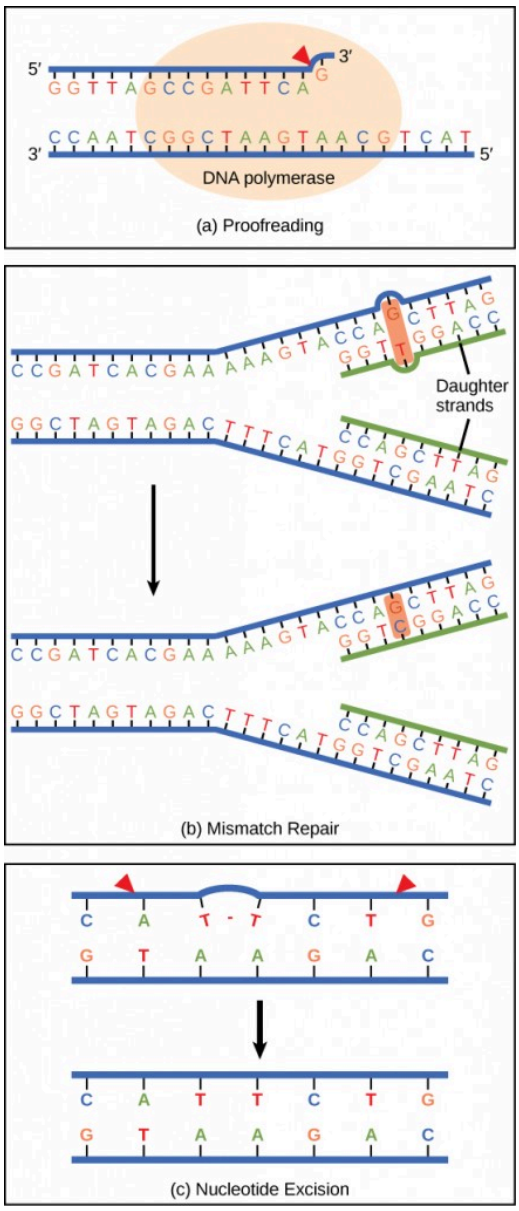


Figure 2.12 Proofreading by DNA polymerase (a) corrects errors during replication. In mismatch repair (b), the incorrectly added base is detected after replication. The mismatch repair proteins detect and remove this base from the newly synthesized strand by nuclease action. The gap is now filled with the correctly paired base. Nucleotide excision (c) repairs thymine dimers. When exposed to UV, thymines lying adjacent can form thymine dimers. In normal cells, they are excised and replaced. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Most mistakes are corrected; if not, they may result in a **variant**—defined as a permanent change in the DNA sequence. Variants in repair genes may lead to serious consequences like cancer.

The second function of DNA (the first was replication) is to **provide the information needed to construct the proteins** necessary so that the cell can perform all of its functions. To do this, the DNA is "read" or transcribed into an mRNA molecule. The mRNA then provides the code to form a protein by a process called translation. Through the processes of transcription and translation, a protein is built with a specific sequence of amino acids that was originally encoded in the DNA. This module discusses the details of transcription.

The Central Dogma: DNA Encodes RNA; RNA Encodes Protein

The central dogma describes the flow of genetic information in cells from DNA to mRNA to protein (Figure 2.13), which states that genes specify the sequences of mRNAs, which in turn specify the sequences of proteins.

Copying DNA to mRNA is relatively straightforward, with one nucleotide being added to the mRNA strand for every complementary nucleotide read in the DNA strand. The translation to protein is more complex because groups of three mRNA nucleotides correspond to one amino acid of the protein sequence. However, as we shall see in the next module, the translation to protein is still systematic, such that nucleotides 1 to 3 correspond to amino acid 1, nucleotides 4 to 6 correspond to amino acid 2, and so on.

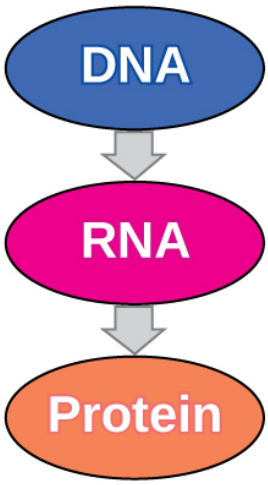


Figure 2.13 The central dogma states that DNA encodes RNA, which encodes protein. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Transcription: from DNA to mRNA

In eukaryotes, the genes are bound in the nucleus, so transcription occurs in the nucleus of the cell and the mRNA transcript must be transported to the cytoplasm. Transcription occurs in three main stages: initiation, elongation, and termination.

Initiation

Transcription requires the DNA double helix to partially unwind in the region of mRNA synthesis. The region of unwinding is called a transcription bubble. The DNA sequence onto which the proteins and enzymes involved in transcription bind to initiate the process is called a **promoter**. In most cases, promoters exist **upstream** of the genes they regulate. The specific sequence of a promoter is very important because it determines whether the corresponding gene is transcribed all of the time, some of the time, or hardly at all (Figure 2.14).

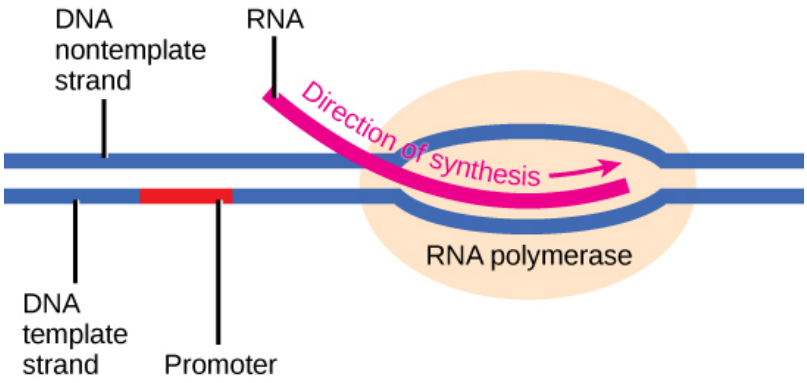


Figure 2.14 The initiation of transcription begins when DNA is unwound, forming a transcription bubble. Enzymes and other proteins involved in transcription bind at the promoter. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0).

Elongation

Transcription always proceeds from one of the two DNA strands, which is called the template strand. The mRNA product is complementary to the **template strand** and is almost identical to the other DNA strand, called the **non-template strand**, except that RNA contains a uracil (U) in place of the thymine (T) found in DNA. During elongation, an enzyme called RNA polymerase proceeds along the DNA template adding nucleotides by base pairing with the DNA template in a manner similar to DNA replication, with the difference that an RNA strand is being synthesized that does not remain bound to the DNA template. As elongation proceeds, the DNA is continuously unwound ahead of the core enzyme and rewound behind it (Figure 2.15).

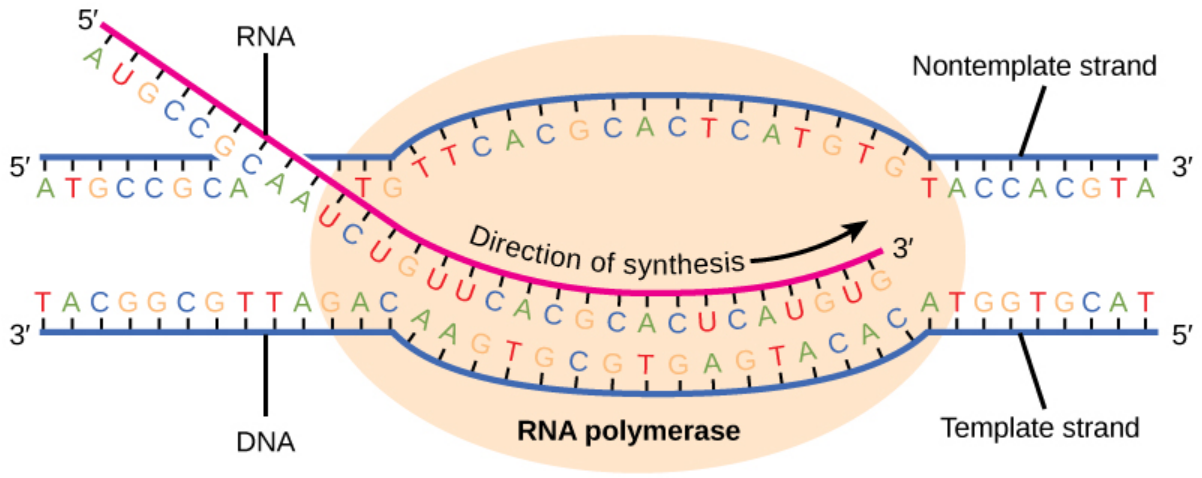


Figure 2.15 During elongation, RNA polymerase tracks along the DNA template, synthesizes mRNA in the 5' to 3' direction, and unwinds then rewinds the DNA as it is read. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Termination

Depending on the gene being transcribed, there are two kinds of termination signals, but both involve repeated nucleotide sequences in the DNA template that result in RNA polymerase stalling, leaving the DNA template, and freeing the mRNA transcript. On termination, the process of transcription is complete.

Eukaryotic RNA Processing

The newly transcribed eukaryotic mRNAs must undergo several processing steps before they can be transferred from the nucleus to the cytoplasm and translated into a protein. The mRNA transcript is first coated in RNA-stabilizing proteins to prevent it from degrading while it is processed and exported out of the nucleus. This occurs while the pre-mRNA is still being synthesized by adding a special nucleotide "cap" to the 5′ end of the growing transcript. In addition to preventing degradation, factors involved in protein synthesis recognize the cap to help initiate translation by ribosomes.

Once elongation is complete, an enzyme then adds a string of approximately 200 adenine residues to the 3′ end, called the **poly-A tail**. This modification further protects the pre-mRNA from degradation and signals to cellular factors that the transcript needs to be exported to the cytoplasm.

Eukaryotic genes are composed of protein-coding sequences called **exons** (*ex*-on signifies that they are *ex*pressed) and *int*ervening sequences called **introns** (*int*-ron denotes their *int*ervening role). Introns are removed from the pre-mRNA during processing. Intron sequences in mRNA do not encode functional proteins. It is essential that all of a pre-mRNA's introns be completely and precisely removed before protein synthesis so that the exons join together to code for the correct amino acids. If the process errs by even a single

nucleotide, the sequence of the rejoined exons would be shifted, and the resulting protein would be nonfunctional. The process of removing introns and reconnecting exons is called splicing (Figure 2.16). Introns are removed and degraded while the pre-mRNA is still in the nucleus.

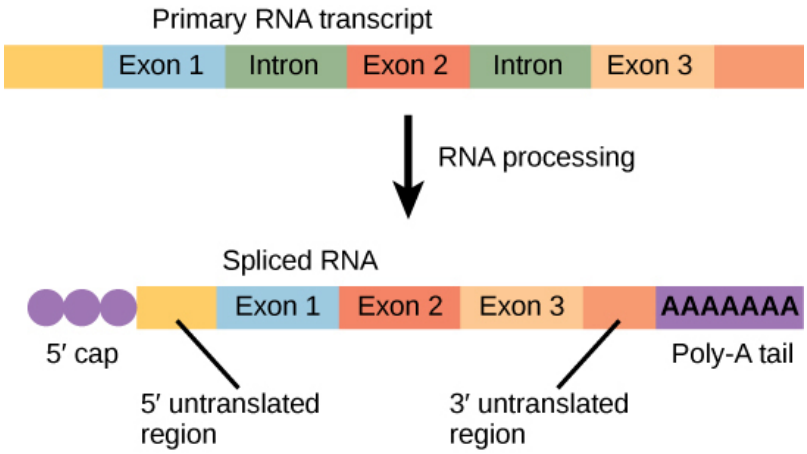


Figure 2.16 Eukaryotic mRNA contains introns that must be spliced out. A 5' cap and 3' tail are also added. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

The synthesis of proteins is one of a cell's most energy-consuming metabolic processes. In turn, proteins account for more mass than any other component of living organisms (with the exception of water), and proteins perform a wide variety of the functions of a cell. Translation, or protein synthesis, involves decoding an mRNA message into a polypeptide product. Amino acids are covalently strung together in lengths ranging from approximately 50 amino acids to more than 1,000.

The Protein Synthesis Machinery

In addition to the mRNA template, many other molecules contribute to the process of translation. The composition of each component may vary across species; for instance, ribosomes may consist of different numbers of ribosomal RNAs (rRNA) and polypeptides, depending on the organism. However, the general structures and functions of the protein synthesis machinery are comparable to those of bacteria and human cells. Translation requires the input of an mRNA template, ribosomes, tRNAs, and various enzymatic factors (Figure 2.17).

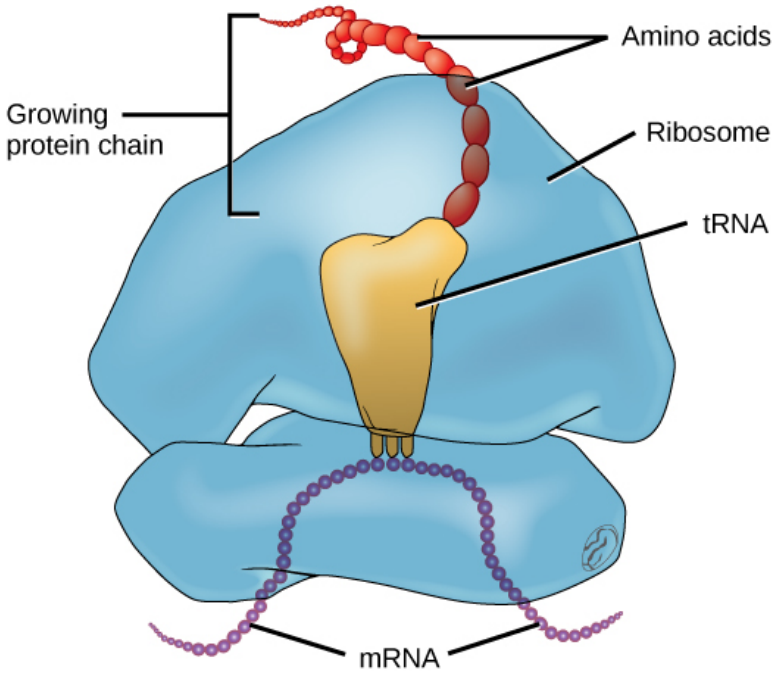


Figure 2.17 The protein synthesis machinery includes the large and small subunits of the ribosome, mRNA, and tRNA. **Source:** modification of work by NIGMS, NIH, *Concepts of Biology* (OpenStax), CC BY 4.0.

In *E. coli*, there are 200,000 ribosomes present in every cell at any given time. A ribosome is a complex macromolecule composed of structural and catalytic rRNAs, and many distinct polypeptides. In eukaryotes, the nucleolus is completely specialized for the synthesis and assembly of rRNAs.

Ribosomes are located in the cytoplasm and endoplasmic reticulum of eukaryotes. Ribosomes are made up of a large and a small subunit that come together for translation. The small subunit is responsible for binding the mRNA template, whereas the large subunit sequentially binds tRNAs, a type of RNA molecule that brings amino acids to the growing chain of the polypeptide. Each mRNA molecule is simultaneously translated by many ribosomes, all synthesizing protein in the same direction.

Depending on the species, 40 to 60 types of tRNA exist in the cytoplasm. Serving as adaptors, specific tRNAs bind to sequences on the mRNA template and add the corresponding amino acid to the polypeptide chain. Therefore, tRNAs are the molecules that actually "translate" the language of RNA into the language of proteins. For each tRNA to function, it must have its specific amino acid bonded to it. In the process of tRNA "charging," each tRNA molecule is bonded to its correct amino acid.

The Genetic Code

Use the interactive slides to watch two videos and check your knowledge, or access the text version of the activity below.

The Genetic Code (text version)
Watch the video: Universality of the Genetic Code (5 mins) on BCCampus (https://media.bccampus.ca/media/Universality+of+the+Genetic+Code/0_gw00p3jq).

1. After watching the first video fill in the missing words in the following statement:
   There are [Blank A] different ways to arrange 4 bases of DNA i groups of [Blank B].
   Since there are 20 amino acids there are more than one codon for each amino acid. This makes the genetic code [Blank C].

Watch the video: Mutations (5 mins) on BCCampus

2. Pause at 2:01. True or false? DNA can have mutations occur spontaneously.
3. Pause at 3:33. True or false? Agents that cause mutations are rarely cancer causing as well.

Check your answers in footnote[3]

Activity source: *Concepts of Biology – 1st Canadian Edition*, CC BY 4.0

To summarize what we know to this point, the cellular process of transcription generates messenger RNA (mRNA), a mobile molecular copy of one or more genes with an alphabet of A, C, G, and uracil (U). Translation of the mRNA template converts nucleotide-based genetic information into a protein product. Protein sequences consist of 20 commonly occurring amino acids; therefore, it can be said that the protein alphabet consists of 20 letters. Each amino acid is defined by a three-nucleotide sequence called the **triplet codon**. The relationship between a nucleotide codon and its corresponding amino acid is called the **genetic code**.

Given the different numbers of "letters" in the mRNA and protein "alphabets," combinations of nucleotides corresponded to single amino acids. Using a three-nucleotide code means that there are a total of 64 (4 × 4 × 4) possible combinations; therefore, a given amino acid is encoded by more than one nucleotide triplet (Figure 2.18).

3. 1. A – 64, B – 3, C – redundant. 2. True. 3. False.

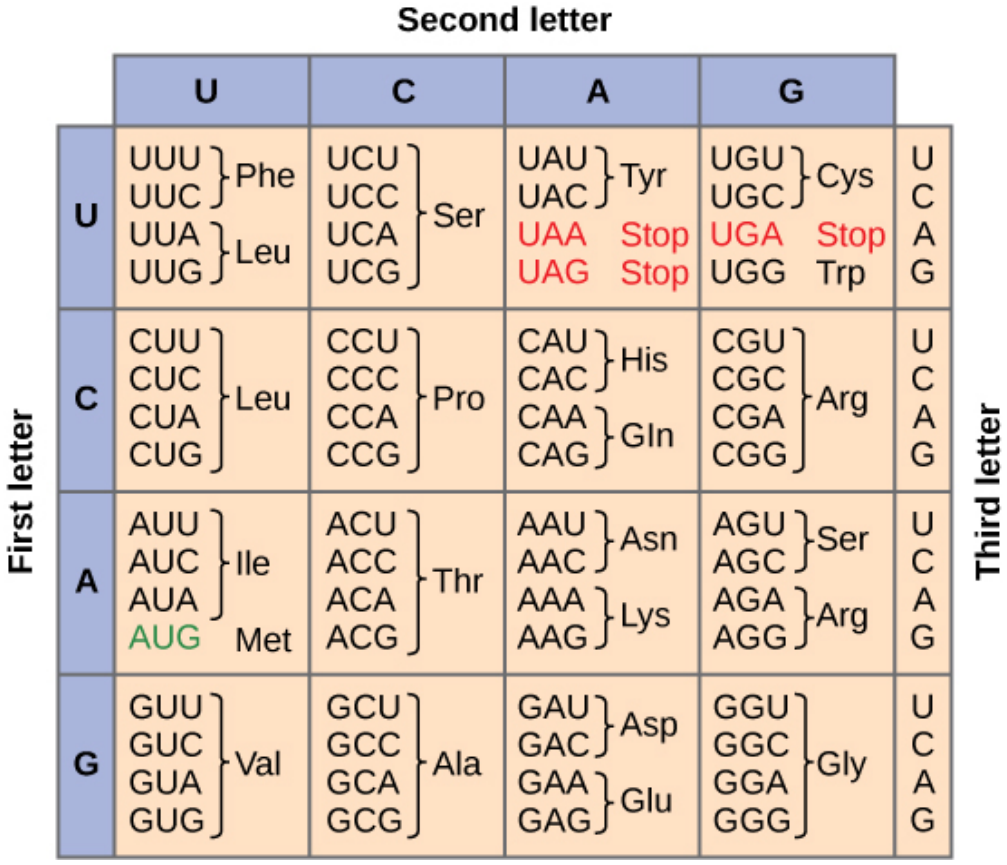
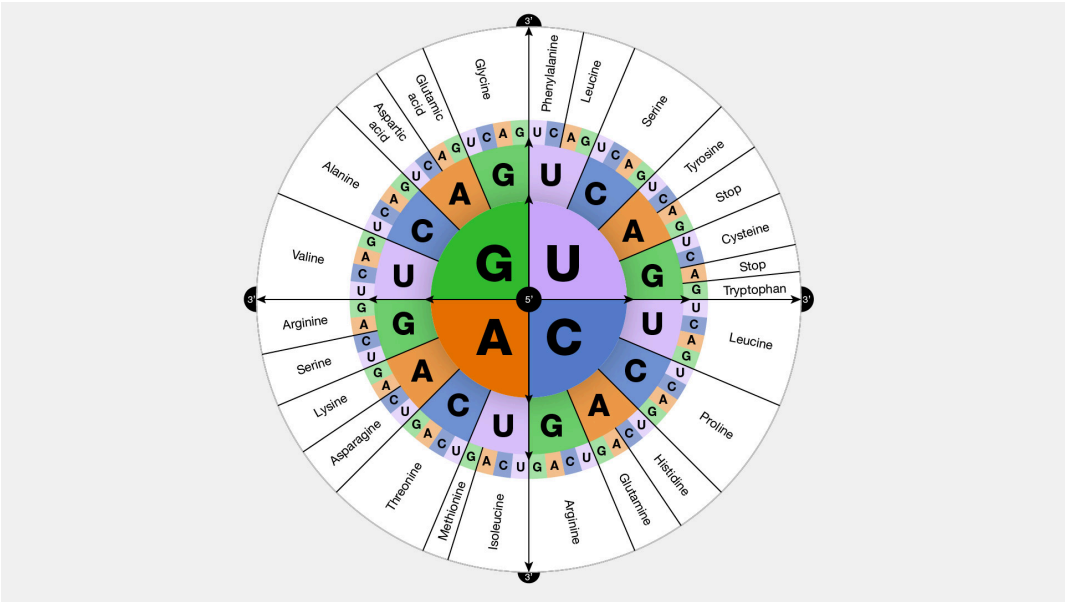


Figure 2.18 This figure shows the genetic code for translating each nucleotide triplet, or codon, in mRNA into an amino acid or a termination signal in a nascent protein. **Source**: modification of work by NIH, *Concepts of Biology* (OpenStax), CC BY 4.0.



Genetic code refers to the instructions contained in a gene that tell a cell how to make a specific protein. Each gene's code uses the four nucleotide bases of DNA: adenine (A), cytosine (C), guanine (G) and thymine (T) — in various ways to spell out three-letter "codons" that specify which amino acid is needed at each position within a protein. **Source:** Genetic Code Courtesy: National Human Genome Research Institute, PDM with attribution.

Three of the 64 codons terminate protein synthesis and release the polypeptide from the translation machinery. These triplets are called **stop codons**. Another codon, AUG, also has a special function. In addition to specifying the amino acid methionine, it also serves as the **start codon** to initiate translation. The reading frame for translation is set by the AUG start codon near the 5′ end of the mRNA. *The genetic code is universal*. With a few exceptions, virtually all species use the same genetic code for protein synthesis, which is powerful evidence that all life on Earth shares a common origin.

The Mechanism of Protein Synthesis

Just as with mRNA synthesis, protein synthesis can be divided into three phases: initiation, elongation, and termination. Here we will explore how translation occurs in *E. coli*, a representative prokaryote, and specify any differences between prokaryotic and eukaryotic translation.

Protein synthesis begins with the formation of an initiation complex. In *E. coli*, this complex involves the small ribosome subunit, the mRNA template, three initiation factors, and a special initiator tRNA. The

initiator tRNA interacts with the AUG start codon, and links to a special form of the amino acid methionine that is typically removed from the polypeptide after translation is complete.

In prokaryotes and eukaryotes, the basics of polypeptide elongation are the same, so we will review elongation from the perspective of *E. coli*. The large ribosomal subunit of *E. coli* consists of three compartments: the A site binds incoming charged tRNAs (tRNAs with their attached specific amino acids). The P site binds charged tRNAs carrying amino acids that have formed bonds with the growing polypeptide chain but have not yet dissociated from their corresponding tRNA. The E site releases dissociated tRNAs so they can be recharged with free amino acids. The ribosome shifts one codon at a time, catalyzing each process that occurs in the three sites. With each step, a charged tRNA enters the complex, the polypeptide becomes one amino acid longer, and an uncharged tRNA departs. The energy for each bond between amino acids is derived from GTP, a molecule similar to ATP (Figure 2.19). Amazingly, the *E. coli* translation apparatus takes only 0.05 seconds to add each amino acid, meaning that a 200-amino acid polypeptide could be translated in just 10 seconds.

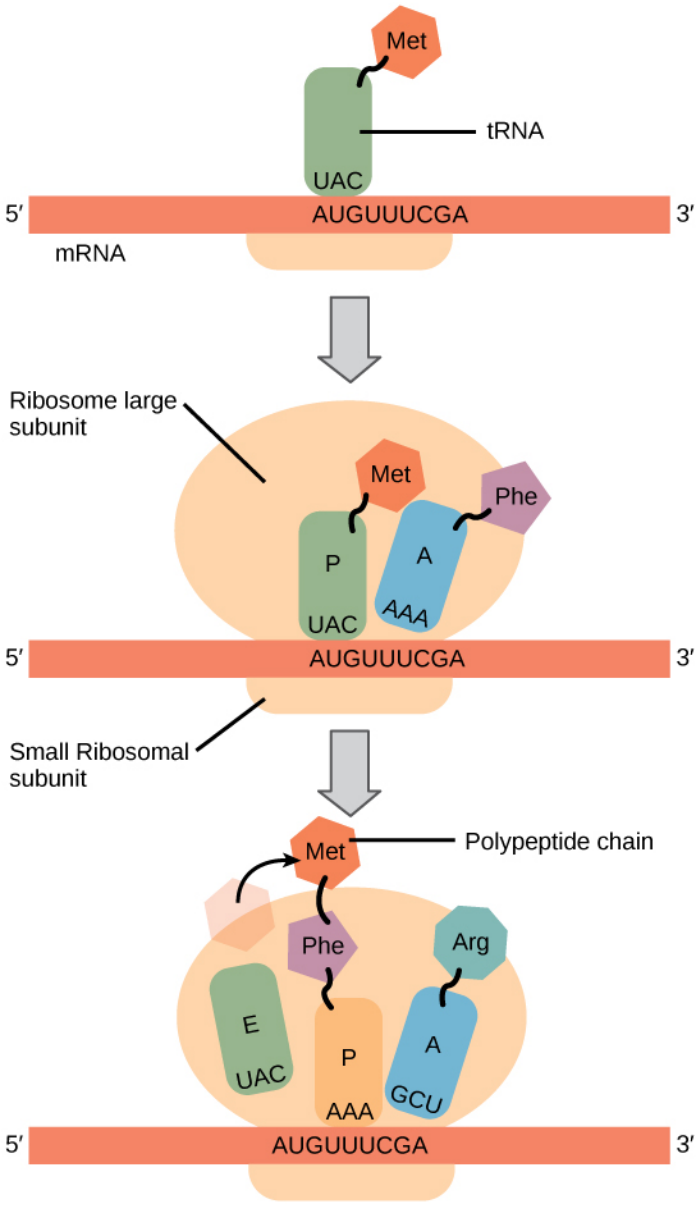


Figure 2.19 Translation begins when a tRNA anticodon recognizes a codon on the mRNA. The large ribosomal subunit joins the small subunit, and a second tRNA is recruited. As the mRNA moves relative to the ribosome, the polypeptide chain is formed. Entry of a release factor into the A site terminates translation and the components dissociate. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Termination of translation occurs when a stop codon (UAA, UAG, or UGA) is encountered. When the ribosome encounters the stop codon, the growing polypeptide is released and the ribosome subunits dissociate and leave the mRNA. After many ribosomes have completed translation, the mRNA is degraded so the nucleotides can be reused in another transcription reaction.

Concept in Action – Transcribe a gene

Visit the Learn Genetics website to transcribe a gene and translate it to protein using complementary pairing and the genetic code .

For a cell to function properly, necessary proteins must be synthesized at the proper time. All organisms and cells control or regulate the transcription and translation of their DNA into protein. The process of turning on a gene to produce RNA and protein is called **gene expression**. Whether in a simple unicellular organism or in a complex multicellular organism, each cell controls when and how its genes are expressed. For this to occur, there must be a mechanism to control when a gene is expressed to make RNA and protein, how much of the protein is made, and when it is time to stop making that protein because it is no longer needed.

Cells in multicellular organisms are specialized; cells in different tissues look very different and perform different functions. For example, a muscle cell is very different from a liver cell, which is very different from a skin cell. These differences are a consequence of the expression of different sets of genes in each of these cells. All cells have certain basic functions they must perform for themselves, such as converting the energy in sugar molecules into energy in ATP. Each cell also has many genes that are not expressed, and expresses many that are not expressed by other cells, such that it can carry out its specialized functions. In addition, cells will turn on or off certain genes at different times in response to changes in the environment or at different times during the development of the organism. Unicellular organisms, also turn on and off genes in response to the demands of their environment so that they can respond to special conditions.

The control of gene expression is extremely complex. Malfunctions in this process are detrimental to the cell and can lead to the development of many diseases, including cancer.

Eukaryotic Gene Expression

To understand how gene expression is regulated, we must first understand how a gene becomes a functional protein in a cell. Eukaryotic cells have intracellular organelles and are complex. Recall that in eukaryotic cells, the DNA is contained inside the cell's nucleus and it is transcribed into mRNA there. The newly synthesized mRNA is then transported out of the nucleus into the cytoplasm, where ribosomes translate the mRNA into protein. The processes of transcription and translation are physically separated by the nuclear membrane; transcription occurs only within the nucleus, and translation only occurs outside the nucleus in the cytoplasm. The regulation of gene expression can occur at all stages of the process (Figure 2.20). Regulation may occur when the DNA is uncoiled and loosened from nucleosomes to bind transcription factors (**epigenetic** level), when the RNA is transcribed (transcriptional level), when RNA is processed and exported

to the cytoplasm after it is transcribed (post-transcriptional level), when the RNA is translated into protein (translational level), or after the protein has been made (post-translational level).

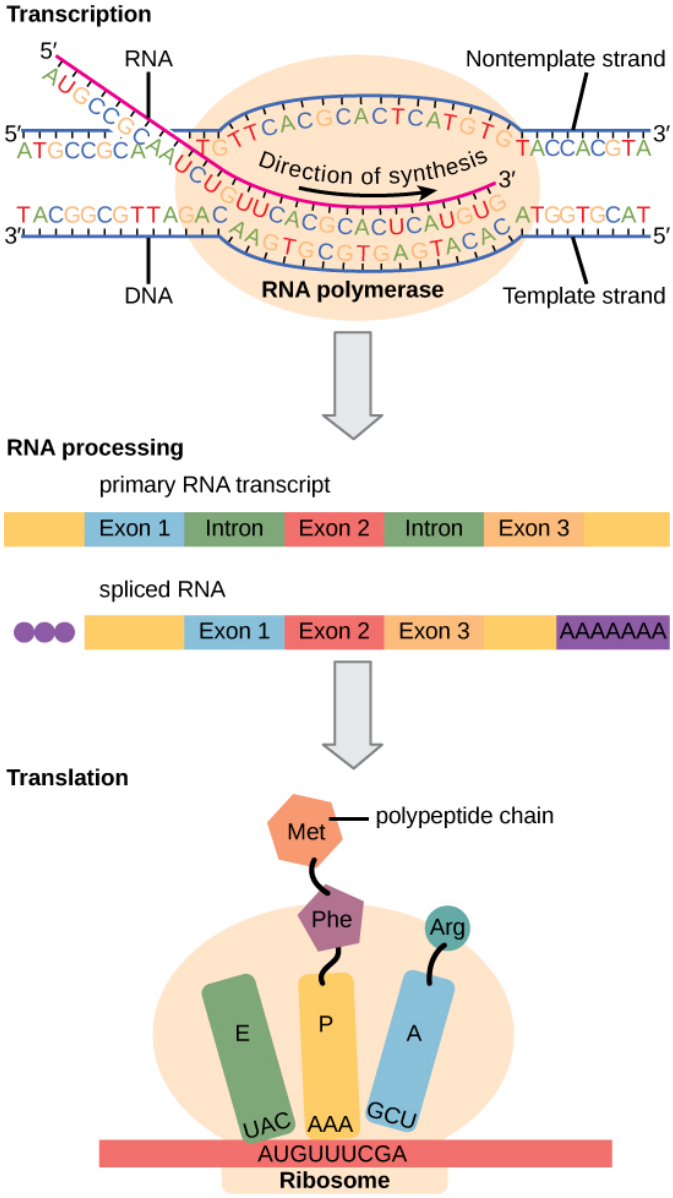


Figure 2.20 Eukaryotic gene expression is regulated during transcription and RNA processing, which take place in the nucleus, as well as during protein translation, which takes place in the cytoplasm. Further regulation may occur through post-translational modifications of proteins. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Alternative RNA Splicing

In the 1970s, genes were first observed that exhibited **alternative RNA splicing**. Alternative RNA splicing

is a mechanism that allows different protein products to be produced from one gene when different combinations of introns (and sometimes exons) are removed from the transcript (Figure 2.21). This alternative splicing can be haphazard, but more often it is controlled and acts as a mechanism of gene regulation, with the frequency of different splicing alternatives controlled by the cell as a way to control the production of different protein products in different cells, or at different stages of development. Alternative splicing is now understood to be a common mechanism of gene regulation in eukaryotes; according to one estimate, 70% of genes in humans are expressed as multiple proteins through alternative splicing.

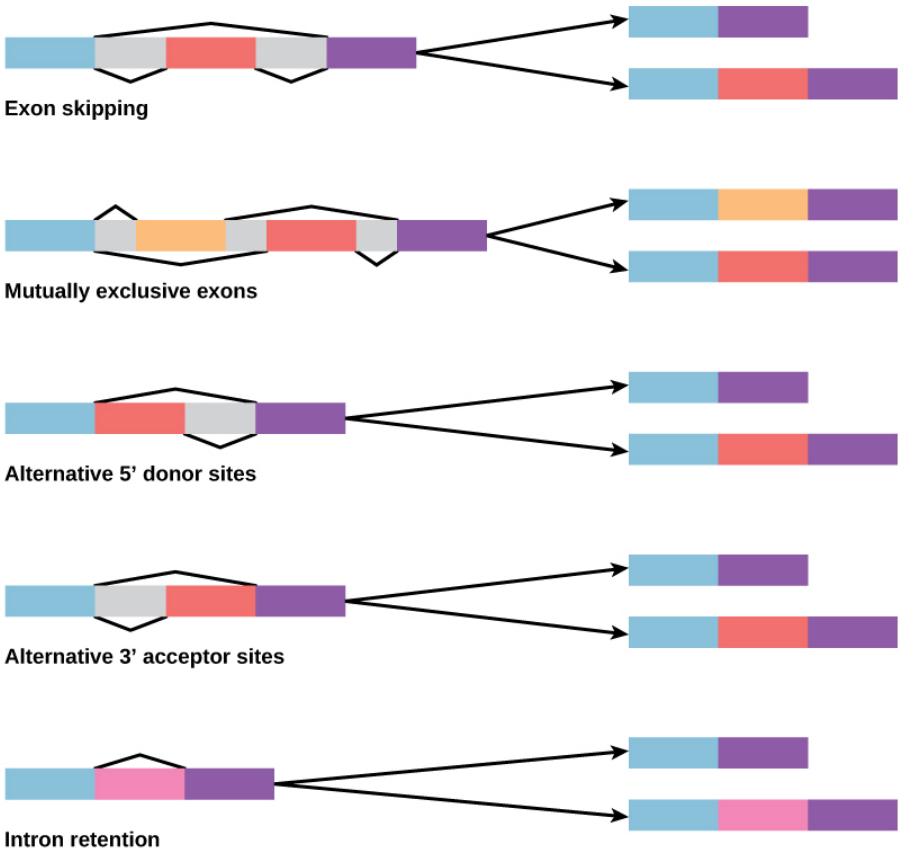


Figure 2.21 There are five basic modes of alternative splicing. Segments of pre-mRNA with exons shown in blue, red, orange, and pink can be spliced to produce a variety of new mature mRNA segments. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

How could alternative splicing evolve? Introns have a beginning and ending recognition sequence, and it is easy to imagine the failure of the splicing mechanism to identify the end of an intron and find the end of the next intron, thus removing two introns and the intervening exon. In fact, there are mechanisms in place to prevent such exon skipping, but variants are likely to lead to their failure. Such "mistakes" would more than likely produce a nonfunctional protein. Indeed, the cause of many genetic diseases is alternative splicing rather than variants in a sequence. However, alternative splicing would create a protein variant without the loss of the original protein, opening up possibilities for adaptation of the new variant to new functions. Gene

duplication has played an important role in the evolution of new functions in a similar way—by providing genes that may evolve without eliminating the original functional protein.

Exercises

Exercises (text version)

1. True or false? Nucleotides are made up of three parts: a base, ribose sugar, and phosphate.
2. Fill in the blanks in the following statements:
    a. a. The letters of the 4 nucleotides are [Blank 1] and [Blank 2] and [Blank 3] and [Blank 4].
    b. b. The base pairing rules are the A always pairs with [Blank 1] and [Blank 2] always pairs with [Blank 3].
    c. DNA replication is said to be [Blank 1]- conservative.
    d. The enzyme that is crucial in copying DNA strands is called [Blank 1].
    e. The central dogma of molecular biology is:
    DNA——1——— arrow to mRNA—2—- arrow to Protein.
    The number that represents Translation is [Blank 1]. The number that represents Transcription is [Blank 2].
    f. Since (with a few exceptions) all organisms use the same genetic code, it is said to be [Blank 1].
    g. DNA functions to provide the information needed to construct [Blank 1]*Protein/Proteins/protein/Protein*.
3. Which of the following does cytosine pair with?
    a. guanine
    b. thymine
    c. adenine
    d. a pyrimidine
4. How are chromosomes arranged and packaged in a eukaryotic cell (select all that apply)?
    a. double-stranded, linear
    b. single-stranded, circular

c. wrapped around histones
d. wrapped around nucleosomes

5. Match the words to the correct blank to describe the organization of the eukaryotic chromosome.
   Words: histones, interphase, fibre, euchromatin, metaphase, heterochromatin
   The DNA is wound around proteins called [Blank A]. These proteins then stack together in a compact form that creates a [Blank B]*fiber* 30-nm thick that is further coiled for greater compactness. During [Blank C] of mitosis, the *chromosome* is at its most compact to facilitate *chromosome* movement. During [Blank D]*interphase*, there are denser areas of chromatin, called [Blank E]*heterochromatin*, that contain DNA that is not expressed, and less dense [Blank F]*euchromatin* that contains DNA that is expressed.
6. Match the words to the correct blank to describe the structure and complementary base pairing of DNA.
   Words: double helix, adenine/thymine, two strands, cytosine/guanine, phosphate group, cytosine/guanine, nucleic acids, nitrogenous, covalently, deoxyribose sugar, hydrogen
   A single strand of DNA is a polymer of [Blank A] joined [Blank B] between the [Blank C] of one and the [Blank D] of the next to form a "backbone" from which the [Blank E] bases stick out. In its natural state, DNA has [Blank F] wound around each other in a [Blank G]. The bases on each strand are bonded to each other with [Blank H] bonds. Only specific bases bond with each other; [Blank i] bonds with [Blank J], and [Blank K] bonds with [Blank L].
7. Fill in the missing word to complete the statement.
   You isolate a cell strain in which the joining together of Okazaki fragments is impaired and suspect that a mutation has occurred in an enzyme found at the replication fork. The enzyme most likely to be altered is [Blank A], as this enzyme joins together Okazaki fragments.
8. DNA replicates by which of the following models?

   a. conservative
   b. semiconservative
   c. dispersive
   d. none of the above

9. What is the initial mechanism for repairing nucleotide errors in DNA?

   a. mismatch repair
   b. DNA polymerase proofreading
   c. nucleotide excision repair

d. thymine dimers

10. True or false? The linear chromosomes in eukaryotes ensure that its ends are replicated completely because telomerase has an inbuilt RNA template that extends the 3' end, so a primer is synthesized and extended, and the ends are protected.
11. What is a promoter?

    a. a specific sequence of DNA nucleotides
    b. a protein that binds to DNA
    c. an enzyme that synthesizes RNA
    d. a specific sequence of RNA nucleotides

12. What is the term for the portions of eukaryotic mRNA sequence that are removed during RNA processing?

    a. exons
    b. caps
    c. poly-A tails
    d. introns

13. Where are the RNA components of ribosomes synthesized?

    a. cytoplasm
    b. nucleus
    c. nucleolus
    d. endoplasmic reticulum

14. How long would the peptide be that is translated from this mRNA sequence: 5'-AUGGGCUACCGA-3'?

    a. 0
    b. 2
    c. 3
    d. 4

15. At what level(s) does the control of gene expression occur in eukaryotic cells?

    a. only the transcriptional level
    b. epigenetic and transcriptional levels
    c. epigenetic, transcriptional, and translational levels

d. epigenetic, transcriptional, post-transcriptional, translational, and post-translational levels

16. What does post-translational control refer to?

    a. the regulation of gene expression after transcription
    b. the regulation of gene expression after translation
    c. the control of epigenetic activation
    d. the period between transcription and translation

17. Match the words into the correct blanks to describe how controlling gene expression will alter the overall protein levels in the cell.
    Words: decrease, stages, Prokaryotic, Eukaryotic, translation, lifespan, Eukaryotic, increase, amount, Prokaryotic,
    The cell controls which protein is expressed, and to what level that protein is expressed, in the cell. [Blank A] cells alter the transcription rate to turn genes on or off. This method will [Blank B] or [Blank C] protein levels in response to what is needed by the cell. [Blank D] cells change the accessibility (epigenetic), transcription, or translation of a gene. This will alter the [Blank E] and [Blank F] of RNA, to alter how much protein exists. These cells also change the protein's [Blank G] to increase or decrease its overall levels. [Blank H] organisms are much more complex than [Blank i] organisms and can manipulate protein levels by changing many [Blank J] in the process.

Check your answers in footnote[4]

4.
1. True. .
2. a. 1: A/G/T/C/a/t/g/c; 2: A/G/T/C/a/t/g/c; 3: A/G/T/C/a/t/g/c; 4: A/G/T/C/a/t/g/c.
   b. 1: T/t; 2: G/g; 3: C/c
   c. 1. semi
   d. 1. DNA polymerase/DNA Polymerase/dna polymerase*.
   e. 1: 2, 2: 1.
   f. 1. universal
   g. Protein/Proteins/protein/Protein
3. a) guanine
4. a) double-stranded, linear
5. A – histones, B – Fiber, C – metaphase, D – interphase, E – heterochromatin, F – euchromatin
6. A – nucleic acids, B – covalently, C – phosphate group, D – deoxyribose sugar, E – nitrogenous, F – two strands, G – double helix, H – hydrogen, i – adenine/thymine, J – adenine/thymine, K – cytosine/guanine, L – cytosine/guanine.

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Attribution & References

Except where otherwise noted, content on this page is adapted from 9.1 The Structure of DNA, 9.2 DNA Replication, 9.3 Transcription, 9.4 Translation, and 9.5 How Genes Are Regulated In *Concepts of Biology – 1st Canadian Edition* by Charles Molnar and Jane Gair, CC BY 4.0. A derivative of *Concepts of Biology (OpenStax),* CC BY 4.0. Access *Concepts of Biology* for free at OpenStax / Adaptations: Individual sections have been combined and streamlined, including minor edits to improve student understanding and provide context.

7. a. Ligase/ligase
8. b. semiconservative
9. b. DNA polymerase proofreading
10. True.
11. a. a specific sequence of DNA nucleotides
12. d. introns
13. c. nucleolus
14. d. 4
15. epigenetic, transcriptional, post-transcriptional, translational, and post-translational levels
16. b. the regulation of gene expression after translation
17. A – Prokaryotic, B – increase, C – decrease, D – Eukaryotic, E – amount, F – lifespan, G – translation, H – Eukaryotic, i – Prokaryotic, J – stages

2.3 THE GENOME AND THE CELL CYCLE

Learning Objectives

- Describe the eukaryotic genome.
- Distinguish between chromosomes, genes, traits, and phenotype.
- Describe the three stages of interphase.
- Discuss the behaviour of chromosomes during mitosis and how the cytoplasmic content divides during cytokinesis.
- Define the quiescent G_0 phase.
- Explain how the three internal control checkpoints occur at the end of G_1, at the G_2–M transition, and during metaphase.

Genomic DNA

Before discussing the steps a cell undertakes to replicate, a deeper understanding of the structure and function of a cell's genetic information is necessary. A cell's complete complement of DNA is called its genome. In eukaryotes, the genome comprises several double-stranded, linear DNA molecules (Figure 2.22) bound with proteins to form complexes called chromosomes. Each eukaryote species has a characteristic number of chromosomes in the nuclei of its cells. Human body cells (somatic cells) have **46 chromosomes,** including **44 autosomes** and **2 sex chromosomes**. A somatic cell contains two matched sets of chromosomes, a configuration known as **diploid**. The letter *n* represents a single set of chromosomes; therefore, a diploid organism is designated 2*n*. Human cells that contain one set of **23 chromosomes** are called **gametes,** or sex cells; these eggs and sperm are designated ***n***, or **haploid**.

The matched pairs of chromosomes in a diploid organism are called homologous chromosomes. **Homologous** chromosomes are the same length and have specific nucleotide segments called genes in exactly the same location, or **locus**. Genes, the functional units of chromosomes, determine specific **characteristics** by coding for specific proteins. An individual's **genotype** refers to the set of genes an organism carries for a

specific trait. **Traits** are the different forms of a characteristic. For example, the shape of earlobes is a characteristic with traits of free or attached. A **phenotype** is the observable physical and physiological traits of an individual resulting from the interaction of its genotype with the environment. The phenotype encompasses all traits, visible or otherwise. Subsequent chapters will discuss how to track phenotypes (specifically diseases) through multiple generations using a pedigree chart.

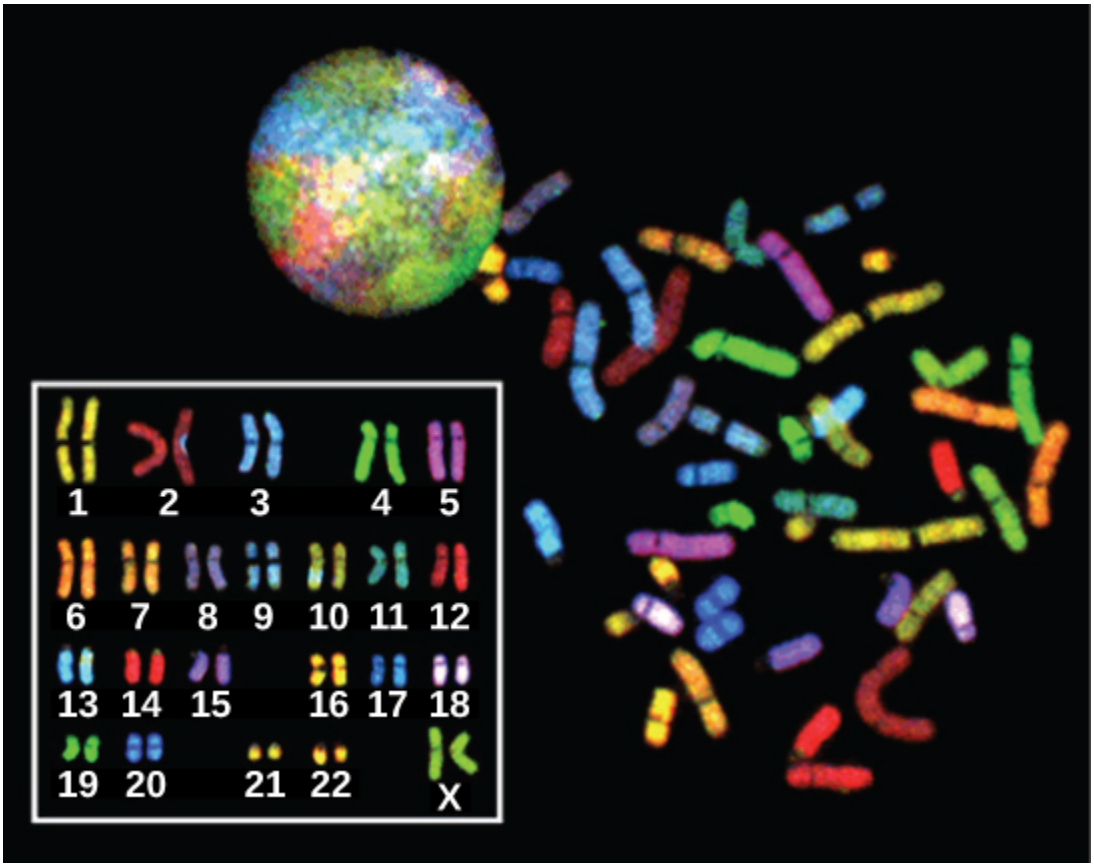

Figure 2.22 There are 23 pairs of homologous chromosomes in a female human somatic cell. These chromosomes are viewed within the nucleus (top), removed from a cell in mitosis (right), and arranged according to length (left) in an arrangement called a karyotype. In this image, the chromosomes were exposed to fluorescent stains to distinguish them. **Source:** Image Courtesy: National Human Genome Research, PDM

Each copy of the homologous pair of chromosomes originates from a different parent; therefore, the copies of each of the genes themselves may not be identical. The **variation** of individuals within a species is caused by the specific combination of the genes inherited from both parents. For example, there are three possible gene sequences on the human chromosome that codes for blood type: sequence A, sequence B, and sequence O. Because all diploid human cells have two copies of the chromosome that determines blood type, the blood type (the trait) is determined by which two versions of the marker gene are inherited. It is possible to have two copies of the same gene sequence, one on each homologous chromosome (for example, AA, BB, or OO), or

two different sequences, such as AB. This is due to incomplete dominance or codominance. Subsequent chapters will discuss these concepts of patterns of inheritance.

Minor variations in traits such as those for blood type, eye color, and height contribute to the natural variation found within a species. However, if the entire DNA sequence from any pair of human homologous chromosomes is compared, the *difference is much less than one percent*. The sex chromosomes, X and Y, are the single exception to the rule of homologous chromosomes; other than a small amount of homology that is necessary to reliably produce gametes, the genes found on the X and Y chromosomes are not the same.

The continuity of life from one cell to another has its foundation in the reproduction of cells by way of the **cell cycle**. The cell cycle is an orderly sequence of events in the life of a cell, from the division of a single parent cell to produce two new daughter cells to the subsequent division of those daughter cells. The mechanisms involved in the cell cycle are highly conserved across eukaryotes.

The Cell Cycle

The cell cycle is an ordered series of events involving cell growth and cell division that produces two new daughter cells. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages of growth, DNA replication, and division that produce two genetically identical cells. The cell cycle has two major phases: **interphase** and the **mitotic phase** (Figure 2.24). During interphase, the cell grows and DNA is replicated. During the mitotic phase, the replicated DNA and cytoplasmic contents are separated and the cell divides.

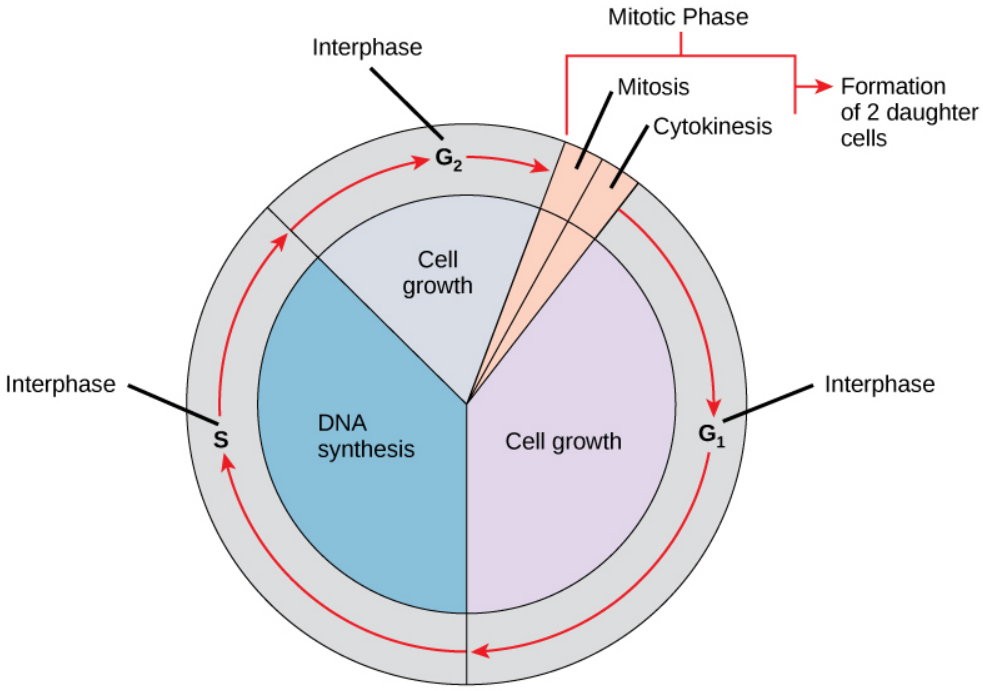

Figure 2.24 A cell moves through a series of phases in an orderly manner. During interphase, G1 involves cell growth and protein synthesis, the S phase involves DNA replication and the replication of the centrosome, and G2 involves further growth and protein synthesis. The mitotic phase follows interphase. Mitosis is nuclear division during which duplicated chromosomes are segregated and distributed into daughter nuclei. Usually the cell will divide after mitosis in a process called cytokinesis in which the cytoplasm is divided and two daughter cells are formed. **Source:** *Concepts of Biology (OpenStax)*, caption edited by *Biology 2e (OpenStax)*, CC BY 4.0.

Interphase

During interphase, the cell undergoes normal processes while also preparing for cell division. For a cell to move from interphase to the mitotic phase, many internal and external conditions must be met. The three stages of interphase are called G_1, S, and G_2.

G_1 Phase

The first stage of interphase is called the **G_1 phase**, or first gap, because little change is visible. However, during the G_1 stage, the cell is quite active at the biochemical level. The cell is accumulating the building blocks of chromosomal DNA and the associated proteins, as well as accumulating enough energy reserves to complete the task of replicating each chromosome in the nucleus.

S Phase

Throughout interphase, nuclear DNA remains in a semi-condensed chromatin configuration. In the **S phase** (synthesis phase), **DNA replication** results in the formation of two identical copies of each chromosome—sister chromatids—that are firmly attached at the centromere region. At this stage, each chromosome is made of two sister chromatids and is a duplicated chromosome. The centrosome is duplicated during the S phase. The two centrosomes will give rise to the **mitotic spindle**, the apparatus that orchestrates the movement of chromosomes during mitosis. The centrosome consists of a pair of rod-like **centrioles** at right angles to each other. Centrioles help organize cell division. Centrioles are not present in the centrosomes of many eukaryotic species, such as plants and most fungi.

G_2 Phase

In the **G_2 phase**, or second gap, the cell replenishes its energy stores and synthesizes the proteins necessary for chromosome manipulation. Some cell organelles are duplicated, and the cytoskeleton is dismantled to provide resources for the mitotic spindle. There may be additional cell growth during G_2. The final preparations for the mitotic phase must be completed before the cell is able to enter the first stage of mitosis.

The Mitotic Phase

To make two daughter cells, the contents of the nucleus and the cytoplasm must be divided. The mitotic phase is a multistep process during which the duplicated chromosomes are aligned, separated, and moved to opposite poles of the cell, and then the cell is divided into two new identical daughter cells. The first portion of the mitotic phase, **mitosis**, is composed of five stages, which accomplish nuclear division. The second portion of the mitotic phase, called **cytokinesis**, is the physical separation of the cytoplasmic components into two daughter cells.

Mitosis

Mitosis is divided into a series of phases— prophase, prometaphase, metaphase, anaphase, and telophase—that result in the division of the cell nucleus (Figure 2.25).

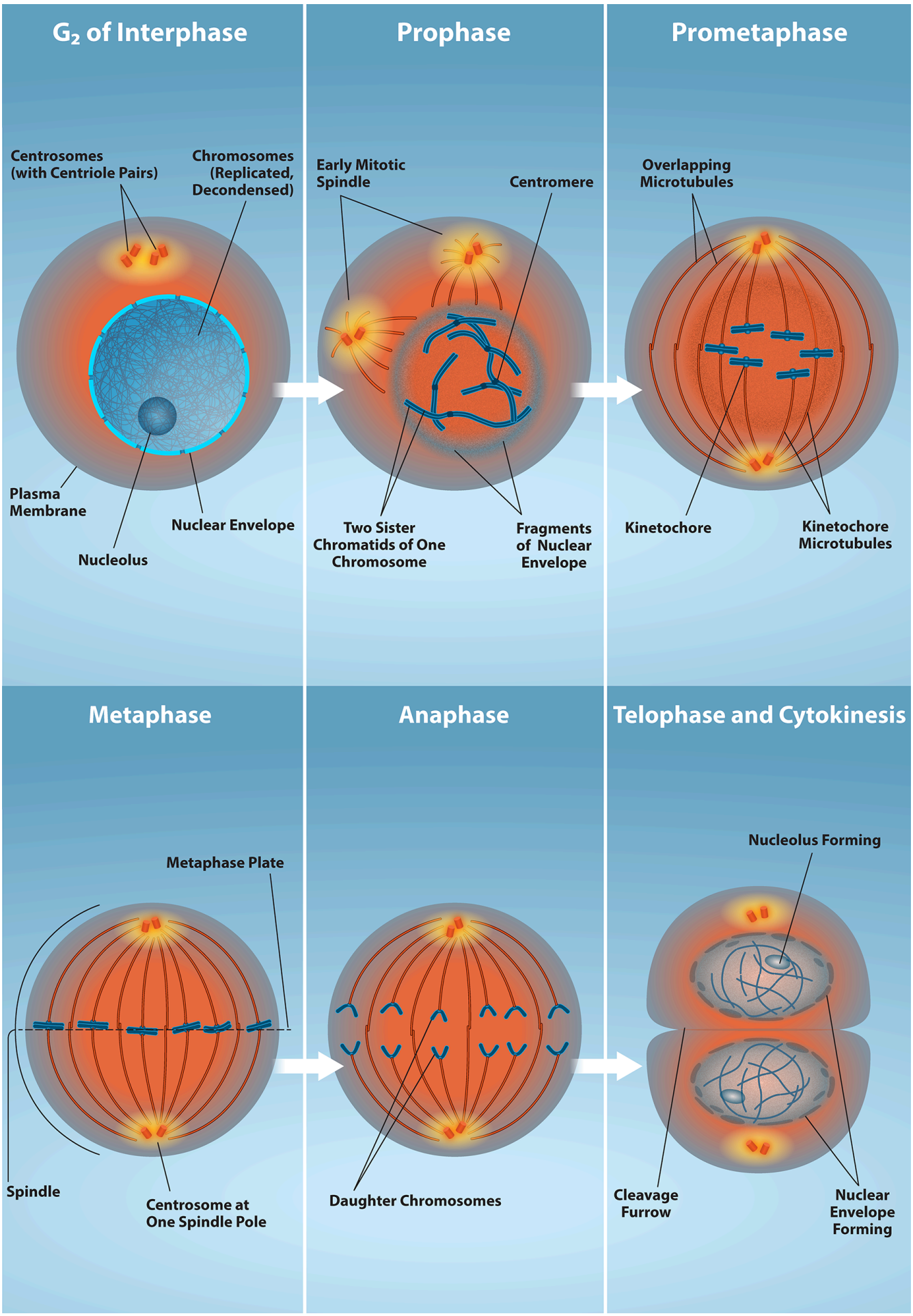
G2 of Interphase
Centrosomes (with Centriole Pairs)
Chromosomes (Replicated, Decondensed)
Plasma Membrane
Nucleolus
Nuclear Envelope
Prophase
Early Mitotic Spindle
Centromere
Two Sister Chromatids of One Chromosome
Fragments of Nuclear Envelope
Prometaphase
Overlapping Microtubules
Kinetochore
Kinetochore Microtubules
Metaphase
Metaphase Plate
Spindle
Centrosome at One Spindle Pole
Anaphase
Daughter Chromosomes
Telophase and Cytokinesis
Nucleolus Forming
Cleavage Furrow
Nuclear Envelope Forming

Figure 2.25 G2 of Interphase – The last stage of interphase is the second gap period, G2. During this stage, cells grow, replenish energy and synthesize needed macromolecules, such as proteins and lipids. Mitosis – When G2 is complete, the cell will enter mitosis. Although there are 5 phases in mitosis, with the exception of the metaphase to anaphase transition, these phases are not discrete and happen as a continuous process. Prophase is the first stage in mitosis. The nuclear envelope begins to break down and chromosomes condense and are now visible. Spindle fibers start to appear and centrosomes begin to move towards opposite poles. Prometaphase – Chromosomes continue to condense and are more visible. Kinetochores appear at the centromere and kinetochore microtubules attach. Centrosomes continue to move towards opposite poles. Metaphase – The mitotic spindle is fully developed and centrosomes are at opposite poles. Chromosomes are aligned at the "equatorial plate", and each sister chromatid rests on one side of the plate, with spindle fibers attached to them. Anaphase – Sister chromatids are pulled apart by spindle fibers and are separated from each other. Each chromatid is now a chromosome. Telophase and Cytokinesis – Chromosomes arrive at opposite poles and start to decondense and become less visible. The nuclear envelope reassembles and begins to surround each new set of chromosomes. The mitotic spindle assembly breaks down and the division of the cytoplasm begins via cytokinesis. This physical separation into two cells are remarkably different processes in plant and animal cells. **Source:** Rao, A., Hawkins, A. and Fletcher, S. Department of Biology, Texas A&M University, *Biology 2e (OpenStax)*, CC BY 4.0.

During **prophase**, the "first phase," several events must occur to provide access to the chromosomes in the nucleus. The nuclear envelope starts to break into small vesicles, and the Golgi apparatus and endoplasmic reticulum fragment and disperse to the periphery of the cell. The nucleolus disappears. The centrosomes begin to move to opposite poles of the cell. The microtubules that form the basis of the mitotic spindle extend between the centrosomes, pushing them farther apart as the microtubule fibers lengthen. The sister chromatids begin to coil more tightly and become visible under a light microscope.

During **prometaphase**, many processes that were begun in prophase continue to advance and culminate in the formation of a connection between the chromosomes and cytoskeleton. The remnants of the nuclear envelope disappear. The mitotic spindle continues to develop as more microtubules assemble and stretch across the length of the former nuclear area. Chromosomes become more condensed and visually discrete. Each sister chromatid attaches to spindle microtubules at the centromere via a protein complex called the kinetochore.

During **metaphase**, all of the chromosomes are aligned in a plane called the **metaphase plate**, or the equatorial plane, midway between the two poles of the cell. The sister chromatids are still tightly attached to each other. At this time, the chromosomes are maximally condensed.

During **anaphase**, the sister chromatids at the equatorial plane are split apart at the centromere. Each chromatid, now called a chromosome, is pulled rapidly toward the centrosome to which its microtubule was attached. The cell becomes visibly elongated as the non-kinetochore microtubules slide against each other at the metaphase plate where they overlap.

During **telophase**, all of the events that set up the duplicated chromosomes for mitosis during the first three phases are reversed. The chromosomes reach the opposite poles and begin to decondense (unravel). The mitotic spindles are broken down into monomers that will be used to assemble cytoskeleton components for each daughter cell. Nuclear envelopes form around chromosomes.

Concept in Action – Mitosis

Watch Mitosis: The Amazing Cell Process that Uses Division to Multiply! (Updated) (6 mins) on YouTube (https://youtu.be/gcz1FOWw0Cg)

Cytokinesis

Cytokinesis is the second part of the mitotic phase during which cell division is completed by the physical separation of the cytoplasmic components into two daughter cells. Although the stages of mitosis are similar for most eukaryotes, the process of cytokinesis is quite different for eukaryotes that have cell walls, such as plant cells.

In cells such as animal cells that lack cell walls, cytokinesis begins following the onset of anaphase. A contractile ring composed of actin filaments forms just inside the plasma membrane at the former metaphase plate. The actin filaments pull the equator of the cell inward, forming a fissure. This fissure, or "crack," is called the **cleavage furrow**. The furrow deepens as the actin ring contracts, and eventually the membrane and cell are cleaved in two (Figure 2.25).

In plant cells, a cleavage furrow is not possible because of the rigid cell walls surrounding the plasma membrane. A new cell wall must form between the daughter cells. During interphase, the Golgi apparatus accumulates enzymes, structural proteins, and glucose molecules prior to breaking up into vesicles and dispersing throughout the dividing cell. During telophase, these Golgi vesicles move on microtubules to collect at the metaphase plate. There, the vesicles fuse from the center toward the cell walls; this structure is called a cell plate. As more vesicles fuse, the cell plate enlarges until it merges with the cell wall at the periphery of the cell. Enzymes use the glucose that has accumulated between the membrane layers to build a new cell wall of cellulose. The Golgi membranes become the plasma membrane on either side of the new cell wall (Figure 2.26).

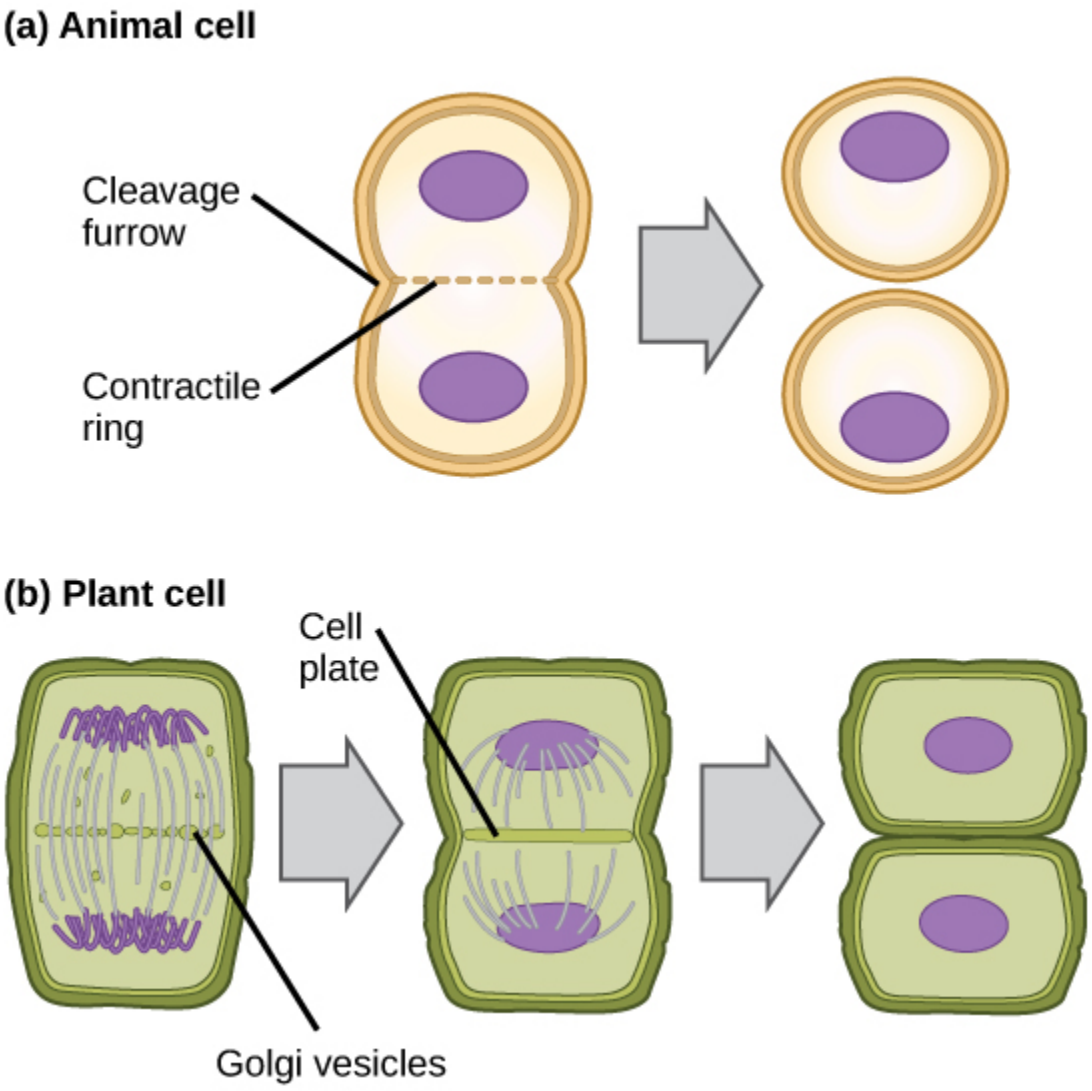

Figure 2.26 In part (a), a cleavage furrow forms at the former metaphase plate in the animal cell. The plasma membrane is drawn in by a ring of actin fibers contracting just inside the membrane. The cleavage furrow deepens until the cells are pinched in two. In part (b), Golgi vesicles coalesce at the former metaphase plate in a plant cell. The vesicles fuse and form the cell plate. The cell plate grows from the center toward the cell walls. New cell walls are made from the vesicle contents. **Source:** *Concepts of Biology (OpenStax)*, CC BY 4.0.

Concept in Action – Cell Cycle

Watch The Cell Cycle by Nucleus Biology (4 mins) on YouTube (https://youtu.be/e6N9_RhD10Q?si=_5hAiWQtpuVCdgQL)

Go Phase

Not all cells adhere to the classic cell-cycle pattern in which a newly formed daughter cell immediately enters interphase, closely followed by the mitotic phase. Cells in the **G_0 phase** are *not actively preparing to divide.* The cell is in a **quiescent (inactive) stage**, having exited the cell cycle. Some cells enter G_0 temporarily until an external signal triggers the onset of G_1. Other cells that never or rarely divide, such as mature cardiac muscle and nerve cells, remain in G_0 permanently (Figure 2.27).

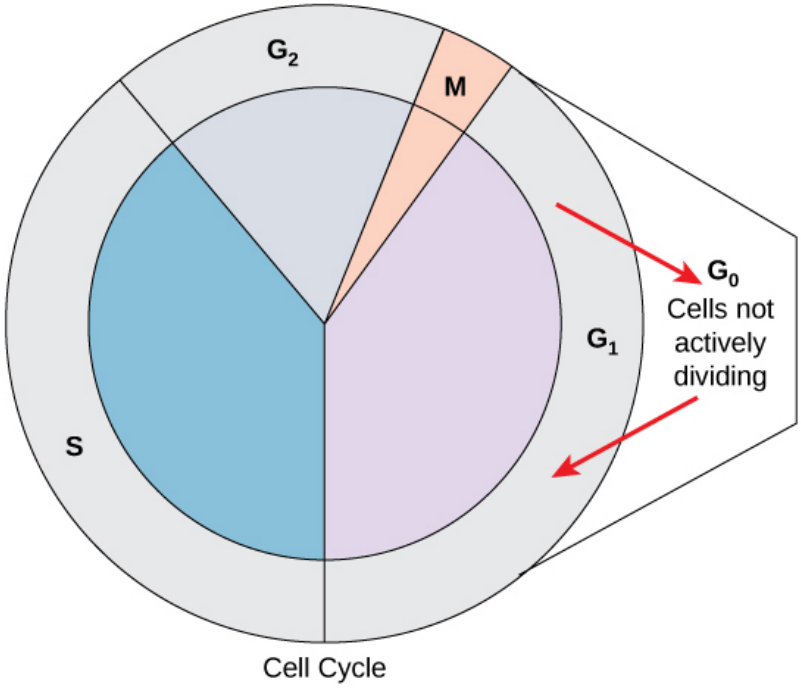

Figure 2.27 Cells that are not actively preparing to divide enter an alternate phase called G0. In some cases, this is a temporary condition until triggered to enter G1. In other cases, the cell will remain in G0 permanently. **Source:** Concepts of Biology (OpenStax), CC BY 4.0.

Control of the Cell Cycle

The length of the cell cycle is highly variable even within the cells of an individual organism. In humans, the frequency of cell turnover ranges from a few hours in early embryonic development to an average of two to five days for epithelial cells, or to an entire human lifetime spent in G_0 by specialized cells such as cortical neurons or cardiac muscle cells. There is also variation in the time that a cell spends in each phase of the cell cycle. When fast-dividing mammalian cells are grown in culture (outside the body under optimal growing conditions), the length of the cycle is approximately 24 hours. In rapidly dividing human cells with a 24-hour cell cycle, the G_1 phase lasts approximately 11 hours. The timing of events in the cell cycle is controlled by mechanisms that are both internal and external to the cell.

Regulation at Internal Checkpoints

It is essential that daughter cells be exact duplicates of the parent cell. Mistakes in the duplication or distribution of the chromosomes lead to gene **variants** (mutations) that may be passed forward to every new cell produced from the abnormal cell. To prevent a compromised cell from continuing to divide, there are internal control mechanisms that operate at three main **cell cycle checkpoints** at which the cell cycle can be stopped until conditions are favorable. These checkpoints occur near the end of G_1, at the **G_2–M transition**, and during metaphase (Figure 2.28).

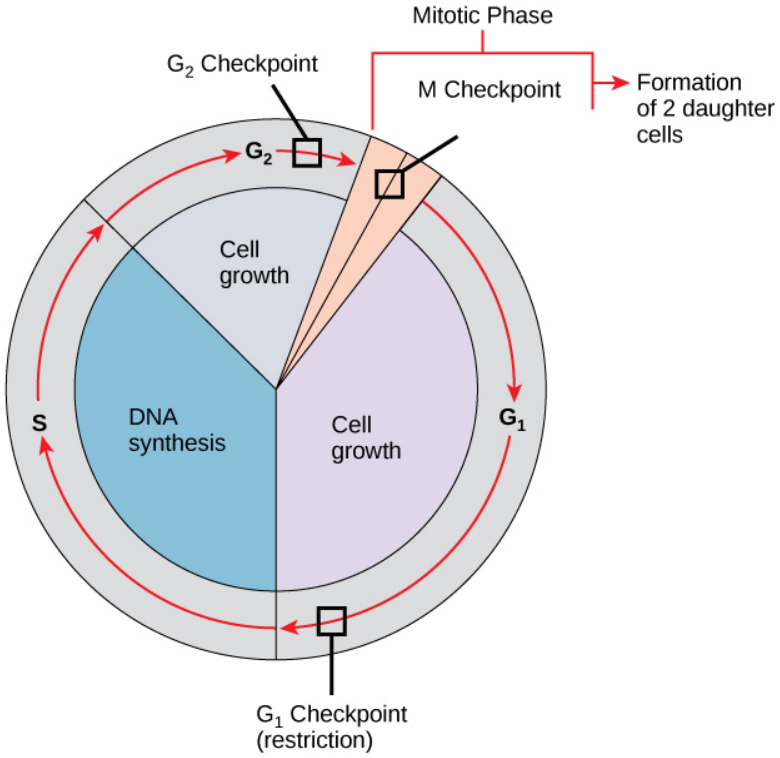

Figure 2.28 The cell cycle is controlled at three checkpoints. Integrity of the DNA is assessed at the G1 checkpoint. Proper chromosome duplication is assessed at the G2 checkpoint. Attachment of each kinetochore to a spindle fiber is assessed at the M checkpoint**. Source:** *Concepts of Biology (OpenStax)*, CC BY 4.0.

The G_1 Checkpoint

The **G_1 checkpoint** determines whether all conditions are favorable for cell division to proceed. The G_1 checkpoint, also called the restriction point, is the point at which the cell irreversibly commits to the cell-division process. In addition to adequate reserves and cell size, there is a check for damage to the genomic DNA at the G_1 checkpoint. A cell that does not meet all the requirements will not be released into the S phase.

The G_2 Checkpoint

The **G_2 checkpoint** bars the entry to the mitotic phase if certain conditions are not met. As in the G_1 checkpoint, cell size and protein reserves are assessed. However, the most important role of the G_2 checkpoint is to ensure that all of the chromosomes have been replicated and that the replicated DNA is not damaged.

The M Checkpoint

The **M checkpoint** occurs near the end of the metaphase stage of mitosis. The M checkpoint is also known as the spindle checkpoint because it determines if all the sister chromatids are correctly attached to the spindle microtubules. Because the separation of the sister chromatids during anaphase is an irreversible step, the cycle will not proceed until the kinetochores of each pair of sister chromatids are firmly anchored to spindle fibers arising from opposite poles of the cell.

Concept in Action – Eukaryotic Cell Cycle

Check out this interactive content that explains these concepts by visiting The Eukaryotic Cell Cycle and Cancer (https://media.hhmi.org/biointeractive/click/cellcycle/?_ga=2.198047532.225804613.1546808178-1471355355.1522416214).

Exercises

Exercises (text version)

1. True or false? The longest phase in the cell cycle is the M or Mitosis phase.
2. Fill in the blanks to complete the statement:
   Matched pairs of chromosomes are called [Blank A] chromosomes. These chromosomes have the same [Blank B] at the same locations. They may have differing [Blank C] , which are differing versions of the same gene.
   The number of chromosomes Humans have is [Blank D].

The term [Blank E] or 2n applies to body cells that have matched pairs of chromosomes. Gametes like sperm and eggs are called [Blank F] or n as they have only one copy of each chromosome.
The process called [Blank G] results in the creation of identical cells. In bacterial (prokaryotic cells) the process of making identical cells is called [Blank H].
The process of [Blank i] occurs in S-phase of interphase.
In the [Blank J] stage of mitosis chromosomes become visible when viewed down the microscope.

3. How many chromosomes does a diploid cell have compared a haploid cell?

    a. one-fourth
    b. one-half
    c. twice
    d. four times

4. What specific combination is inherited that determines an organism's traits?

    a. cells
    b. genes
    c. proteins
    d. chromatids

5. Match the words into the correct blanks to compare the characteristics of a human somatic cell to a human gamete.
   Words: haploid/n, one, forty-six, twenty-three, n/haploid, 2n/diploid, non-homologous, homologous, twenty-two, diploid/2n
   Human somatic cells have [Blank A] chromosomes, including [Blank B] [Blank C] pairs and [Blank D] pair of [Blank E] sex chromosomes. This is the [Blank F], or [Blank G], condition.
   Human gametes have one each of [Blank H] unique chromosomes. This is the [Blank i], or [Blank J] condition.
6. Which of the following statements describes the correct order of events in mitosis?

    a. Sister chromatids line up at the metaphase plate. The kinetochore becomes attached to the mitotic spindle. The nucleus re-forms and the cell divides. The sister chromatids separate.
    b. The kinetochore becomes attached to the mitotic spindle. The sister chromatids separate. Sister chromatids line up at the metaphase plate. The nucleus re-forms and the cell divides.

c. The kinetochore becomes attached to metaphase plate. Sister chromatids line up at the metaphase plate. The kinetochore breaks down and the sister chromatids separate. The nucleus re-forms and the cell divides.
d. The kinetochore becomes attached to the mitotic spindle. Sister chromatids line up at the metaphase plate. The kinetochore breaks apart and the sister chromatids separate. The nucleus re-forms and the cell divides.

7. In what portion of the cell cycle are chromosomes duplicated?

a. G_1 phase
b. S phase
c. prophase
d. prometaphase

8. In what stage of mitosis is the separation of the sister chromatids characteristic?

a. prometaphase
b. metaphase
c. anaphase
d. telophase

9. In what stage of mitosis do the individual chromosomes become visible with a light microscope?

a. prophase
b. prometaphase
c. metaphase
d. anaphase

10. What condition is necessary for a cell to pass the G_2 checkpoint?

a. cell has reached a sufficient size
b. an adequate stockpile of nucleotides
c. accurate and complete DNA replication
d. proper attachment of mitotic spindle fibers to kinetochores

Check your answers in footnote[1]

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Individual sections have been combined and streamlined, including minor edits to improve student understanding and provide context.

1. 1. False.
   2. A – homologous, B – genes, C – alleles, D – 46, E -diploid, F – haploid – G – mitosis, H – binary fission, i – replication/DNA replication, J – prophase
   3. c) twice
   4. b) genes
   5. A – forty-six, B – twenty-two, C – homologous, D – one, E – non-homologous, F – 2n/diploid, G – diploid/2n, H – twenty-three, i – n/haploid, J – haploid/n
   6. d) The kinetochore becomes attached to the mitotic spindle. Sister chromatids line up at the metaphase plate. The kinetochore breaks apart and the sister chromatids separate. The nucleus re-forms and the cell divides.
   7. b) S phase
   8. c) anaphase
   9. a) prophase
   10. c) accurate and complete DNA replication

2.4 CANCER AND THE CELL CYCLE

Learning Objectives

- Explain how cancer is caused by uncontrolled cell division.
- Identify how proto-oncogenes become oncogenes.
- Describe how tumor suppressors function to stop the cell cycle until certain events are completed.
- Explain how tumor suppressor variants cause cancer.

This chapter examines cancer from cellular perspective to provide a foundation for further discussion of the polygenic nature of diseases such as cancer (ch. 4.5), and cancer genomics (ch. 12.3).

Cancer is a collective name for many different diseases caused by a common mechanism: uncontrolled cell division. Despite the redundancy and overlapping levels of cell-cycle control, errors occur. One of the critical processes monitored by the cell-cycle checkpoint surveillance mechanism is the proper **replication of DNA** during the S phase. Even when all of the cell-cycle controls are fully functional, a small percentage of replication errors (variants) will be passed on to the daughter cells. If one of these changes to the DNA nucleotide sequence occurs within a gene, a gene variant results. All cancers begin when a gene variant gives rise to a faulty protein that participates in the process of cell reproduction. The change in the cell that results from the malformed protein may be minor. Even minor mistakes, however, may allow subsequent mistakes to occur more readily. Over and over, small, uncorrected errors are passed from parent cell to daughter cells and accumulate as each generation of cells produces more non-functional proteins from uncorrected DNA damage. Eventually, the pace of the cell cycle speeds up as the effectiveness of the control and repair mechanisms decreases. Uncontrolled growth of the altered cells outpaces the growth of normal cells in the area, and a tumor can result.

Proto-oncogenes

The genes that code for the **positive cell-cycle regulators** are called **proto-oncogenes**. Proto-oncogenes are normal genes that, when altered, become **oncogenes**—genes that cause a cell to become cancerous. Consider what might happen to the cell cycle in a cell with a recently acquired oncogene. In most instances, the alteration of the DNA sequence will result in a less functional (or non-functional) protein. The result is detrimental to the cell and will likely prevent the cell from completing the cell cycle; however, the organism is not harmed because the variant will not be carried forward. If a cell cannot reproduce, the variant is not propagated and the damage is minimal. Occasionally, however, a gene variant causes a change that increases the activity of a positive regulator. For example, a variant that allows Cdk, a protein involved in cell-cycle regulation, to be activated before it should be could push the cell cycle past a checkpoint before all of the required conditions are met. If the resulting daughter cells are too damaged to undertake further cell divisions, the variant would not be propagated and no harm comes to the organism. However, if the atypical daughter cells are able to divide further, the subsequent generation of cells will likely accumulate even more variants, some possibly in additional genes that regulate the cell cycle.

The Cdk example is only one of many genes that are considered proto-oncogenes. In addition to the cell-cycle regulatory proteins, any protein that influences the cycle can be altered in such a way as to override cell-cycle checkpoints. **Once a proto-oncogene has been altered such that there is an increase in the rate of the cell cycle, it is then called an oncogene**.

Tumor Suppressor Genes

Like proto-oncogenes, many of the **negative cell-cycle regulatory proteins** were discovered in cells that had become cancerous. **Tumor suppressor genes** are genes that code for the **negative regulator proteins**, the type of regulator that—when activated—can prevent the cell from undergoing uncontrolled division. The collective function of the best-understood tumor suppressor gene proteins, retinoblastoma protein (RB1), p53, and p21, is to put up a roadblock to cell-cycle progress until certain events are completed. A cell that carries a varied form of a negative regulator might not be able to halt the cell cycle if there is a problem.

Altered p53 genes have been identified in more than half of all human tumor cells. This discovery is not surprising in light of the multiple roles that the p53 protein plays at the G_1 checkpoint. The p53 protein activates other genes whose products halt the cell cycle (allowing time for DNA repair), activates genes whose products participate in DNA repair, or activates genes that initiate cell death when DNA damage cannot be repaired. A damaged p53 gene can result in the cell behaving as if there are no variants (Figure 2.29). This allows cells to divide, propagating the variant in daughter cells and allowing the accumulation of new variants. In addition, the damaged version of p53 found in cancer cells cannot trigger cell death.

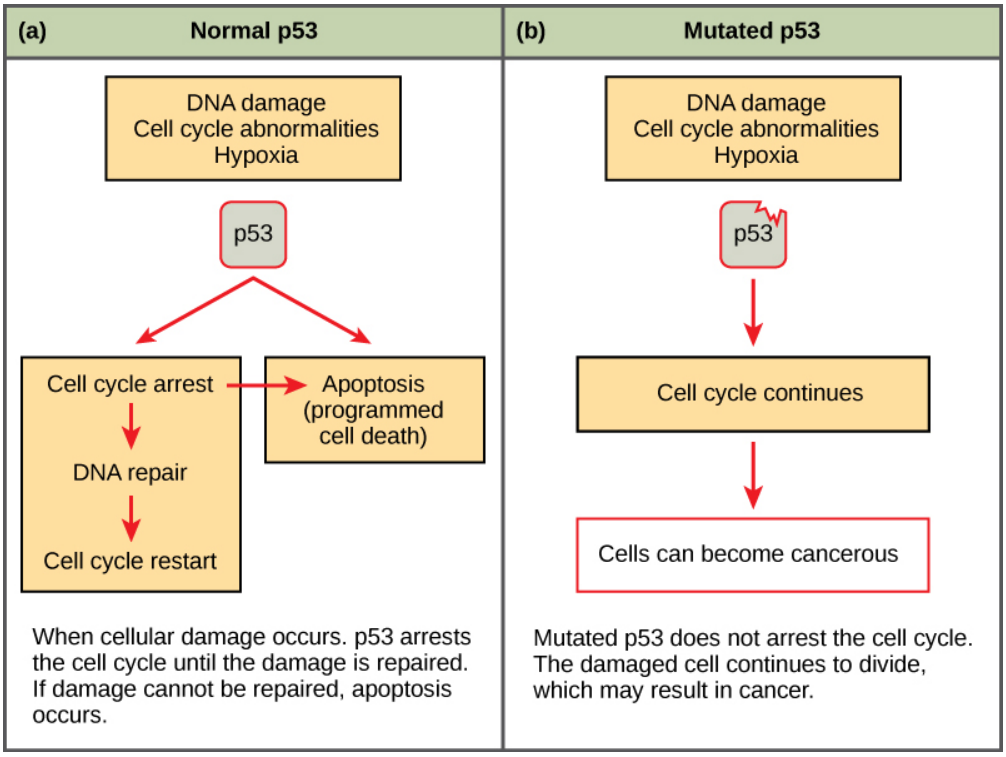

Figure 2.29 (a) The role of p53 is to monitor DNA. If damage is detected, p53 triggers repair mechanisms. If repairs are unsuccessful, p53 signals apoptosis. (b) A cell with an abnormal p53 protein cannot repair damaged DNA and cannot signal apoptosis. Cells with abnormal p53 can become cancerous. **Source:** modification of work by Thierry Soussi from *Concepts of Biology* (OpenStax), CC BY 4.0.

Concept in Action

Watch The Cell Cycle (and cancer) [Updated] (9 mins) on YouTube (https://youtu.be/QVCjdNxJreE)

Exercises

Exercises (text version)

1. What are changes to the nucleotides called in a segment of DNA that codes for a protein?

    a. proto-oncogenes
    b. tumor suppressor genes
    c. gene variants
    d. negative regulators

2. What is a gene called that codes for a positive cell cycle regulator?

    a. kinase inhibitor
    b. tumor suppressor gene
    c. proto-oncogene
    d. oncogene

3. Match the words to the correct blanks to describe the steps that lead to a cell becoming cancerous.
   Words: proteins, un-repaired, regulator, altered, cell-cycle
   The steps that lead to a cell becoming cancerous occur when one of the genes that produce [Blank A] proteins becomes [Blank B], and produces a malformed, possibly non-functional, [Blank C] regulator. This increases the chance that more variants will be left [Blank D] in the cell. Each subsequent generation of cells sustains more damage. The cell cycle can speed up as a result of loss of functional checkpoint [Blank E]. The cells can lose the ability to self-destruct.
4. Match the words to the correct blanks to describe the steps that lead to a cell becoming cancerous.
   Words: overactive, negative, underactive, positive, oncogene
   The difference between a proto-oncogene and a tumor suppressor gene is a proto-oncogene is the segment of DNA that codes for one of the [Blank A] cell-cycle regulators. If that gene becomes altered to a form that is [Blank B], it is considered an [Blank C]. A tumor suppressor gene is a segment of DNA that codes for one of the [Blank D] cell-cycle regulators. If that gene becomes altered to a form that is [Blank E], the cell cycle will run unchecked.

Check your answers in footnote[1]

1. a. c) gene variants
   b. c) proto-oncogene

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c. A – regulator, B – altered, C – cell-cycle, D – un-repaired, E – proteins
d. A – positive, B – overactive, C – oncogene, D – negative, E – underactive

2.5 THE CELLULAR BASIS OF INHERITANCE

Learning Objectives

- Explain why variation among offspring is a potential evolutionary advantage resulting from sexual reproduction.
- Identify why a gamete can not be identical to either of the parent gametes.
- Examine cellular events and chromosomal behavior during meiosis.
- Distinguish the differences between meiosis and mitosis.

Watch Sexual Reproduction (4 mins) from BCCampus (https://media.bccampus.ca/media/Sexual+Reproduction/0_25x7u748) and answer the question when prompted to check your learning.

Sexual reproduction (text version)

Watch Sexual Reproduction (4 mins) from BCCampus (https://media.bccampus.ca/media/Sexual+Reproduction/0_25x7u748)

1. Pause the video at 3:20. True or false? The processes that create variation in meiosis include both crossing over and independent assortment.
2. Pause the video at 4:20. True or false? Meiosis makes each human genetically unique.

Check your answer in footnote[1]

Activity source: *Concepts of Biology – 1st Canadian Edition*, CC BY 4.0.

1. 1. True. 2. True.

Life Cycles of Sexually Reproducing Organisms

Sexual reproduction requires **fertilization**, a union of two cells from two individual organisms. Fertilization occurs with the fusion of two gametes, usually from different individuals, restoring the diploid state. If those two cells each contain one set of chromosomes, then the resulting cell contains two sets of chromosomes. The number of sets of chromosomes in a cell is called its ploidy level. Haploid cells contain one set of chromosomes. Cells containing two sets of chromosomes are called diploid. If the reproductive cycle is to continue, the diploid cell must somehow reduce its number of chromosome sets before fertilization can occur again, or there will be a continual doubling in the number of chromosome sets in every generation. So, in addition to fertilization, sexual reproduction includes a nuclear division, known as meiosis, that reduces the number of chromosome sets. The variation that sexual reproduction creates among offspring is very important to the survival and reproduction of those offspring. In addition, variants are continually reshuffled from one generation to the next when different parents combine their unique genomes, and the genes are mixed into different combinations by the process of meiosis. Meiosis is the division of the contents of the nucleus that divides the chromosomes among gametes. Variation is introduced during meiosis, as well as when the gametes combine in fertilization.

Most animals and plants are diploid, containing two sets of chromosomes; in each **somatic** cell (the nonreproductive cells of a multicellular organism), the nucleus contains two copies of each chromosome that are referred to as homologous chromosomes. Somatic cells are sometimes referred to as "body" cells. Homologous chromosomes are matched pairs containing genes for the same traits in identical locations along their length. Diploid organisms inherit one copy of each homologous chromosome from each parent; all together, they are considered a full set of chromosomes. In animals, haploid cells containing a single copy of each homologous chromosome are found only within **gametes**. Gametes fuse with another haploid gamete to produce a diploid cell.

The nuclear division that forms haploid cells (meiosis) is related to mitosis. As you have learned, mitosis is part of a cell reproduction cycle that results in identical daughter nuclei that are also genetically identical to the original parent nucleus. In mitosis, both the parent and the daughter nuclei contain the same number of chromosome sets—diploid for most plants and animals. Meiosis employs many of the same mechanisms as mitosis. However, the starting nucleus is always diploid and the nuclei that result at the end of a meiotic cell division are haploid. To achieve the reduction in chromosome number, meiosis consists of one round of chromosome duplication and two rounds of nuclear division. Because the events that occur during each of the division stages are analogous to the events of mitosis, the same stage names are assigned. However, because there are two rounds of division, the stages are designated with a "I" or "II." Thus, meiosis I is the first round of meiotic division and consists of prophase I, prometaphase I, and so on. Meiosis I reduces the number of chromosome sets from two to one. The genetic information is also mixed during this division to create unique **recombinant** chromosomes. Meiosis II, in which the second round of meiotic division takes place in a way that is similar to mitosis, includes prophase II, prometaphase II, and so on.

Interphase

Meiosis is preceded by an interphase consisting of the G_1, S, and G_2 phases, which are nearly identical to the phases preceding mitosis. The G_1 phase is the first phase of interphase and is focused on cell growth. In the S phase, the DNA of the chromosomes is replicated. Finally, in the G_2 phase, the cell undergoes the final preparations for meiosis.

During DNA duplication of the S phase, each chromosome becomes composed of two identical copies (called sister chromatids) that are held together at the centromere until they are pulled apart during meiosis II. In an animal cell, the centrosomes that organize the microtubules of the meiotic spindle also replicate. This prepares the cell for the first meiotic phase.

Meiosis I

Early in prophase I, the chromosomes can be seen clearly microscopically. As the nuclear envelope begins to break down, the proteins associated with homologous chromosomes bring the pair close to each other. The tight pairing of the homologous chromosomes is called **synapsis**. In synapsis, the genes on the chromatids of the homologous chromosomes are precisely aligned with each other. An exchange of chromosome segments between non-sister homologous chromatids occurs and is called **crossing over**. This process is revealed visually after the exchange as **chiasmata (singular = *chiasma*)** (Figure 2.30).

As prophase I progresses, the close association between homologous chromosomes begins to break down, and the chromosomes continue to condense, although the homologous chromosomes remain attached to each other at chiasmata. The number of chiasmata varies with the species and the length of the chromosome. At the end of prophase I, the pairs are held together only at chiasmata (Figure 2.30) and are called **tetrads** because the four sister chromatids of each pair of homologous chromosomes are now visible.

The crossover events are the first source of genetic variation produced by meiosis. A single crossover event between homologous non-sister chromatids leads to a reciprocal exchange of equivalent DNA between a maternal chromosome and a paternal chromosome. Now, when that sister chromatid is moved into a gamete, it will carry some DNA from one parent of the individual and some DNA from the other parent. The recombinant sister chromatid has a combination of maternal and paternal genes that did not exist before the crossover.

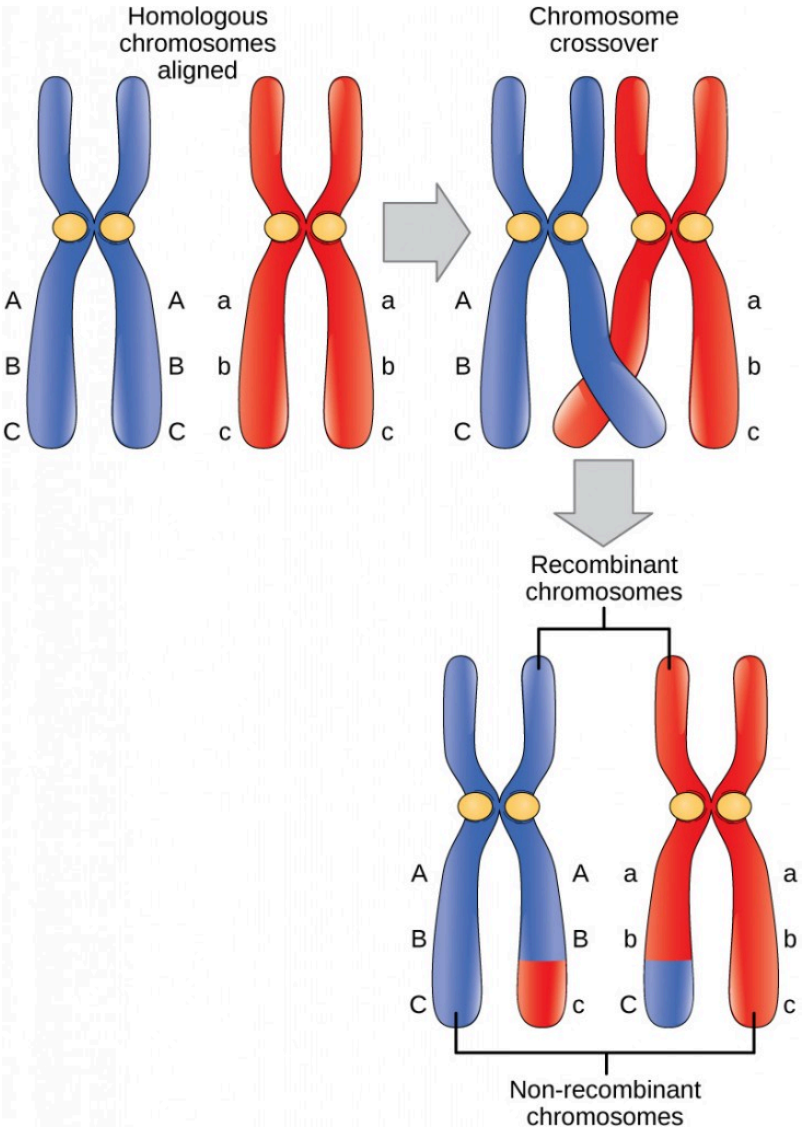


Figure 2.30 In this illustration of the effects of crossing over, the blue chromosome came from the individual's father and the red chromosome came from the individual's mother. Crossover occurs between non-sister chromatids of homologous chromosomes. The result is an exchange of genetic material between homologous chromosomes. The chromosomes that have a mixture of maternal and paternal sequence are called recombinant and the chromosomes that are completely paternal or maternal are called non-recombinant. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

The key event in prometaphase I is the attachment of the spindle fiber microtubules to the kinetochore proteins at the centromeres. The microtubules assembled from centrosomes at opposite poles of the cell grow toward the middle of the cell. At the end of prometaphase I, each tetrad is attached to microtubules from both poles, with one homologous chromosome attached at one pole and the other homologous chromosome

attached to the other pole. The homologous chromosomes are still held together at chiasmata. In addition, the nuclear membrane has broken down entirely.

During metaphase I, the homologous chromosomes are arranged in the center of the cell with the **kinetochores** facing opposite poles. The orientation of each pair of homologous chromosomes at the center of the cell is random.

This randomness, called **independent assortment**, is the physical basis for the generation of the second form of genetic variation in offspring. Consider that the homologous chromosomes of a sexually reproducing organism are originally inherited as two separate sets, one from each parent. Using humans as an example, one set of 23 chromosomes is present in the egg donated by the mother. The father provides the other set of 23 chromosomes in the sperm that fertilizes the egg. In metaphase I, these pairs line up at the midway point between the two poles of the cell. Because there is an equal chance that a microtubule fiber will encounter a maternally or paternally inherited chromosome, the arrangement of the tetrads at the metaphase plate is random. Any maternally inherited chromosome may face either pole. Any paternally inherited chromosome may also face either pole. The orientation of each tetrad is independent of the orientation of the other 22 tetrads.

In each cell that undergoes meiosis, the arrangement of the tetrads is different. The number of variations depends on the number of chromosomes making up a set. There are two possibilities for orientation (for each tetrad); thus, the possible number of alignments equals 2^n where n is the number of chromosomes per set. Humans have 23 chromosome pairs, which results in over eight million (2^{23}) possibilities. This number does not include the variability previously created in the sister chromatids by crossover. Given these two mechanisms, it is highly unlikely that any two haploid cells resulting from meiosis will have the same genetic composition (Figure 2.31).

To summarize the genetic consequences of meiosis I: the maternal and paternal genes are recombined by crossover events occurring on each homologous pair during prophase I; in addition, the random assortment of tetrads at metaphase produces a unique combination of maternal and paternal chromosomes that will make their way into the gametes.

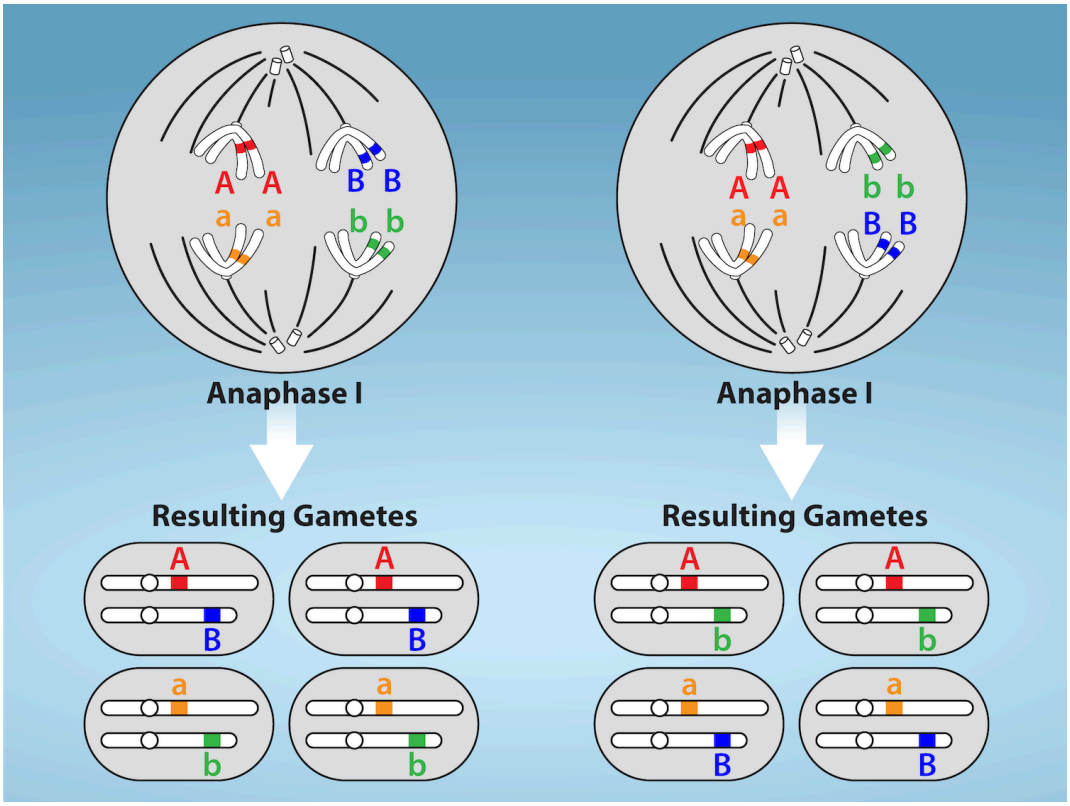


Figure 2.31 To demonstrate random, independent assortment at metaphase I, consider a cell with n = 2. In this case, there are two possible arrangements at the equatorial plane in metaphase I, as shown in the upper cell of each panel. These two possible orientations lead to the production of genetically different gametes. With more chromosomes, the number of possible arrangements increases dramatically. **Source:** *Biology 2e* (OpenStax), a derivative of *Concepts of Biology* (OpenStax), CC BY 4.0.

In anaphase I, the spindle fibers pull the linked chromosomes apart. The sister chromatids remain tightly bound together at the centromere. It is the chiasma connections that are broken in anaphase I as the fibers attached to the fused kinetochores pull the homologous chromosomes apart.

In telophase I, the separated chromosomes arrive at opposite poles. The remainder of the typical telophase events may or may not occur depending on the species. In some organisms, the chromosomes decondense and nuclear envelopes form around the chromatids in telophase I.

Cytokinesis, the physical separation of the cytoplasmic components into two daughter cells, occurs without reformation of the nuclei in other organisms. In nearly all species, cytokinesis separates the cell contents by either a cleavage furrow (in animals and some fungi), or a cell plate that will ultimately lead to formation of cell walls that separate the two daughter cells (in plants). At each pole, there is just one member

of each pair of the homologous chromosomes, so only one full set of the chromosomes is present. This is why the cells are considered haploid—there is only one chromosome set, even though there are duplicate copies of the set because each homolog still consists of two sister chromatids that are still attached to each other. However, although the sister chromatids were once duplicates of the same chromosome, they are no longer identical at this stage because of crossovers.

Meiosis II

In meiosis II, the connected sister chromatids remaining in the haploid cells from meiosis I will be split to form four haploid cells. In some species, cells enter a brief interphase, or **interkinesis**, that lacks an S phase, before entering meiosis II. Chromosomes are not duplicated during interkinesis. The two cells produced in meiosis I go through the events of meiosis II in synchrony. Overall, meiosis II resembles the mitotic division of a haploid cell.

In prophase II, if the chromosomes decondensed in telophase I, they condense again. If nuclear envelopes were formed, they fragment into vesicles. The centrosomes duplicated during interkinesis move away from each other toward opposite poles, and new spindles are formed. In prometaphase II, the nuclear envelopes are completely broken down, and the spindle is fully formed. Each sister chromatid forms an individual kinetochore that attaches to microtubules from opposite poles. In metaphase II, the sister chromatids are maximally condensed and aligned at the center of the cell. In anaphase II, the sister chromatids are pulled apart by the spindle fibers and move toward opposite poles.

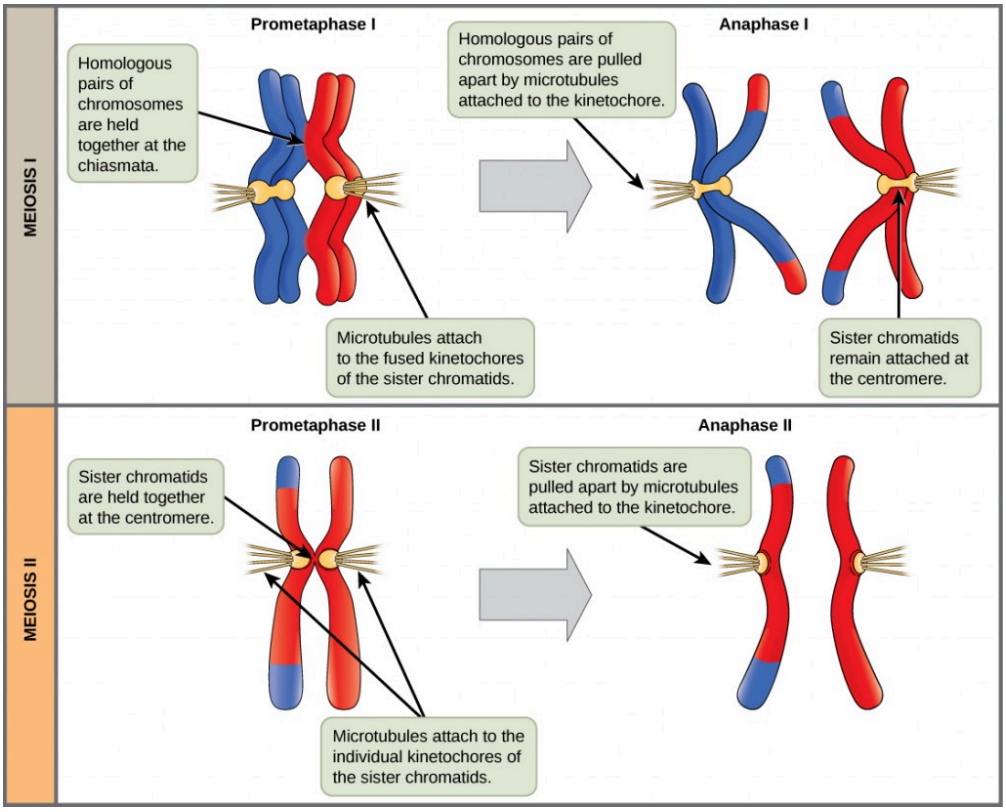


Figure 2.32 In prometaphase I, microtubules attach to the fused kinetochores of homologous chromosomes. In anaphase I, the homologous chromosomes are separated. In prometaphase II, microtubules attach to individual kinetochores of sister chromatids. In anaphase II, the sister chromatids are separated. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

In telophase II, the chromosomes arrive at opposite poles and begin to decondense. Nuclear envelopes form around the chromosomes. Cytokinesis separates the two cells into four genetically unique haploid cells. At this point, the nuclei in the newly produced cells are both haploid and have only one copy of the single set of chromosomes. The cells produced are genetically unique because of the random assortment of paternal and maternal homologs and because of the recombination of maternal and paternal segments of chromosomes—with their sets of genes—that occurs during crossover.

Concept in Action – Meiosis

Watch Meiosis 3D Animation (7 mins) on YouTube (https://youtu.be/GoJCer_acIQ)

Comparing Meiosis and Mitosis

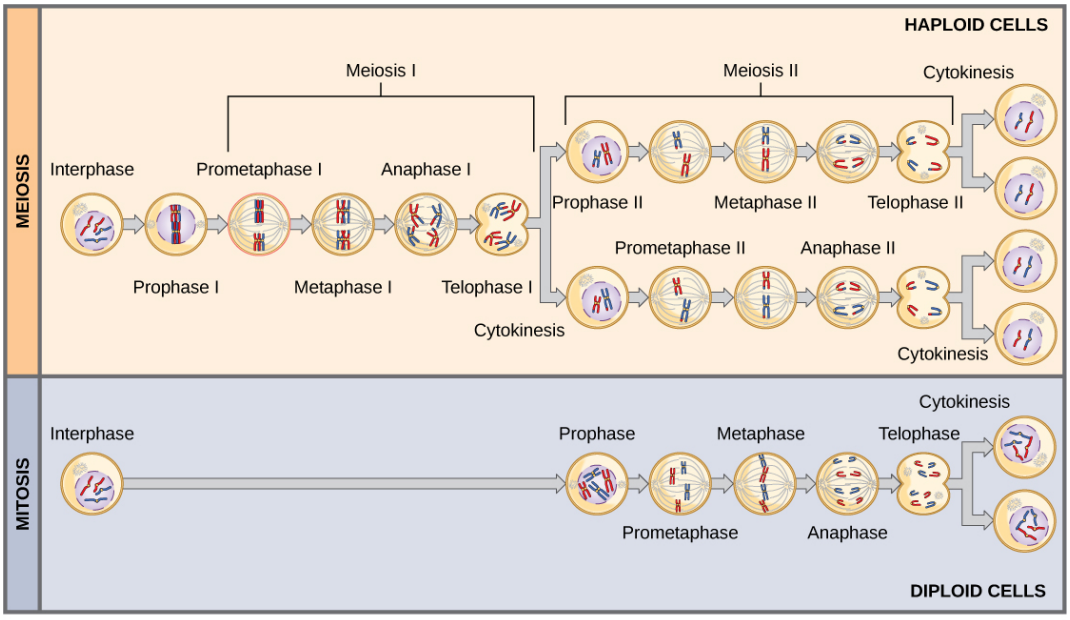
Mitosis and meiosis, which are both forms of division of the nucleus in eukaryotic cells, share some similarities, but also exhibit distinct differences that lead to their very different outcomes. Mitosis is a single nuclear division that results in two nuclei, usually partitioned into two new cells. The nuclei resulting from a mitotic division are genetically identical to the original. They have the same number of sets of chromosomes: one in the case of haploid cells, and two in the case of diploid cells. On the other hand, meiosis is two nuclear divisions that result in four nuclei, usually partitioned into four new cells. The nuclei resulting from meiosis are never genetically identical, and they contain one chromosome set only—this is half the number of the original cell, which was diploid.

The differences in the outcomes of meiosis and mitosis occur because of differences in the behavior of the chromosomes during each process. Most of these differences in the processes occur in meiosis I, which is a very different nuclear division than mitosis. In meiosis I, the homologous chromosome pairs become associated with each other, are bound together, experience chiasmata and crossover between sister chromatids, and line up along the metaphase plate in tetrads with spindle fibers from opposite spindle poles attached to each kinetochore of a homolog in a tetrad. All of these events occur only in meiosis I, never in mitosis.

Homologous chromosomes move to opposite poles during meiosis I so the number of sets of chromosomes in each nucleus-to-be is reduced from two to one. For this reason, meiosis I is referred to as a reduction division. There is no such reduction in ploidy level in mitosis.

Meiosis II is much more analogous to a mitotic division. In this case, duplicated chromosomes (only one set of them) line up at the center of the cell with divided kinetochores attached to spindle fibers from opposite poles. During anaphase II, as in mitotic anaphase, the kinetochores divide and one sister chromatid is pulled to one pole and the other sister chromatid is pulled to the other pole. If it were not for the fact that there had been crossovers, the two products of each meiosis II division would be identical as in mitosis; instead, they are different because there has always been at least one crossover per chromosome. Meiosis II is not a reduction division because, although there are fewer copies of the genome in the resulting cells, there is still one set of chromosomes, as there was at the end of meiosis I.

Cells produced by mitosis will function in different parts of the body as a part of growth or replacing dead or damaged cells. Cells produced by meiosis in a diploid-dominant organism such as an animal will only participate in sexual reproduction.



						OUTCOME
PROCESS	DNA synthesis	Synapsis of homologous chromosomes	Crossover	Homologous chromosomes line up at metaphase plate	Sister chromatids line up at metaphase plate	Number and genetic composition of daughter cells
MEIOSIS	Occurs in S phase of interphase	During prophase I	During prophase I	During metaphase I	During metaphase II	Four haploid cells at the end of meiosis II
MITOSIS	Occurs in S phase of interphase	Does not occur in mitosis	Does not occur in mitosis	Does not occur in mitosis	During metaphase	Two diploid cells at the end of mitosis

Figure 2.33 Meiosis and mitosis are both preceded by one round of DNA replication; however, meiosis includes two nuclear divisions. The four daughter cells resulting from meiosis are haploid and genetically distinct. The daughter cells resulting from mitosis are diploid and identical to the parent cell. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0

Concept in Action – Mitosis & Meiosis

For an animation comparing mitosis and meiosis, go to How Cells Divide: Mitosis vs. Meiosis (https://www.pbs.org/wgbh/nova/baby/divi_text.html)

Exercises

Exercises (text version)

1. True or false? Sexual reproduction is so common because it creates uniformity in its offspring.
2. Fill in the missing words to complete the statement:
   Mitosis has only one division but meiosis has [Blank A] divisions. The first of these divisions is called [Blank B] and is said to be reductional because in humans the chromosome number is reduced from 46 to [Blank C].
   Humans have a [Blank D] dominant lifecycle.
   The tight pairing of homolous chromosomes in Prophase 1 is called [Blank E].
   Independent assortment of homologous pairs in Meiosis 1 produces 2 to the 23rd power of possible combinations. That is over [Blank F] million combinations.
   Two processes create unique gametes in Meiosis. In prophase 1 the homologous chromosomes pair and [Blank G] mixes the genetic material. In Metaphase 1 the process of Independent [Blank H] occurs.
3. Which event leads to a diploid cell in a life cycle?

   a. meiosis
   b. fertilization
   c. alternation of generations
   d. mutation

4. Match the words to the correct blanks to describe the two events that are common to all sexually reproducing organisms, and how they fit into the different life cycles of those organisms.
   Words: mitosis, fertilization, meiosis
   The two events common to all sexually reproducing organisms are [Blank A] and [Blank B]. In [Blank C] the diploid cell is reduced to a haploid state. The haploid cell may divide through [Blank D] to produce an organism, some of whose cells will combine during [Blank E], or the haploid cells produced by [Blank F] may immediately combine in [Blank G] to produce a diploid cell that divides to produce an organism.
5. At which stage of meiosis are sister chromatids separated from each other?

   a. prophase I
   b. prophase II
   c. anaphase I
   d. anaphase II

6. How many daughter cells does meiosis produce?

   a. two haploid

b. two diploid
c. four haploid
d. four diploid

7. What is the part of meiosis that is similar to mitosis?

   a. meiosis I
   b. anaphase I
   c. meiosis II
   d. interkinesis

8. If a muscle cell of a typical organism has 32 chromosomes, how many chromosomes will be in a gamete of that same organism?

   a. 8
   b. 16
   c. 32
   d. 64

9. Match the words to the correct blanks to explain how the random alignment of homologous chromosomes during metaphase I contributes to variation in gametes produced by meiosis.
   Words: random, anaphase I, center, orientation, differently, unique, equal, metaphase I, sperm, egg
   Random alignment leads to new combinations of traits. The chromosomes that were originally inherited by the gamete-producing individual came equally from the [Blank A] and the [Blank B]. In [Blank C], the duplicated copies of these maternal and paternal homologous chromosomes line up across the [Blank D] of the cell to form a tetrad. The [Blank E] of each tetrad is [Blank F] There is an [Blank G] chance that the maternally derived chromosomes will be facing either pole. The same is true of the paternally derived chromosomes. The alignment should occur [Blank H] in almost every meiosis. As the homologous chromosomes are pulled apart in [Blank i], any combination of maternal and paternal chromosomes will move toward each pole. The gametes formed from these two groups of chromosomes will have a mixture of traits from the individual's parents. Each gamete is [Blank J].
10. Match the words to the correct blanks to describe the ways meiosis II is similar to and different from mitosis of a diploid cell.
    Words: two, meiosis I, half, chromatids, individually,
    The two divisions are similar in that the chromosomes line up along the metaphase plate [Blank A], meaning unpaired with other chromosomes (as in meiosis I). In addition, each

chromosome consists of [Blank B] sister [Blank C] that will be pulled apart. The two divisions are different because in meiosis II there are [Blank D] the number of chromosomes that are present in a diploid cell of the same species undergoing mitosis. This is because [Blank E] reduced the number of chromosomes to a haploid state.

Check your answers in footnote[2]

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Glossary

Summary of additional key terms introduced in this chapter:

Alternation of generations: a life-cycle type in which the diploid and haploid stages alternate

Life cycle: the sequence of events in the development of an organism and the production of cells that produce offspring

2.

1. False. Sexual reproduction is so common because it creates variation in its offspring.
2. A – 2/two, B – meiosis 1, C – 23, D – 2n/diploid, E – synapsis, F – 8/eight, G – crossing over, H – assortment
3. c) fertilization
4. A – meiosis, B – fertilization, C – meiosis, D – mitosis, E – fertilization, F – meiosis, G – fertilization
5. d) anaphase II
6. c) four haploid
7. c) meiosis II
8. b) 16
9. A – egg, B – sperm, C – metaphase I, D – center, E – orientation, F – random, G – equal, H – differently, i – anaphase I, J – unique
10. A – individually, B – two, C – chromatids, D – half, E – meiosis I

Attribution & References

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Adaptations: Individual sections have been combined and streamlined, including minor edits to improve student understanding and provide context.

2.6 PATTERNS OF INHERITANCE

Learning Objectives

- Describe the expected outcomes of monohybrid crosses involving dominant and recessive alleles.
- Explain the relationship between genotypes and phenotypes in dominant and recessive gene systems.
- Use a Punnett square to calculate the expected proportions of genotypes and phenotypes in a monohybrid cross.
- Explain Mendel's law of segregation and independent assortment in terms of genetics and the events of meiosis.
- Identify non-Mendelian inheritance patterns such as incomplete dominance, codominance, multiple alleles, and sex linkage from the results of crosses.
- Explain the effect of linkage and recombination on gamete genotypes.
- Explain the phenotypic outcomes of epistatic effects among genes.
- Explain polygenic inheritance.

Watch the interactive video on the history of Johann Gregor Mendel and his experiments (4 mins) on BCCampus (https://media.bccampus.ca/media/0_sexo3iqx), which paved the way for the discipline we now know as Genetics.

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://ecampusontario.pressbooks.pub/personalizedhealthnursing/?p=765#h5p-12

Mendel and the Gene Idea (text version)

Watch Johann Gregor Mendel and his experiments (4 mins) on BCCampus (https://media.bccampus.ca/media/0_sexo3iqx)

Pause the video at 0:38 and answer the following question:

True or false? Mendel used garden peas as his experimental organism.

Check your answer in footnote[1]

Activity source: *Concepts of Biology – 1st Canadian Edition*, CC BY 4.0

Johann Gregor Mendel (1822–1884) was a lifelong learner, teacher, scientist, and man of faith. As a young adult, he joined the Augustinian Abbey of St. Thomas in Brno in what is now the Czech Republic. Supported by the monastery, he taught physics, botany, and natural science courses at the secondary and university levels. In 1856, he began a decade-long research pursuit involving inheritance patterns in honeybees and plants, ultimately settling on pea plants as his primary **model system** (a system with convenient characteristics that is used to study a specific biological phenomenon to gain understanding to be applied to other systems). In 1865, Mendel presented the results of his experiments with nearly 30,000 pea plants to the local natural history society. He demonstrated that traits are transmitted faithfully from parents to offspring in specific patterns. In 1866, he published his work, *Experiments in Plant Hybridization,*[2] in the Natural History Society of Brünn proceedings.

Mendel's work went virtually unnoticed by the scientific community, which incorrectly believed that the inheritance process involved a blending of parental traits that produced an intermediate physical appearance in offspring. This hypothetical process appeared to be correct because of what we know now as **continuous variation**. Continuous variation is the range of small differences we see among individuals in a characteristic like human height. It does appear that offspring are a "blend" of their parents' traits when we look at characteristics that exhibit continuous variation. Mendel worked instead with traits that show **discontinuous variation**. Discontinuous variation is the variation seen among individuals when each individual shows one of two—or a very few—easily distinguishable traits, such as violet or white flowers. Mendel's choice of these kinds of traits allowed him to see experimentally that the traits were not blended in the offspring as would have been expected at the time, but that they were inherited as distinct traits. In 1868, Mendel became abbot of the monastery and exchanged his scientific pursuits for his pastoral duties. He was not recognized for his

1. True.

2. Johann Gregor Mendel, "Versuche über Pflanzenhybriden." *Verhandlungen des naturforschenden Vereines in Brünn*, Bd. IV für das Jahr, 1865 Abhandlungen (1866):3–47. [for English translation, see http://www.mendelweb.org/Mendel.plain.html]; Sumiti Vinayak et al., "Origin and Evolution of Sulfadoxine Resistant *Plasmodium falciparum," PLoS Pathogens* 6 (2010): e1000830.

extraordinary scientific contributions during his lifetime; in fact, it was not until 1900 that his work was rediscovered, reproduced, and revitalized by scientists on the brink of discovering the chromosomal basis of heredity.

Mendel's Crosses

Mendel's seminal work was accomplished using the garden pea, *Pisum sativum*, to study inheritance. This species naturally self-fertilizes, meaning that pollen encounters ova within the same flower. The flower petals remain sealed tightly until pollination is completed to prevent the pollination of other plants. The result is highly inbred, or "true-breeding," pea plants. These are plants that always produce offspring that look like the parent. By experimenting with true-breeding pea plants, Mendel avoided the appearance of unexpected traits in offspring that might occur if the plants were not true breeding. The garden pea also grows to maturity within one season, meaning that several generations could be evaluated over a relatively short time. Finally, large quantities of garden peas could be cultivated simultaneously, allowing Mendel to conclude that his results did not come about simply by chance.

Mendel performed **hybridizations**, which involve mating two true-breeding individuals that have different traits. In the pea, which is naturally self-pollinating, this is done by manually transferring pollen from the anther of a mature pea plant of one variety to the stigma of a separate mature pea plant of the second variety.

Plants used in first-generation crosses were called P, or parental generation, plants (Figure 2.34). Mendel collected the seeds produced by the P plants that resulted from each cross and grew them the following season. These offspring were called the **F_1, or the first filial** (filial = daughter or son), generation. Once Mendel examined the characteristics in the F_1 generation of plants, he allowed them to self-fertilize naturally. He then collected and grew the seeds from the F_1 plants to produce the **F_2, or second filial, generation**. Mendel's experiments extended beyond the F_2 generation to the F_3 generation, F_4 generation, and so on, but it was the ratio of characteristics in the P, F_1, and F_2 generations that were the most intriguing and became the basis of Mendel's postulates.

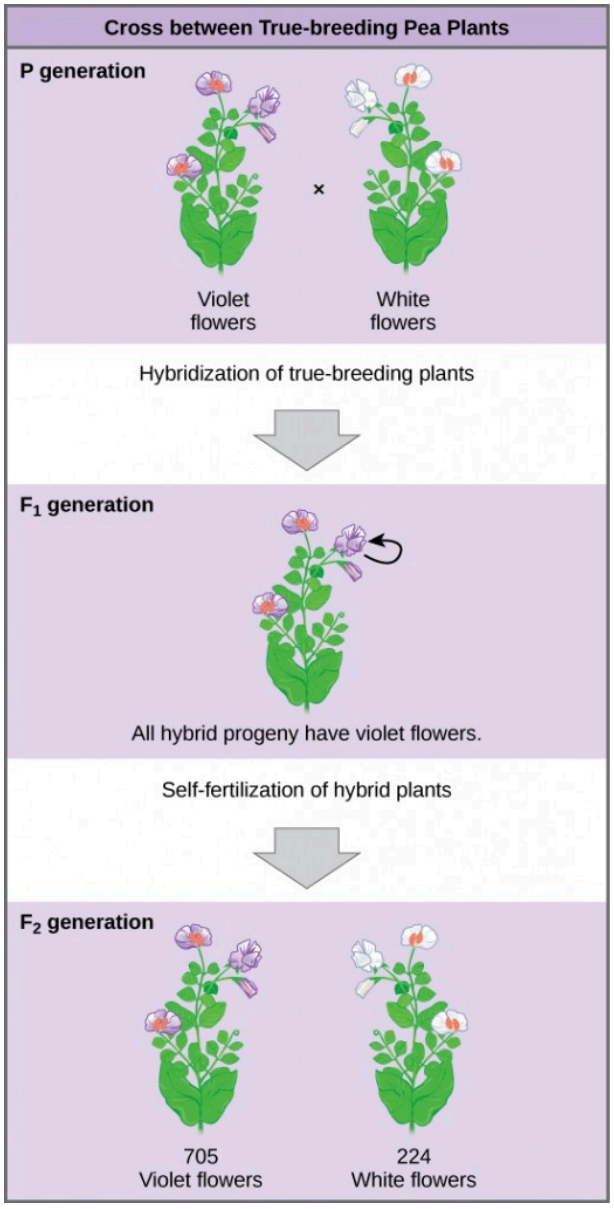

Figure 2.34 Mendel's process for performing crosses included examining flower color. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Garden Pea Characteristics Revealed the Basics of Heredity

In his 1865 publication, Mendel reported the results of his crosses involving seven different characteristics, each with two contrasting traits. A trait is defined as a variation in the physical appearance of a heritable characteristic. The characteristics included plant height, seed texture, seed color, flower color, pea-pod size, pea-pod color, and flower position. For the characteristic of flower color, for example, the two contrasting

traits were white versus violet. To fully examine each characteristic, Mendel generated large numbers of F_1 and F_2 plants and reported results from thousands of F_2 plants.

What results did Mendel find in his crosses for flower color? First, Mendel confirmed that he was using plants that bred true for white or violet flower color. Irrespective of the number of generations that Mendel examined, all self-crossed offspring of parents with white flowers had white flowers, and all self-crossed offspring of parents with violet flowers had violet flowers. In addition, Mendel confirmed that, other than flower color, the pea plants were physically identical. This was an important check to make sure that the two varieties of pea plants only differed with respect to one trait, flower color.

Once these validations were complete, Mendel applied the pollen from a plant with violet flowers to the stigma of a plant with white flowers. After gathering and sowing the seeds that resulted from this cross, Mendel found that 100 percent of the F_1 hybrid generation had violet flowers. Conventional wisdom at that time would have predicted the hybrid flowers to be pale violet or for hybrid plants to have equal numbers of white and violet flowers. In other words, the contrasting parental traits were expected to blend in the offspring. Instead, Mendel's results demonstrated that the white flower trait had completely disappeared in the F_1 generation.

Importantly, Mendel did not stop his experimentation there. He allowed the F_1 plants to self-fertilize and found that 705 plants in the F_2generation had violet flowers and 224 had white flowers. This was a ratio of 3.15 violet flowers to one white flower, or approximately 3:1. When Mendel transferred pollen from a plant with violet flowers to the stigma of a plant with white flowers and vice versa, he obtained approximately the same ratio irrespective of which parent—male or female—contributed which trait. This is called a **reciprocal cross**—a paired cross in which the respective traits of the male and female in one cross become the respective traits of the female and male in the other cross. For the other six characteristics that Mendel examined, the F_1 and F_2 generations behaved in the same way that they behaved for flower color. One of the two traits would disappear completely from the F_1 generation, only to reappear in the F_2 generation at a ratio of roughly 3:1 (Figure 2.35).

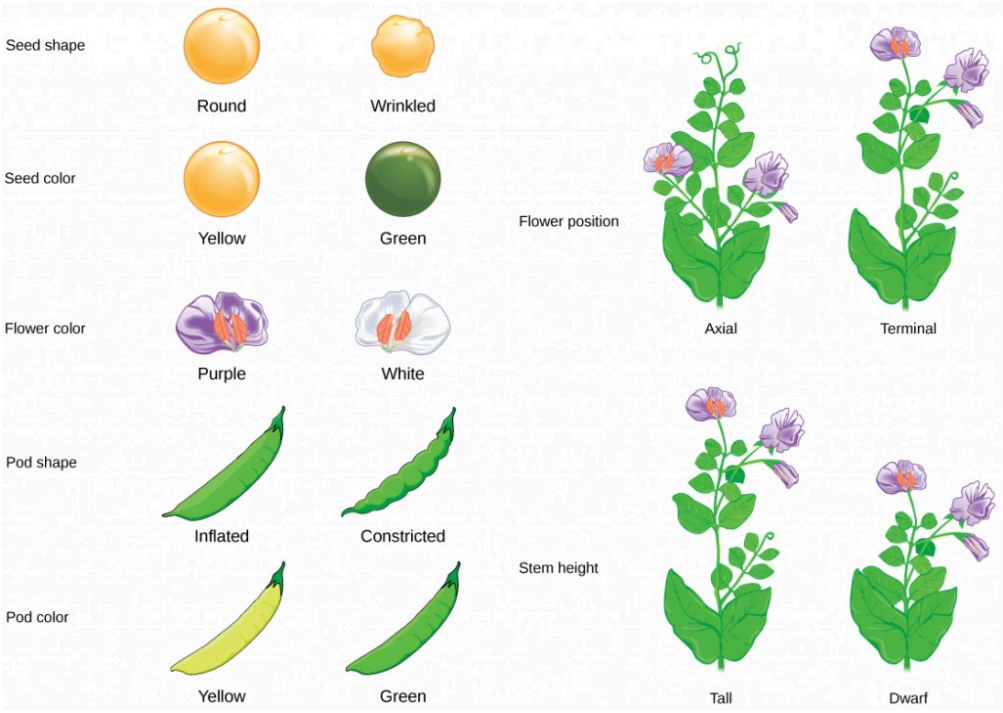

Figure 2.35 Mendel identified seven pea plant characteristics. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0

Upon compiling his results for many thousands of plants, Mendel concluded that the characteristics could be divided into expressed and latent traits. He called these dominant and recessive traits, respectively. Dominant traits are those that are inherited unchanged in a hybridization. Recessive traits become latent, or disappear in the offspring of a hybridization. The recessive trait does, however, reappear in the progeny of the hybrid offspring. An example of a dominant trait is the violet-colored flower trait. For this same characteristic (flower color), white-colored flowers are a recessive trait. The fact that the recessive trait reappeared in the F_2 generation meant that the traits remained separate (and were not blended) in the plants of the F_1 generation. Mendel proposed that this was because the *plants possessed two copies of the trait for the flower-color characteristic*, and that each parent transmitted one of their two copies to their offspring, where they came together. Moreover, the physical observation of a dominant trait could mean that the genetic composition of the organism included two dominant versions of the characteristic, or that it included one dominant and one recessive version. Conversely, the observation of a recessive trait meant that the organism lacked any dominant versions of this characteristic.

The seven characteristics that Mendel evaluated in his pea plants were each expressed as one of two versions, or traits. Mendel deduced from his results that each individual had two discrete copies of the characteristic that are passed individually to offspring. We now call those two copies **genes**, which are carried on chromosomes. The reason we have two copies of each gene is that we inherit one from each parent. In fact, it is the chromosomes we inherit and the two copies of each gene are located on paired chromosomes. Recall

that in meiosis these chromosomes are separated out into haploid gametes. This **separation, or segregation**, of the homologous chromosomes means also that only one of the copies of the gene gets moved into a gamete. The offspring are formed when that gamete unites with one from another parent and the two copies of each gene (and chromosome) are restored.

For cases in which a single gene controls a single characteristic, a diploid organism has two genetic copies that may or may not encode the same version of that characteristic. For example, one individual may carry a gene that determines white flower color and a gene that determines violet flower color. Gene variants that arise by mutation and exist at the same relative locations on homologous chromosomes are called **alleles**. Mendel examined the inheritance of genes with just two allele forms, but it is common to encounter more than two alleles for any given gene in a natural population.

Phenotypes and Genotypes

Two alleles for a given gene in a diploid organism are expressed and interact to produce physical characteristics. The observable traits expressed by an organism are referred to as its **phenotype**. An organism's underlying genetic makeup, consisting of both the physically visible and the non-expressed alleles, is called its **genotype**. Mendel's hybridization experiments demonstrate the difference between phenotype and genotype. For example, the phenotypes that Mendel observed in his crosses between pea plants with differing traits are connected to the diploid genotypes of the plants in the P, F_1, and F_2 generations. We will use a second trait that Mendel investigated, seed color, as an example. Seed color is governed by a single gene with two alleles. The yellow-seed allele is dominant and the green-seed allele is recessive. When true-breeding plants were cross-fertilized, in which one parent had yellow seeds and one had green seeds, all of the F_1 hybrid offspring had yellow seeds. That is, the hybrid offspring were phenotypically identical to the true-breeding parent with yellow seeds. However, we know that the allele donated by the parent with green seeds was not simply lost because it reappeared in some of the F_2 offspring (Figure 2.36). Therefore, the F_1 plants must have been genotypically different from the parent with yellow seeds.

The P plants that Mendel used in his experiments were each **homozygous** for the trait he was studying. Diploid organisms that are homozygous for a gene have two identical alleles, one on each of their homologous chromosomes. The genotype is often written as *YY* or *yy*, for which each letter represents one of the two alleles in the genotype. The dominant allele is capitalized and the recessive allele is lower case. The letter used for the gene (seed color in this case) is usually related to the dominant trait (yellow allele, in this case, or "*Y*"). Mendel's parental pea plants always bred true because both produced gametes carried the same allele. When P plants with contrasting traits were cross-fertilized, all of the offspring were **heterozygous** for the contrasting trait, meaning their genotype had different alleles for the gene being examined. For example, the F_1 yellow plants that received a *Y* allele from their yellow parent and a *y* allele from their green parent had the genotype *Yy*.

Note: though in classical Mendelian genetics the convention was to name the gene after the dominant trait, modern genetics often names genes after the mutant phenotype, since this is usually what is first observed and studied. For example, is Drosophila, a variant that causes abnormally small wings, called vestigial, is denoted *vg*. Additionally, Mendelian genetics provide a foundation for understanding these basic concepts. Traits that follow Mendelian inheritance are often associated with genetic disorders (e.g. cystic fibrosis or Huntington's disease). Please keep in mind that inheritance is not always so straight-forward and that multiple genetic and environmental factors can interact to influence gene expression.

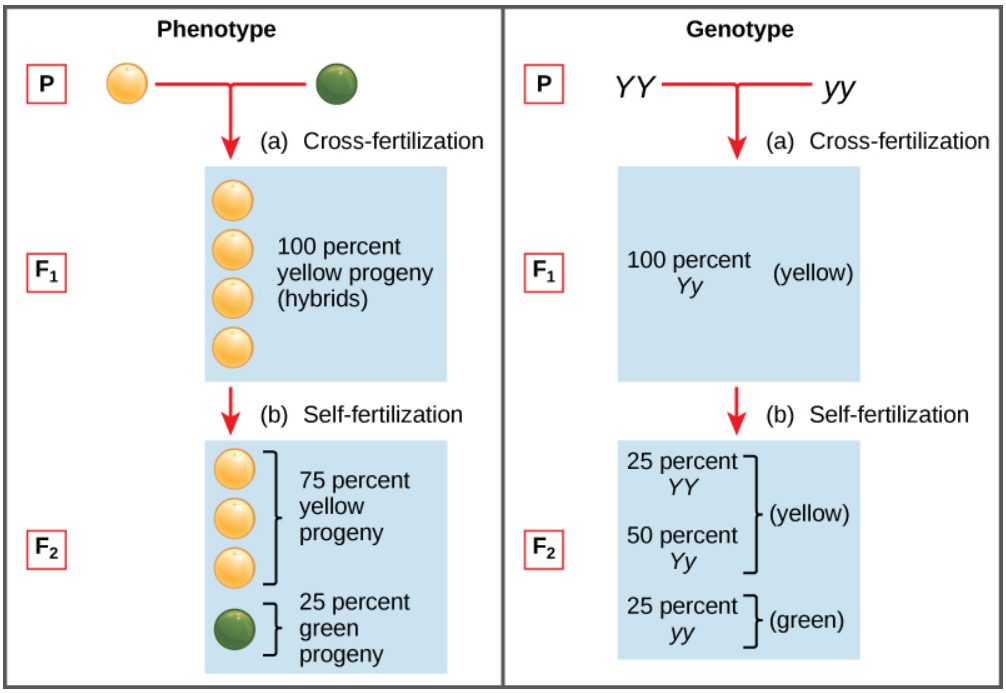

Figure 2.36 Phenotypes are physical expressions of traits that are transmitted by alleles. Capital letters represent dominant alleles and lowercase letters represent recessive alleles. The phenotypic ratios are the ratios of visible characteristics. The genotypic ratios are the ratios of gene combinations in the offspring, and these are not always distinguishable in the phenotypes. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Law of Dominance

Our discussion of homozygous and heterozygous organisms brings us to why the F_1 heterozygous offspring were identical to one of the parents, rather than expressing both alleles. In all seven pea-plant characteristics, one of the two contrasting alleles was dominant, and the other was recessive. Mendel called the dominant allele the expressed unit factor; the recessive allele was referred to as the latent unit factor. We now know that these so-called unit factors are actually genes on homologous chromosomes. For a gene that is expressed in a dominant and recessive pattern, *homozygous dominant and heterozygous organisms will look identical* (that is,

they will have different genotypes but the same phenotype), and the *recessive allele will only be observed in homozygous recessive individuals*.

Correspondence between Genotype and Phenotype for a Dominant-Recessive Characteristic.

Type	Homozygous	Heterozygous	Homozygous
Genotype	*YY*	*Yy*	*yy*
Phenotype	yellow	yellow	green

Mendel's **law of dominance** states that in a heterozygote, one trait will conceal the presence of another trait for the same characteristic. For example, when crossing true-breeding violet-flowered plants with true-breeding white-flowered plants, all of the offspring were violet-flowered, even though they all had one allele for violet and one allele for white. Rather than both alleles contributing to a phenotype, the dominant allele will be expressed exclusively. The recessive allele will remain latent, but will be transmitted to offspring in the same manner as that by which the dominant allele is transmitted. The recessive trait will only be expressed by offspring that have two copies of this allele (Figure 2.37), and these offspring will breed true when self-crossed.

Figure 2.37 The allele for albinism, expressed here in humans, is recessive. Both of this child's parents carried the recessive allele. **Source:** Image by Amapola89, PDM .

Monohybrid Cross and the Punnett Square

When fertilization occurs between two true-breeding parents that differ by only the characteristic being studied, the process is called a **monohybrid cross**, and the resulting offspring are called monohybrids. Mendel performed seven types of monohybrid crosses, each involving contrasting traits for different characteristics. Out of these crosses, all of the F_1 offspring had the phenotype of one parent, and the F_2 offspring had a 3:1 phenotypic ratio. On the basis of these results, Mendel postulated that each parent in the monohybrid cross contributed one of two paired unit factors to each offspring, and every possible combination of unit factors was equally likely.

The results of Mendel's research can be explained in terms of probabilities, which are mathematical measures of likelihood. The probability of an event is calculated by the number of times the event occurs divided by the total number of opportunities for the event to occur. A probability of one (100 percent) for

some event indicates that it is guaranteed to occur, whereas a probability of zero (0 percent) indicates that it is guaranteed to not occur, and a probability of 0.5 (50 percent) means it has an equal chance of occurring or not occurring.

To demonstrate this with a monohybrid cross, consider the case of true-breeding pea plants with yellow versus green seeds. The dominant seed color is yellow; therefore, the parental genotypes were *YY* for the plants with yellow seeds and *yy* for the plants with green seeds. A Punnett square, devised by the British geneticist Reginald Punnett, is useful for determining probabilities because it is drawn to predict all possible outcomes of all possible random fertilization events and their expected frequencies. Figure 2.39 shows a Punnett square for a cross between a plant with yellow peas and one with green peas. To prepare a **Punnett square**, all possible combinations of the parental alleles (the genotypes of the gametes) are listed along the top (for one parent) and side (for the other parent) of a grid. The combinations of egg and sperm gametes are then made in the boxes in the table on the basis of which alleles are combining. Each box then represents the diploid genotype of a zygote, or fertilized egg. Because each possibility is equally likely, genotypic ratios can be determined from a Punnett square. If the pattern of inheritance (dominant and recessive) is known, the phenotypic ratios can be inferred as well. For a monohybrid cross of two true-breeding parents, each parent contributes one type of allele. In this case, only one genotype is possible in the F_1 offspring. All offspring are *Yy* and have yellow seeds.

When the F_1 offspring are crossed with each other, each has an equal probability of contributing either a *Y* or a *y* to the F_2 offspring. The result is a 1 in 4 (25 percent) probability of both parents contributing a *Y*, resulting in an offspring with a yellow phenotype; a 25 percent probability of parent A contributing a *Y* and parent B a *y*, resulting in offspring with a yellow phenotype; a 25 percent probability of parent A contributing a *y* and parent B a *Y*, also resulting in a yellow phenotype; and a (25 percent) probability of both parents contributing a *y*, resulting in a green phenotype. When counting all four possible outcomes, there is a 3 in 4 probability of offspring having the yellow phenotype and a 1 in 4 probability of offspring having the green phenotype. This explains why the results of Mendel's F_2 generation occurred in a 3:1 phenotypic ratio. Using large numbers of crosses, Mendel was able to calculate probabilities, found that they fit the model of inheritance, and use these to predict the outcomes of other crosses.

Law of Segregation

Observing that true-breeding pea plants with contrasting traits gave rise to F_1 generations that all expressed the dominant trait and F_2 generations that expressed the dominant and recessive traits in a 3:1 ratio, Mendel proposed the **law of segregation**. This law states that paired unit factors (genes) must segregate equally into gametes such that offspring have an equal likelihood of inheriting either factor. For the F_2 generation of a monohybrid cross, the following three possible combinations of genotypes result: homozygous dominant, heterozygous, or homozygous recessive. Because heterozygotes could arise from two different pathways (receiving one dominant and one recessive allele from either parent), and because heterozygotes and

homozygous dominant individuals are phenotypically identical, the law supports Mendel's observed 3:1 phenotypic ratio. The equal segregation of alleles is the reason we can apply the Punnett square to accurately predict the offspring of parents with known genotypes. The physical basis of Mendel's law of segregation is the first division of meiosis in which the homologous chromosomes with their different versions of each gene are segregated into daughter nuclei. This process was not understood by the scientific community during Mendel's lifetime (Figure 2.38).

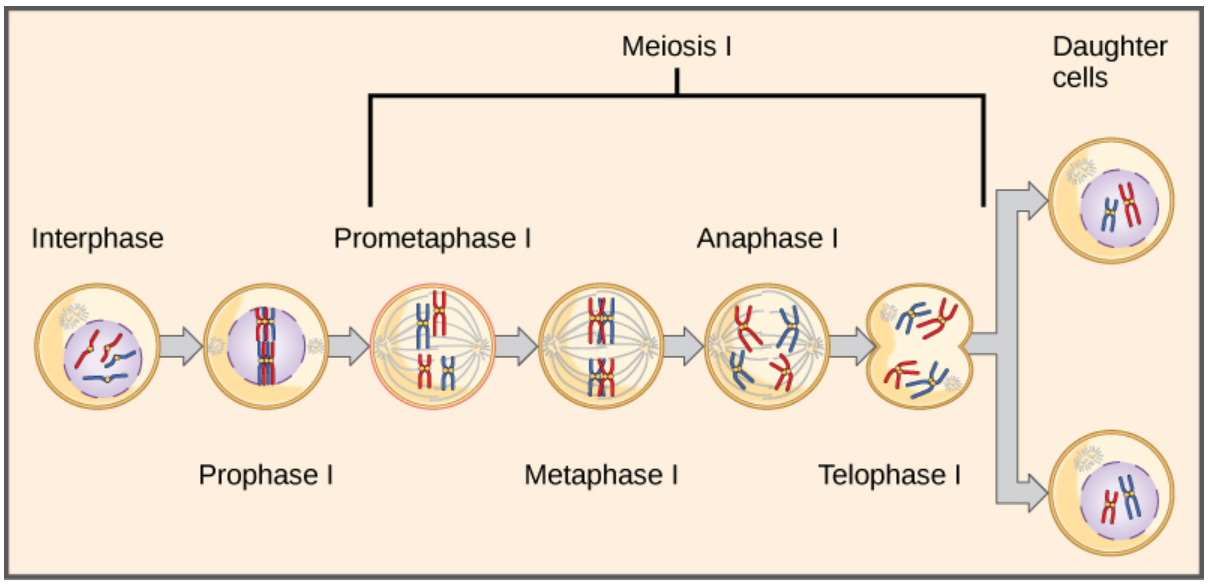

Figure 2.38 The first division in meiosis is shown. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Test Cross

Beyond predicting the offspring of a cross between known homozygous or heterozygous parents, Mendel also developed a way to determine whether an organism that expressed a dominant trait was a heterozygote or a homozygote. Called the **test cross**, this technique is still used by plant and animal breeders. In a test cross, the **d**ominant-expressing organism is crossed with an organism that is homozygous recessive for the same characteristic. If the dominant-expressing organism is a homozygote, then all F_1 offspring will be heterozygotes expressing the dominant trait (Figure 2.39). Alternatively, if the dominant-expressing organism is a heterozygote, the F_1 offspring will exhibit a 1:1 ratio of heterozygotes and recessive homozygotes (Figure 2.40). The test cross further validates Mendel's postulate that pairs of unit factors segregate equally.

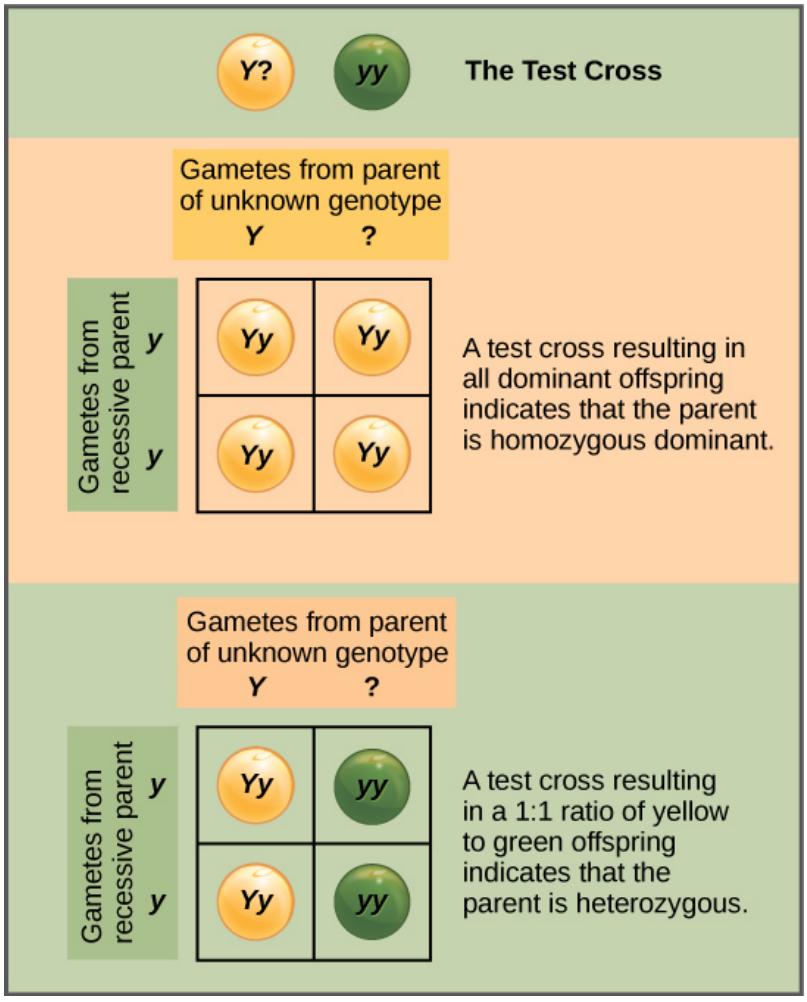

Figure 2.39 A test cross can be performed to determine whether an organism expressing a dominant trait is a homozygote or a heterozygote. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

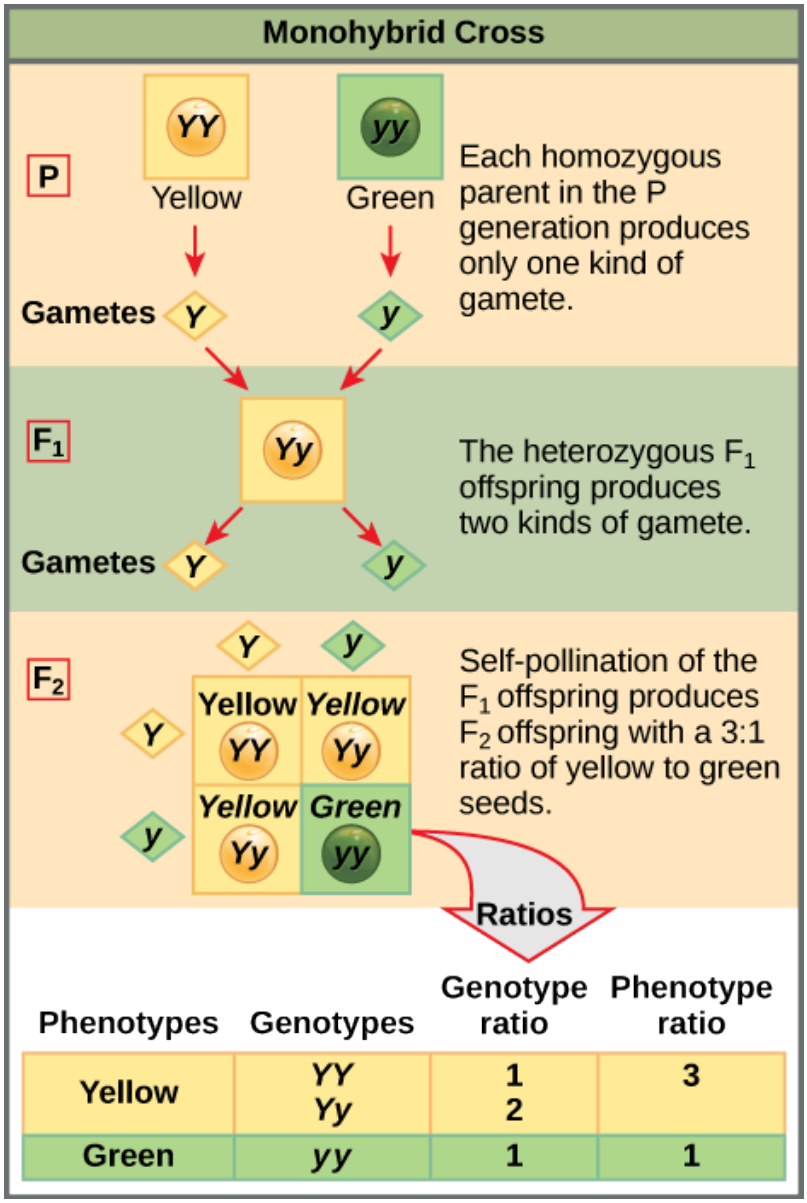

Figure 2.40 This Punnett square shows the cross between plants with yellow seeds and green seeds. The cross between the true-breeding P plants produces F1 heterozygotes that can be self-fertilized. The self-cross of the F1 generation can be analyzed with a Punnett square to predict the genotypes of the F2 generation. Given an inheritance pattern of dominant–recessive, the genotypic and phenotypic ratios can then be determined. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

In pea plants, round peas (*R*) are dominant to wrinkled peas (*r*). You do a test cross between a pea plant with wrinkled peas (genotype *rr*) and a plant of unknown genotype that has round peas. You end up with three plants, all which have round peas. From this data, can you tell if the parent plant is homozygous dominant or heterozygous?

You cannot be sure if the plant is homozygous or heterozygous as the data set is too small: by random chance, all three plants might have acquired only the dominant gene even if the recessive one is present.

Concept in Action – Punnett Square

Watch How to use a Punnett Square (with genetics practice questions) (27 mins) on YouTube (https://youtu.be/uDoNTugVtCM)

Law of Independent Assortment

Mendel's **law of independent assortment** states that **genes do not influence each other with regard to the sorting of alleles into gametes**, and every possible combination of alleles for every gene is equally likely to occur. Independent assortment of genes can be illustrated by the **dihybrid** cross, a cross between two true-breeding parents that express different traits for two characteristics. Consider the characteristics of seed color and seed texture for two pea plants, one that has wrinkled, green seeds (*rryy*) and another that has round, yellow seeds (*RRYY*). Because each parent is homozygous, the law of segregation indicates that the gametes for the wrinkled–green plant all are *ry*, and the gametes for the round–yellow plant are all *RY*. Therefore, the F_1 generation of offspring all are *RrYy* (Figure 2.41).

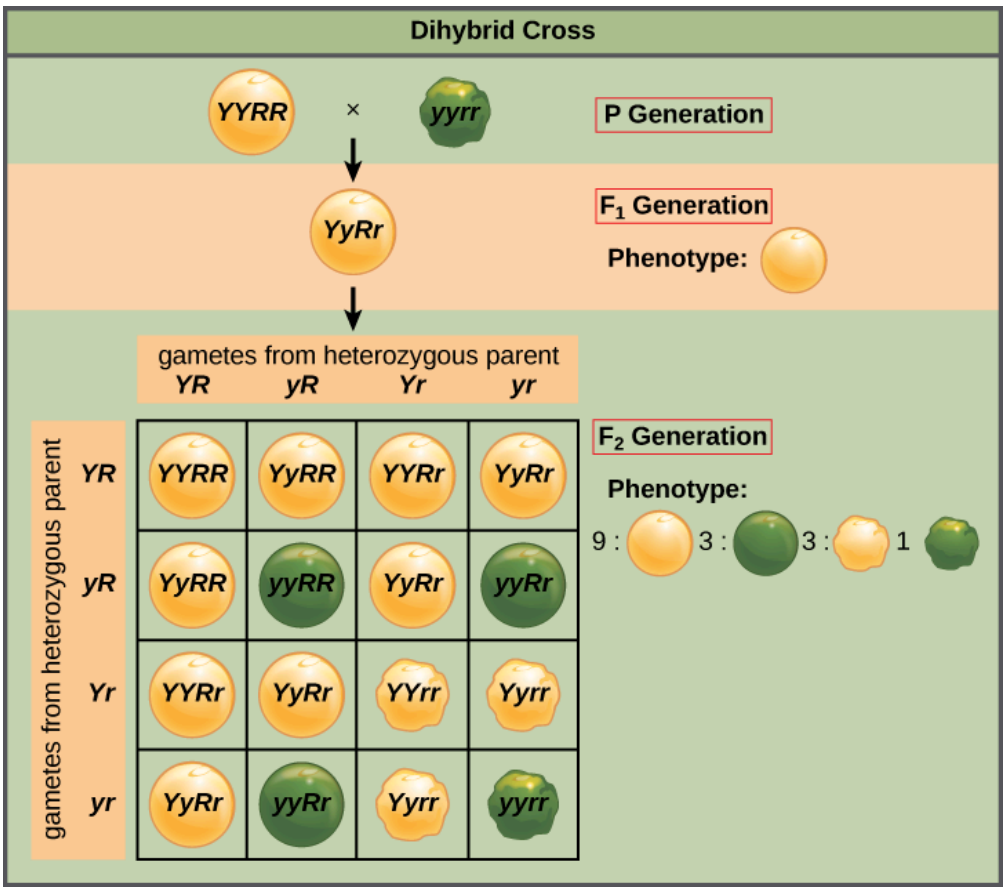

Figure 2.41 A dihybrid cross in pea plants involves the genes for seed color and texture. The P cross produces F1 offspring that are all heterozygous for both characteristics. The resulting 9:3:3:1 F2 phenotypic ratio is obtained using a Punnett square. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

In pea plants, purple flowers (*P*) are dominant to white (*p*), and yellow peas (*Y*) are dominant to green (*y*). What are the possible genotypes and phenotypes for a cross between *PpYY* and *ppYy* pea plants? How many squares would you need to complete a Punnett square analysis of this cross?

The possible genotypes are PpYY, PpYy, ppYY, and ppYy. The former two genotypes would result in plants with purple flowers and yellow peas, while the latter two genotypes would result in plants with white flowers with yellow peas, for a 1:1 ratio of each phenotype. You only need a 2 × 2 Punnett square (four squares total) to do this analysis because two of the alleles are homozygous.

The gametes produced by the F_1 individuals must have one allele from each of the two genes. For example, a gamete could get an *R* allele for the seed shape gene and either a *Y* or a *y* allele for the seed color gene. It cannot get both an *R* and an *r* allele; each gamete can have only one allele per gene. The law of independent assortment states that a gamete into which an *r* allele is sorted would be equally likely to contain either a *Y* or a *y* allele. Thus, there are four equally likely gametes that can be formed when the *RrYy* heterozygote is self-crossed, as follows: *RY*, *rY*, *Ry*, and *ry*. Arranging these gametes along the top and left of a 4 × 4 Punnett

square gives us 16 equally likely genotypic combinations. From these genotypes, we find a phenotypic ratio of 9 round–yellow:3 round–green:3 wrinkled–yellow:1 wrinkled–green. These are the offspring ratios we would expect, assuming we performed the crosses with a large enough sample size.

The physical basis for the law of independent assortment also lies in meiosis I, in which the different homologous pairs line up in random orientations. Each gamete can contain any combination of paternal and maternal chromosomes (and therefore the genes on them) because the orientation of tetrads on the metaphase plane is random (Figure 2.42).

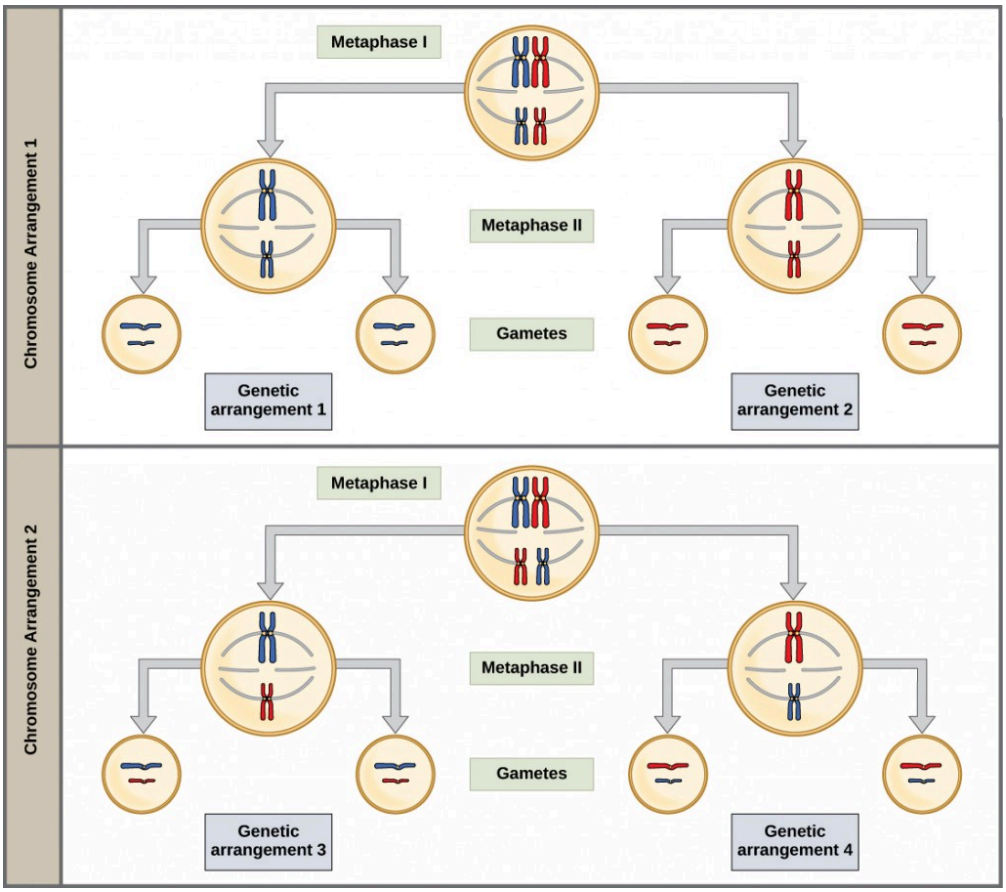

Figure 2.42 The random segregation into daughter nuclei that happens during the first division in meiosis can lead to a variety of possible genetic arrangements. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Probability Basics

Probabilities are mathematical measures of likelihood. The empirical probability of an event is calculated by dividing the number of times the event occurs by the total number of opportunities for the event to occur. It is also possible to calculate theoretical probabilities by dividing the number of times that an event is expected to occur by the number of times that it could occur. Empirical probabilities come from observations, like those of Mendel. Theoretical probabilities come from knowing how the events are produced and assuming

that the probabilities of individual outcomes are equal. A probability of one for some event indicates that it is guaranteed to occur, whereas a probability of zero indicates that it is guaranteed not to occur. An example of a genetic event is a round seed produced by a pea plant. In his experiment, Mendel demonstrated that the probability of the event "round seed" occurring was one in the F_1 offspring of true-breeding parents, one of which has round seeds and one of which has wrinkled seeds. When the F_1 plants were subsequently self-crossed, the probability of any given F_2 offspring having round seeds was now three out of four. In other words, in a large population of F_2 offspring chosen at random, 75 percent were expected to have round seeds, whereas 25 percent were expected to have wrinkled seeds. Using large numbers of crosses, Mendel was able to calculate probabilities and use these to predict the outcomes of other crosses.

The Product Rule and Sum Rule

Mendel demonstrated that the pea-plant characteristics he studied were transmitted as discrete units from parent to offspring. As will be discussed, Mendel also determined that different characteristics, like seed color and seed texture, were transmitted independently of one another and could be considered in separate probability analyses. For instance, performing a cross between a plant with green, wrinkled seeds and a plant with yellow, round seeds still produced offspring that had a 3:1 ratio of green:yellow seeds (ignoring seed texture) and a 3:1 ratio of round:wrinkled seeds (ignoring seed color). The characteristics of color and texture did not influence each other.

The **product rule of probability** can be applied to this phenomenon of the independent transmission of characteristics. The product rule states that *the probability of two independent events occurring together can be calculated by multiplying the individual probabilities of each event occurring alone*. To demonstrate the product rule, imagine that you are rolling a six-sided die (D) and flipping a penny (P) at the same time. The die may roll any number from 1–6 ($D_{\#}$), whereas the penny may turn up heads (P_H) or tails (P_T). The outcome of rolling the die has no effect on the outcome of flipping the penny and vice versa. There are 12 possible outcomes of this action, and each event is expected to occur with equal probability.

Twelve Equally Likely Outcomes of Rolling a Die and Flipping a Penny

Rolling Die	Flipping Penny
D_1	P_H
D_1	P_T
D_2	P_H
D_2	P_T
D_3	P_H
D_3	P_T
D_4	P_H
D_4	P_T
D_5	P_H
D_5	P_T
D_6	P_H
D_6	P_T

Of the 12 possible outcomes, the die has a 2/12 (or 1/6) probability of rolling a two, and the penny has a 6/12 (or 1/2) probability of coming up heads. By the product rule, the probability that you will obtain the combined outcome 2 and heads is: $(D_2) \times (P_H) = (1/6) \times (1/2)$ or 1/12. Notice the word "and" in the description of the probability. **The "and" is a signal to apply the product rule**. For example, consider how the product rule is applied to the dihybrid cross: the probability of having both dominant traits in the F_2 progeny is the product of the probabilities of having the dominant trait for each characteristic, as shown here:

$$3/4 \times 3/4 = 9/16$$

On the other hand, the **sum rule of probability** is applied when considering two mutually exclusive outcomes that can come about by more than one pathway. The sum rule states that *the probability of the occurrence of one event or the other event, of two mutually exclusive events, is the sum of their individual probabilities*. Notice the word "or" in the description of the probability. **The "or" indicates that you should apply the sum rule.** In this case, let's imagine you are flipping a penny (P) and a quarter (Q). What is the probability of one coin coming up heads and one coin coming up tails? This outcome can be achieved by two cases: the penny may be heads (P_H) and the quarter may be tails (Q_T), or the quarter may be heads (Q_H) and the penny may be tails (P_T). Either case fulfills the outcome. By the sum rule, we calculate the probability of obtaining one head and one tail as $[(P_H) \times (Q_T)] + [(Q_H) \times (P_T)] = [(1/2) \times (1/2)] + [(1/2) \times (1/2)] = 1/2$. You should also notice that we used the product rule to calculate the probability of P_H and Q_T, and also the

probability of P_T and Q_H, before we summed them. Again, the sum rule can be applied to show the probability of having just one dominant trait in the F_2 generation of a dihybrid cross:

$$3/16 + 3/4 = 15/16$$

The Product Rule and Sum Rule

Product Rule	Sum Rule
For independent events A and B, the probability (P) of them both occurring (A ***and*** B) is ($P_A \times P_B$)	For mutually exclusive events A and B, the probability (P) that at least one occurs (A ***or*** B) is ($P_A + P_B$)

To use probability laws in practice, it is necessary to work with large sample sizes because small sample sizes are prone to deviations caused by chance. The large quantities of pea plants that Mendel examined allowed him calculate the probabilities of the traits appearing in his F_2 generation. As you will learn, this discovery meant that when parental traits were known, the offspring's traits could be predicted accurately even before fertilization.

Example – Pedigree chart

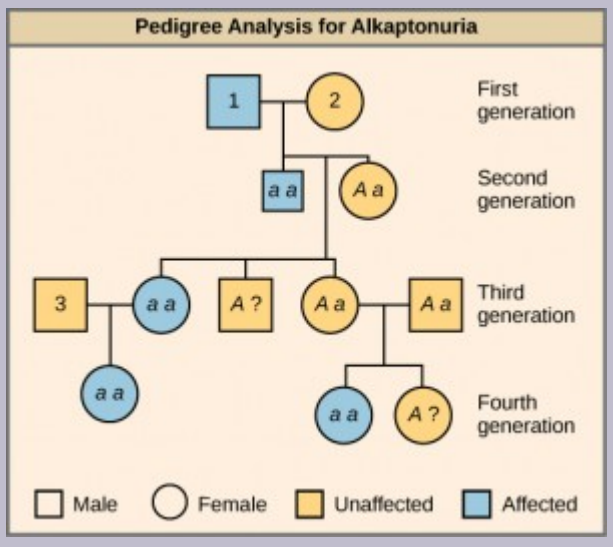

Figure 2.43. Pedigree chart of family with recessive disorder alkaptonuria. **Source:** *Biology 2e (OpenStax)*, CC BY 4.0.

Figure 2.43 shows a pedigree of a family that carries the recessive disorder alkaptonuria. In the second generation, an unaffected mother and an affected father have three children. One child has the disorder, so the genotype of the mother must be Aa and the genotype of the father is aa. One unaffected child goes on to have two children, one affected and one unaffected. Because her husband was not affected, she and her husband must both be heterozygous. The genotype of their unaffected child is unknown, and is designated A?. In the third generation, the other unaffected child had no offspring, and his genotype is therefore also unknown. The affected third-generation child goes on to have one child with the disorder. Her husband is unaffected and is labeled "3." The first

generation father is affected and is labeled "1." The first generation mother is unaffected and is labeled "2." The Art Connection question asks the genotype of the three numbered individuals.

Alkaptonuria is a recessive genetic disorder in which two amino acids, phenylalanine and tyrosine, are not properly metabolized. Affected individuals may have darkened skin and brown urine, and may suffer joint damage and other complications. In this pedigree, individuals with the disorder are indicated in blue and have the genotype *aa*. Unaffected individuals are indicated in yellow and have the genotype *AA* or *Aa*. Note that it is often possible to determine a person's genotype from the genotype of their offspring. For example, if neither parent has the disorder but their child does, they must be heterozygous. Two individuals on the pedigree have an unaffected phenotype but unknown genotype. Because they do not have the disorder, they must have at least one normal allele, so their genotype gets the "*A?*" designation.

What are the genotypes of the individuals labeled 1, 2 and 3?

Alternatives to Dominance and Recessiveness

Mendel's experiments with pea plants suggested that: 1) two types of "units" or alleles exist for every gene; 2) alleles maintain their integrity in each generation (no blending); and 3) in the presence of the dominant allele, the recessive allele is hidden, with no contribution to the phenotype. Therefore, recessive alleles can be "carried" and not expressed by individuals. Such **heterozygous individuals** are sometimes referred to as "**carriers**." Since then, genetic studies in other organisms have shown that much more complexity exists, but that the fundamental principles of Mendelian genetics still hold true. In the sections to follow, we consider some of the extensions of Mendelism.

Incomplete Dominance

Figure 2.44 These pink flowers of a heterozygote snapdragon result from incomplete dominance. **Source:** Image by storebukkebruse, CC BY 2.0.

Mendel's results, demonstrating that traits are inherited as dominant and recessive pairs, contradicted the view at that time that offspring exhibited a blend of their parents' traits. However, the heterozygote phenotype occasionally does appear to be intermediate between the two parents. For example, in the snapdragon, *Antirrhinum majus* (Figure 2.44), a cross between a homozygous parent with white flowers ($C^{W}C^{W}$) and a homozygous parent with red flowers ($C^{R}C^{R}$) will produce offspring with pink flowers ($C^{R}C^{W}$). (Note that different genotypic abbreviations are used for Mendelian extensions to distinguish these patterns from simple dominance and recessiveness.) This pattern of inheritance is described as **incomplete dominance**, meaning that one of the alleles appears in the phenotype in the heterozygote, but not to the exclusion of the other, which can also be seen. The allele for red flowers is incompletely dominant over the allele for white flowers. However, the results of a heterozygote self-cross can still be predicted, just as with Mendelian dominant and recessive crosses. In this case, the genotypic ratio would be 1 $C^{R}C^{R}$:2 $C^{R}C^{W}$:1 $C^{W}C^{W}$, and the phenotypic ratio would be 1:2:1 for red:pink:white. The basis for the intermediate color in the heterozygote is simply that the pigment produced by the red allele (anthocyanin) is diluted in the heterozygote and therefore appears pink because of the white background of the flower petals.

Codominance

A variation on incomplete dominance is **codominance**, in which both alleles for the same characteristic are **simultaneously expressed** in the heterozygote. An example of codominance occurs in the ABO blood groups of humans. The A and B alleles are expressed in the form of A or B molecules present on the surface of red blood cells. Homozygotes ($I^{A}I^{A}$ and $I^{B}I^{B}$) express either the A or the B phenotype, and heterozygotes ($I^{A}I^{B}$) express both phenotypes equally. The $I^{A}I^{B}$ individual has blood type AB. In a self-cross between heterozygotes expressing a codominant trait, the three possible offspring genotypes are phenotypically distinct. However, the 1:2:1 genotypic ratio characteristic of a Mendelian monohybrid cross still applies (Figure 2.45).

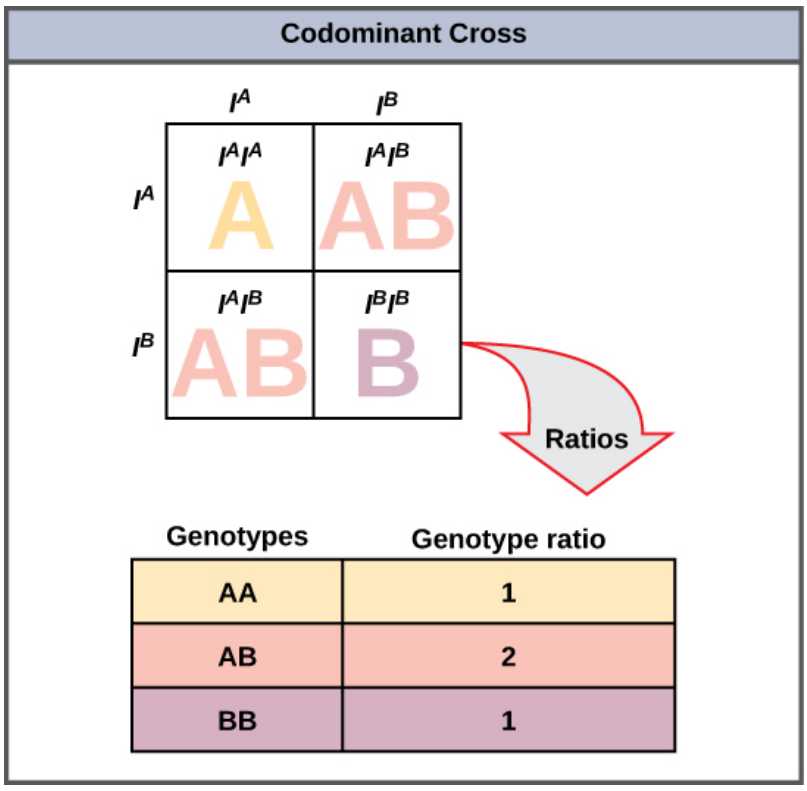

Figure 2.45 This Punnett square shows an AB/AB blood type cross. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Multiple Alleles

Mendel implied that only two alleles, one dominant and one recessive, could exist for a given gene. We now know that this is an oversimplification. Although individual humans (and all diploid organisms) can only have two alleles for a given gene, multiple alleles may exist at the population level, such that many combinations of two alleles are observed. Note that when many alleles exist for the same gene, the convention is to denote the most common phenotype or genotype in the natural population as the **wild type** (often abbreviated "+"). All other phenotypes or genotypes are considered variants (mutants) of this typical form, meaning they deviate from the wild type. The variant may be recessive or dominant to the wild-type allele.

An example of multiple alleles is the ABO blood-type system in humans. In this case, there are three alleles circulating in the population. The I^A allele codes for A molecules on the red blood cells, the I^B allele codes for B molecules on the surface of red blood cells, and the i allele codes for no molecules on the red blood cells. In this case, the I^A and I^B alleles are codominant with each other and are both dominant over the i allele. Although there are three alleles present in a population, each individual only gets two of the alleles from their parents. This produces the genotypes and phenotypes shown in Figure 2.46. Notice that instead of three genotypes, there are six different genotypes when there are three alleles. The number of possible phenotypes depends on the dominance relationships between the three alleles.

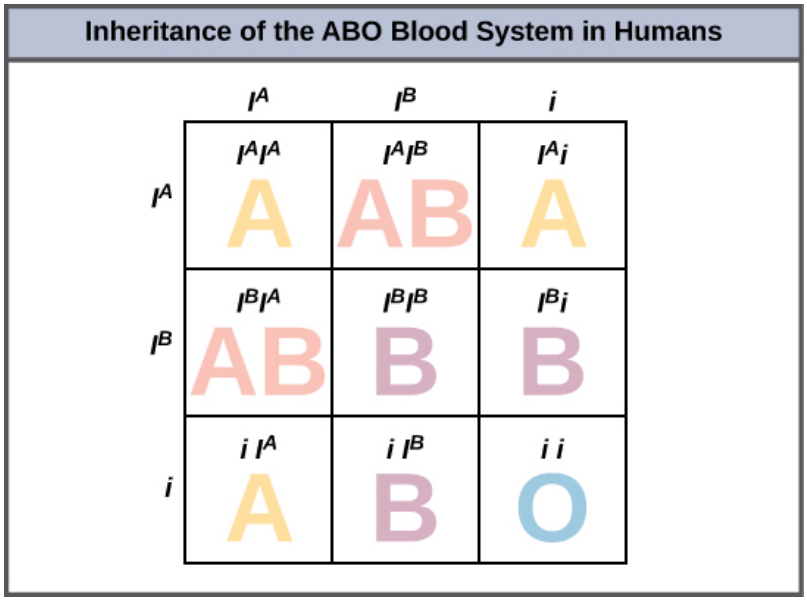

Figure 2.46 Inheritance of the ABO blood system in humans is shown. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Multiple Alleles Confer Drug Resistance in the Malaria Parasite

Malaria is a parasitic disease in humans that is transmitted by infected female mosquitoes, including *Anopheles gambiae*, and is characterized by cyclic high fevers, chills, flu-like symptoms, and severe anemia. *Plasmodium falciparum* and *P. vivax* are the most common causative agents of malaria, and *P. falciparum* is the most deadly. When promptly and correctly treated, *P. falciparum* malaria has a mortality rate of 0.1 percent. However, in some parts of the world, the parasite has evolved resistance to commonly used malaria treatments, so the most effective malarial treatments can vary by geographic region.

In Southeast Asia, Africa, and South America, *P. falciparum* has developed resistance to the anti-malarial drugs chloroquine, mefloquine, and sulfadoxine-pyrimethamine. *P. falciparum*, which is haploid during the life stage in which it is infective to humans, has evolved multiple drug-resistant mutant alleles of the *dhps* gene. Varying degrees of sulfadoxine resistance are associated with each of these alleles. Being haploid, *P. falciparum* needs only one drug-resistant allele to express this trait.

In Southeast Asia, different sulfadoxine-resistant alleles of the *dhps* gene are localized to different geographic regions. This is a common evolutionary phenomenon that comes about because drug-resistant mutants arise in a population and interbreed with other *P. falciparum* isolates in close proximity. Sulfadoxine-resistant parasites cause considerable human hardship in regions in which this drug is widely used as an over-the-counter malaria remedy. As is common with pathogens that multiply to large numbers within an infection cycle, *P. falciparum* evolves relatively rapidly (over a decade or so) in response to the selective

pressure of commonly used anti-malarial drugs. For this reason, scientists must constantly work to develop new drugs or drug combinations to combat the worldwide malaria burden[3].

Sex-Linked Traits

In humans, as well as in many other animals and some plants, the sex of the individual is determined by sex chromosomes—one pair of non-homologous chromosomes. Until now, we have only considered inheritance patterns among non-sex chromosomes, or autosomes. In addition to 22 homologous pairs of autosomes, human females have a homologous pair of X chromosomes, whereas human males have an XY chromosome pair. Although the Y chromosome contains a small region of similarity to the X chromosome so that they can pair during meiosis, the Y chromosome is much shorter and contains fewer genes. When a gene being examined is present on the X, but not the Y, chromosome, it is **X-linked**.

Eye color in *Drosophila*, the common fruit fly, was the first X-linked trait to be identified. Thomas Hunt Morgan mapped this trait to the X chromosome in 1910. Like humans, *Drosophila* males have an XY chromosome pair, and females are XX. In flies the wild-type eye color is red (X^W) and is dominant to white eye color (X^w) (Figure 2.47). Because of the location of the eye-color gene, reciprocal crosses do not produce the same offspring ratios. Males are said to be **hemizygous**, in that they have only one allele for any X-linked characteristic. Hemizygosity makes descriptions of dominance and recessiveness irrelevant for XY males. *Drosophila* males lack the white gene on the Y chromosome; that is, their genotype can only be X^WY or X^wY. In contrast, females have two allele copies of this gene and can be X^WX^W, X^WX^w, or X^wX^w.

3. Sumiti Vinayak et al., "Origin and Evolution of Sulfadoxine Resistant *Plasmodium falciparum*," *PLoS Pathogens* 6 (2010): e1000830.

Figure 2.47 In Drosophila, the gene for eye color is located on the X chromosome. Red eye color is wild-type and is dominant to white eye color. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

In an X-linked cross, the genotypes of F_1 and F_2 offspring depend on whether the recessive trait was expressed by the male or the female in the P generation. With respect to *Drosophila* eye color, when the P male expresses the white-eye phenotype and the female is homozygously red-eyed, all members of the F_1 generation exhibit red eyes (Figure 2.48). The F_1 females are heterozygous (X^WX^w), and the males are all X^WY, having received their X chromosome from the homozygous dominant P female and their Y chromosome from the P male. A subsequent cross between the X^WX^w female and the X^WY male would produce only red-eyed females (with X^WX^W or X^WX^w genotypes) and both red- and white-eyed males (with X^WY or X^wY genotypes). Now, consider a cross between a homozygous white-eyed female and a male with red eyes. The F_1 generation would exhibit only heterozygous red-eyed females (X^WX^w) and only white-eyed males (X^wY). Half of the F_2 females would be red-eyed (X^WX^w) and half would be white-eyed (X^wX^w). Similarly, half of the F_2 males would be red-eyed (X^WY) and half would be white-eyed (X^wY).

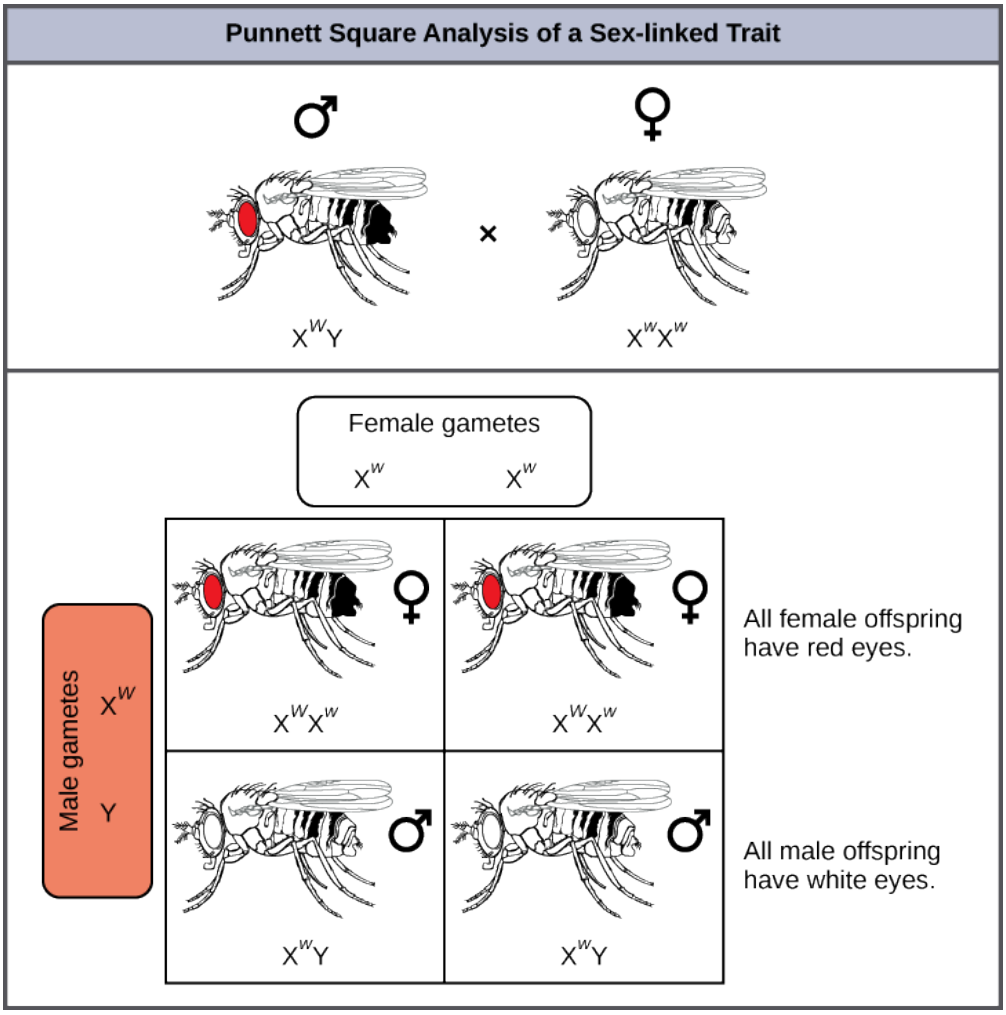

Figure 2.48 Crosses involving sex-linked traits often give rise to different phenotypes for the different sexes of offspring, as is the case for this cross involving red and white eye color in Drosophila. In the diagram, w is the white-eye mutant allele and W is the wild-type, red-eye allele. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0).

What ratio of offspring would result from a cross between a white-eyed male and a female that is heterozygous for red eye color?

Half of the female offspring would be heterozygous (X^WX^w) with red eyes, and half would be homozygous recessive (X^wX^w) with white eyes. Half of the male offspring would be hemizygous dominant (X^WY) with red eyes, and half would be hemizygous recessive (X^wY) with white eyes.

Discoveries in fruit fly genetics can be applied to human genetics. When a female parent is homozygous for a recessive X-linked trait, she will pass the trait on to 100 percent of her male offspring, because the males will receive the Y chromosome from the male parent. In humans, the alleles for certain conditions (some color-blindness, hemophilia, and muscular dystrophy) are X-linked. Females who are heterozygous for these diseases

are said to be carriers and may not exhibit any phenotypic effects. These females will pass the disease to half of their sons and will pass carrier status to half of their daughters; therefore, X-linked traits appear more frequently in males than females.

In some groups of organisms with sex chromosomes, the sex with the non-homologous sex chromosomes is the female rather than the male. This is the case for all birds. In this case, sex-linked traits will be more likely to appear in the female, in whom they are hemizygous.

Concept in Action – Sex Linked Traits

Watch Sex Linked Traits: Baldness and Hemophilia (4 mins) on YouTube (https://youtu.be/-6RGz1YM11o)

Linked Genes Violate the Law of Independent Assortment

Although all of Mendel's pea plant characteristics behaved according to the law of independent assortment, we now know that some allele combinations are not inherited independently of each other. Genes that are located on separate, non-homologous chromosomes will always sort independently. However, each chromosome contains hundreds or thousands of genes, organized linearly on chromosomes like beads on a string. The segregation of alleles into gametes can be influenced by linkage, in which genes that are located physically close to each other on the same chromosome are more likely to be inherited as a pair. However, because of the process of **recombination**, or "crossover," it is possible for two genes on the same chromosome to behave independently, or as if they are not linked. To understand this, let us consider the biological basis of gene linkage and recombination.

Homologous chromosomes possess the same genes in the same order, though the specific alleles of the gene can be different on each of the two chromosomes. Recall that during interphase and prophase I of meiosis, homologous chromosomes first replicate and then synapse, with like genes on the homologs aligning with each other. At this stage, segments of homologous chromosomes exchange linear segments of genetic material (Figure 2.49). This process is called recombination, or crossover, and it is a common genetic process. Because the genes are aligned during recombination, the gene order is not altered. Instead, the result of recombination is that maternal and paternal alleles are combined onto the same chromosome. Across a given chromosome, several recombination events may occur, causing extensive shuffling of alleles.

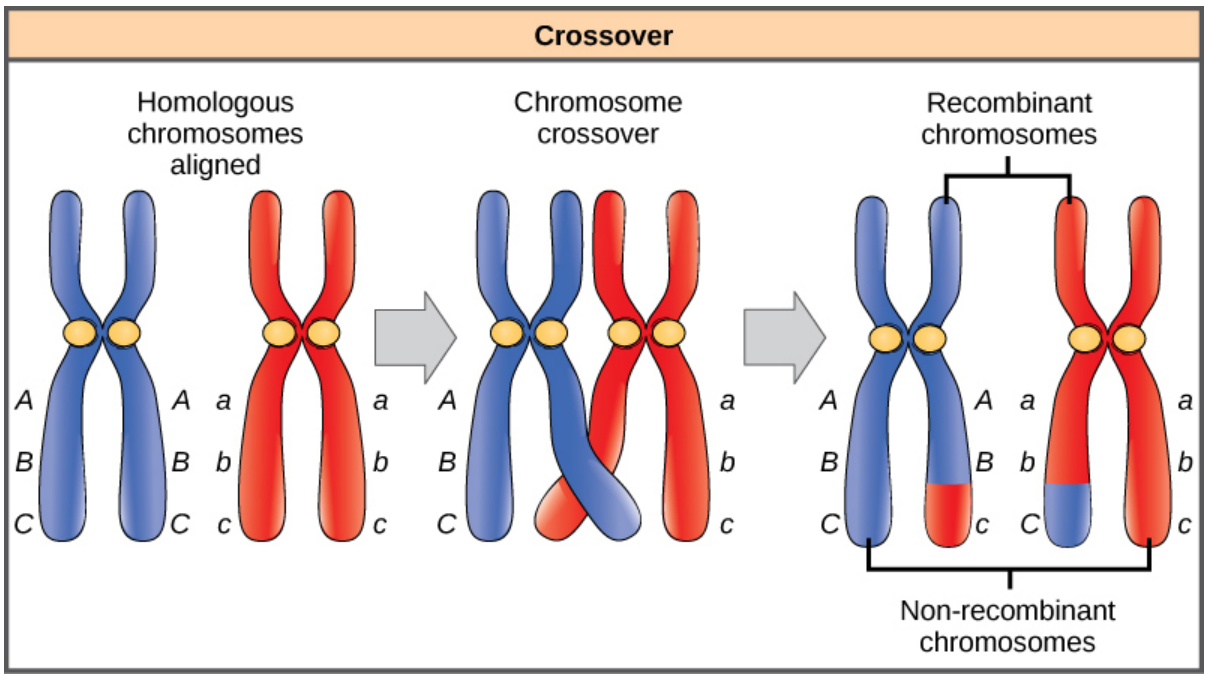

Figure 2.49 The process of crossover, or recombination, occurs when two homologous chromosomes align and exchange a segment of genetic material. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

When two genes are located on the same chromosome, they are considered linked, and their alleles tend to be transmitted through meiosis together. To exemplify this, imagine a dihybrid cross involving flower color and plant height in which the genes are next to each other on the chromosome. If one homologous chromosome has alleles for tall plants and red flowers, and the other chromosome has genes for short plants and yellow flowers, then when the gametes are formed, the tall and red alleles will tend to go together into a gamete and the short and yellow alleles will go into other gametes. These are called the parental genotypes because they have been inherited intact from the parents of the individual producing gametes. But unlike if the genes were on different chromosomes, there will be no gametes with tall and yellow alleles and no gametes with short and red alleles. If you create a Punnett square with these gametes, you will see that the classical Mendelian prediction of a 9:3:3:1 outcome of a dihybrid cross would not apply. As the distance between two genes increases, the probability of one or more crossovers between them increases and the genes behave more like they are on separate chromosomes. Geneticists have used the proportion of recombinant gametes (the ones not like the parents) as a measure of how far apart genes are on a chromosome. Using this information, they have constructed linkage maps of genes on chromosomes for well-studied organisms, including humans.

Mendel's seminal publication makes no mention of linkage, and many researchers have questioned whether he encountered linkage but chose not to publish those crosses out of concern that they would invalidate his independent assortment postulate. The garden pea has seven chromosomes, and some have suggested that his choice of seven characteristics was not a coincidence. However, even if the genes he examined were not

located on separate chromosomes, it is possible that he simply did not observe linkage because of the extensive shuffling effects of recombination.

Epistasis

Mendel's studies in pea plants implied that the sum of an individual's phenotype was controlled by genes (or as he called them, unit factors), such that every characteristic was distinctly and completely controlled by a single gene. In fact, single observable characteristics are almost always under the influence of multiple genes (each with two or more alleles) acting in unison. For example, at least eight genes contribute to eye color in humans.

In some cases, several genes can contribute to aspects of a common phenotype without their gene products ever directly interacting. In the case of organ development, for instance, genes may be expressed sequentially, with each gene adding to the complexity and specificity of the organ. Genes may function in complementary or synergistic fashions, such that two or more genes expressed simultaneously affect a phenotype. An apparent example of this occurs with human skin color, which appears to involve the action of at least three (and probably more) genes. Cases in which inheritance for a characteristic like skin color or human height depend on the combined effects of numerous genes are called polygenic inheritance.

Genes may also oppose each other, with one gene suppressing the expression of another. In **epistasis**, the interaction between genes is antagonistic, such that one gene masks or interferes with the expression of another. "Epistasis" is a word composed of Greek roots meaning "standing upon." The alleles that are being masked or silenced are said to be hypostatic to the epistatic alleles that are doing the masking. Often the biochemical basis of epistasis is a gene pathway in which expression of one gene is dependent on the function of a gene that precedes or follows it in the pathway.

An example of epistasis is pigmentation in mice. The wild-type coat color, agouti (AA) is dominant to solid-colored fur (aa). However, a separate gene C, when present as the recessive homozygote (cc), negates any expression of pigment from the A gene and results in an albino mouse (Figure 2.50). Therefore, the genotypes *AAcc*, *Aacc*, and *aacc* all produce the same albino phenotype. A cross between heterozygotes for both genes (*AaCc* x *AaCc*) would generate offspring with a phenotypic ratio of 9 agouti:3 black:4 albino (Figure 2.50). In this case, the *C* gene is epistatic to the *A* gene.

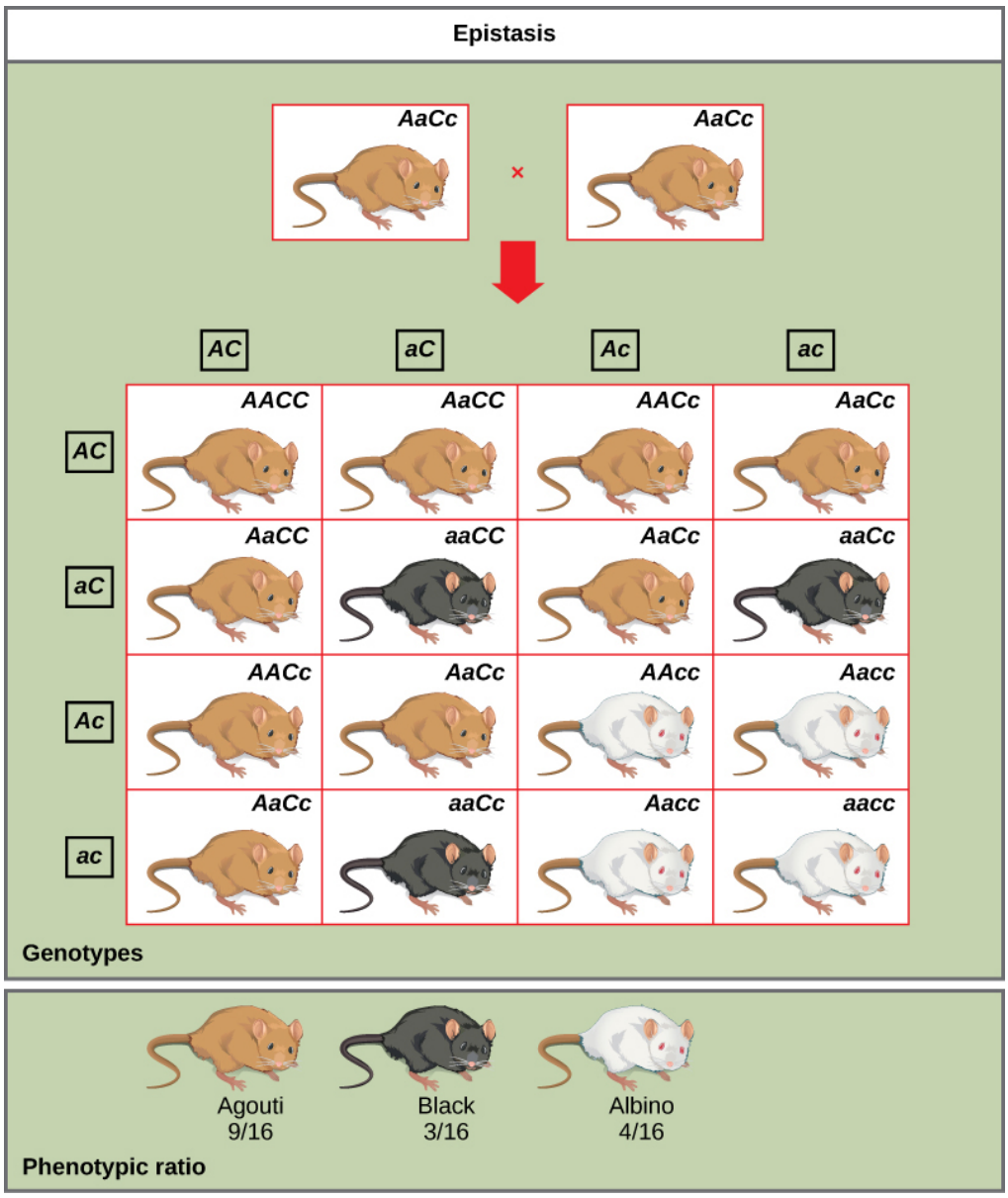

Figure 2.50 In this example of epistasis, one gene (C) masks the expression of another (A) for coat color. When the C allele is present, coat color is expressed; when it is absent (cc), no coat color is expressed. Coat color depends on the A gene, which shows dominance, with the recessive homozygote showing a different phenotype than the heterozygote or dominant homozygote. **Source:** *Concepts of Biology* (OpenStax), CC BY 4.0.

Exercises

Exercises (text version)

1. Match words into the correct blanks to complete the statements.

    A. Mendel's experiments measured quantitative traits and his analysis was of [Blank a] sample sizes.
    B. One of the incorrect ideas about inheritance prior to Mendel's experiments was that inheritance was a [Blank b] of parental traits.
    C. Mendel worked with common garden [Blank c] plants. The traits showed [Blank d] variation.
    D. The trait that masks the other recessive trait is called [Blank e].
    E. Gene variants that exist at the same chromosomal location are called [Blank f].
    F. Observable traits expressed by an organism are referred to as its [Blank g] where the underlying genetic make-up is known as the [Blank h].
    G. The P generation plants Mendel crossed had 2 alike alleles and are therefore [Blank i] the F1 plants they produced have differing alleles and are therefore [Blank j].
    H. Mendels' Law of [Blank k] refers to the separation of 2 alleles so that gametes contain only one or the other alleles.
    I. If the F1 progeny of a cross show a phenotype that is "in between" the parental phenotypes the trait is said to display [Blank l] dominance.
    J. If the F1 progeny of a cross display both traits displayed in the parents the trait is said to exhibit [Blank m]dominance.
    K. Traits on chromosomes 1-22 are said to be [Blank n] traits and genes on the X chromosome are called [Blank o] linked traits.
    L. Human eye colour is determined by [Blank p] alleles.
    M. Some genes can block or "stand upon" other genes. This is called [Blank q].

2. What traits of pea seed color would you expect to observe in F1 offspring if you cross true-breeding parents with green seeds and yellow seeds, and the yellow seed color is dominant over green?

    a. only yellow-green seeds

b. only yellow seeds
c. 1:1 yellow seeds:green seeds
d. 1:3 green seeds:yellow seeds

3. Which of the following experimental results, in terms of numbers of plants are closest to what you would expect in the F2 progeny of a cross involving seed surface texture in garden pea plants? True-breeding round and wrinkled parents were crossed to obtain F1 offspring.

   a. 810 round seeds
   b. 810 wrinkled seeds
   c. 405:395 round seeds:wrinkled seeds
   d. 610:190 round seeds:wrinkled seeds

4. True or false? One of the reasons that the garden pea was an excellent choice of model systems for studying inheritance is that the flowers close tightly during self-pollination to prevent accidental or unintentional fertilizations that could have diminished the accuracy of Mendel's data.
5. Select the correct words from the pair in bold type to answer the question.
   Question: Based on the following data, can you tell if the parent plant is homozygous dominant or heterozygous? In pea plants, round peas (*R*) are dominant to wrinkled peas (*r*). You do a test cross between a pea plant with wrinkled peas (genotype *rr*) and a plant of unknown genotype that has round peas. You end up with three plants, all which have round peas.
   Answer: You cannot be sure if the plant is homozygous or heterozygous as the data set is too **[Pair A: large or small]**: by **[Pair B: mathematical or random]** chance, all three plants might have acquired only the **[Pair C: recessive or dominant*]** gene even if the **[Pair D: recessive or dominant]** one is present.
6. Fill in the missing words to answer the questions:
   Question: What are the possible genotypes and phenotypes for a cross between *PpYY* and *ppYy* pea plants where purple flowered pea plants (*P*) are dominant to white flowered pea plants (*p*), and yellow peas (*Y*) are dominant to green (*y*)? How many squares would you need to complete a Punnett square analysis of this cross?
   Answer: The possible genotypes are [Blank A]**PpYY/PpYy**, [Blank B]**PpYY/PpYy**, [Blank C]**ppYY/ppYy**, and [Blank D]**ppYY/ppYy**. The former two genotypes would result in plants with [Blank E]*purple* flowers and [Blank F]*yellow* peas, while the latter two genotypes would result in plants with [Blank G]*white* flowers with [Blank H]*yellow* peas, for a 1:1 ratio of each phenotype. You only need a [Blank i]*2 × 2* Punnett square, [Blank J]*four*

squares total to do this analysis because two of the alleles are homozygous.

7. What are the observable traits expressed by an organism called?

    a. phenotype
    b. genotype
    c. alleles
    d. zygote

8. What is it called when a recessive trait will be observed in individuals?

    a. heterozygous
    b. homozygous or heterozygous
    c. homozygous
    d. diploid

9. What are the types of gametes that can be produced by an individual with the genotype *AaBb?*

    a. *Aa*, *Bb*
    b. *AA*, *aa*, *BB*, *bb*
    c. *AB*, *Ab*, *aB*, *ab*
    d. *AB*, *ab*

10. What is the reason for doing a test cross?

    a. to identify heterozygous individuals with the dominant phenotype
    b. to determine which allele is dominant and which is recessive
    c. to identify homozygous recessive individuals in the F2
    d. to determine if two genes assort independently

11. Match the words to the correct blanks to answer the question.
    Question: What is the phenotypic ratio of the offspring where a Punnett square is used to predict the offspring in a cross between a dwarf pea plant (homozygous recessive) and a tall pea plant (heterozygous)?
    Words: 2 × 2 , genotypes, tall, t and t, T and t, dwarf
    Answer: The phenotypic ratio will be 1 [Blank A]:1 [Blank B], and the Punnett square would be [Blank C] and will have [Blank D] along the top and [Blank E] along the left side. Clockwise from the top left, the [Blank F] listed within the boxes will be Tt, tt, tt, and Tt.

12. Match the words to the correct blanks to answer the question.

Question: Describe a Punnett square used to predict the offspring in a cross between a tall pea plant (heterozygous) and a tall pea plant (heterozygous). What is the genotypic ratio of the offspring?

Words: 1TT, 2 × 2, Tt, 1tt, TT, tt, 2Tt, T and t

Answer: The Punnett square will be [Blank A] and will have [Blank B] along the top and [Blank C] along the left side. Clockwise from the top left, the genotypes listed within the boxes will be [Blank D], [Blank E], [Blank F], and [Blank G]. The genotypic ratio will be [Blank H]: [Blank i]: [Blank J].

Check your answers in footnote[4]

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Glossary

Summary of additional key terms introduced in this chapter:

4.

1. a) large, b) blend, c) pea, d) discontinuous, e) dominant, f) alleles, g) phenotype, h) genotype, i) homozygous, j) heterozygous, k) segregation, l) incomplete, m) co-, n) autosomal, o) X/sex, p) multiple, q) epistasis.
2. b) only yellow seeds
3. d) 610:190 round seeds:wrinkled seeds
4. True. The garden pea has flowers that close tightly during self-pollination. This helps to prevent accidental or unintentional fertilizations that could have diminished the accuracy of Mendel's data.
5. A: small, B: random, C: dominant, D: recessive
6. A – *PpYY/PpYy*, B – *PpYY/PpYy,* C – *ppYY/ppYy,* D – *ppYY/ppYy,* E – purple, F – yellow, G – white, H – yellow, i – 2 × 2, J – four
7. a) phenotype
8. c) homozygous
9. c) *AB*, *Ab*, *aB*, *ab*
10. a) to identify heterozygous individuals with the dominant phenotype
11. A – tall, B – dwarf, C – 2 × 2, D – T and t, E – t and t, F – genotypes
12. A – 2 × 2, B – T and t, C – T and t, D – TT, E – Tt, F – Tt, G – tt, H- 1TT, i – 2Tt, J – 1tt.

P: the parental generation in a cross

Attribution & References

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2.7 UNIT SUMMARY AND REVIEW

Key Takeaways

The Genome

Eukaryotes have multiple, linear chromosomes surrounded by a nuclear membrane. Human somatic cells have 46 chromosomes consisting of two sets of 22 homologous chromosomes and a pair of nonhomologous sex chromosomes. This is the 2n, or diploid, state. Human gametes have 23 chromosomes or one complete set of chromosomes. This is the n, or haploid, state. Genes are segments of DNA that code for a specific protein or RNA molecule. An individual's traits are the observable or measurable features of an organism which are determined in large part by the genes inherited from each parent, but also by the environment that they experience. An individual's phenotype encompasses all traits, including those that are visible and those that are not (such as behavior). Genes are expressed as characteristics of the organism, and each characteristic may have different variants called traits that are caused by differences in the DNA sequence for a gene, which can be the distinguishing feature between two individuals.

The Cell Cycle

The cell cycle is an orderly sequence of events. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages. In eukaryotes, the cell cycle consists of a long preparatory period, called interphase. Interphase is divided into G1, S, and G2 phases. Mitosis consists of five stages: prophase, prometaphase, metaphase, anaphase, and telophase. Mitosis is usually accompanied by cytokinesis, during which the cytoplasmic components of the daughter cells are separated by an actin ring (animal cells). Each step of the cell cycle is monitored by internal controls called checkpoints. There are three major checkpoints in the cell cycle: one near the end of G1, a second at the G2–M transition, and the third during metaphase.

Cancer and the Cell Cycle

Cancer is the result of unchecked cell division caused by a breakdown of the mechanisms regulating the cell cycle. The loss of control begins with a change in the DNA sequence of a gene that codes for one of the regulatory molecules. Faulty instructions lead to a protein that does not function as it should. Any disruption of the monitoring system can allow other mistakes to be passed on to the daughter cells. Each successive cell division will give rise to daughter cells with even more accumulated damage. Eventually, all checkpoints become nonfunctional, and rapidly reproducing cells crowd out normal cells, resulting in tumorous growth.

The Cellular Basis of Inheritance

Nearly all eukaryotes undergo sexual reproduction. The variation introduced into the reproductive cells by meiosis appears to be one of the advantages of sexual reproduction that has made it so successful. Meiosis and fertilization alternate in sexual life cycles. The process of meiosis produces genetically unique reproductive cells called gametes, which have half the number of chromosomes as the parent cell. Fertilization, the fusion of haploid gametes from two individuals, restores the diploid condition. Thus, sexually reproducing organisms alternate between haploid and diploid stages. However, the ways in which reproductive cells are produced and the timing between meiosis and fertilization vary greatly. There are three main categories of life cycles: diploid-dominant, demonstrated by most animals; haploid-dominant, demonstrated by all fungi and some algae; and alternation of generations, demonstrated by plants and some algae.

Meiosis

Sexual reproduction requires that diploid organisms produce haploid cells that can fuse during fertilization to form diploid offspring. The process that results in haploid cells is called meiosis. Meiosis is a series of events that arrange and separate chromosomes into daughter cells. During the interphase of meiosis, each chromosome is duplicated. In meiosis, there are two rounds of nuclear division resulting in four nuclei and usually four haploid daughter cells, each with half the number of chromosomes as the parent cell. During meiosis, variation in the daughter nuclei is introduced because of crossover in prophase I and random alignment at metaphase I. The cells that are produced by meiosis are genetically unique.

Meiosis and mitosis share similarities, but have distinct outcomes. Mitotic divisions are single nuclear divisions that produce daughter nuclei that are genetically identical and have the same

number of chromosome sets as the original cell. Meiotic divisions are two nuclear divisions that produce four daughter nuclei that are genetically different and have one chromosome set rather than the two sets the parent cell had. The main differences between the processes occur in the first division of meiosis. The homologous chromosomes separate into different nuclei during meiosis I causing a reduction of ploidy level. The second division of meiosis is much more similar to a mitotic division.

Patterns of Inheritance

Working with garden pea plants, Mendel found that crosses between parents that differed for one trait produced F1 offspring that all expressed one parent's traits. The traits that were visible in the F1 generation are referred to as dominant, and traits that disappear in the F1 generation are described as recessive. When the F1 plants in Mendel's experiment were self-crossed, the F2 offspring exhibited the dominant trait or the recessive trait in a 3:1 ratio, confirming that the recessive trait had been transmitted faithfully from the original P parent. Reciprocal crosses generated identical F1 and F2 offspring ratios. By examining sample sizes, Mendel showed that traits were inherited as independent events.

When true-breeding, or homozygous, individuals that differ for a certain trait are crossed, all of the offspring will be heterozygous for that trait. If the traits are inherited as dominant and recessive, the F1 offspring will all exhibit the same phenotype as the parent homozygous for the dominant trait. If these heterozygous offspring are self-crossed, the resulting F2 offspring will be equally likely to inherit gametes carrying the dominant or recessive trait, giving rise to offspring of which one quarter are homozygous dominant, half are heterozygous, and one quarter are homozygous recessive. Because homozygous dominant and heterozygous individuals are phenotypically identical, the observed traits in the F2 offspring will exhibit a ratio of three dominant to one recessive.

Mendel postulated that genes (characteristics) are inherited as pairs of alleles (traits) that behave in a dominant and recessive pattern. Alleles segregate into gametes such that each gamete is equally likely to receive either one of the two alleles present in a diploid individual. In addition, genes are assorted into gametes independently of one another. That is, in general, alleles are not more likely to segregate into a gamete with a particular allele of another gene.

Alleles do not always behave in dominant and recessive patterns. Incomplete dominance describes situations in which the heterozygote exhibits a phenotype that is intermediate between the homozygous phenotypes. Codominance describes the simultaneous expression of both of the alleles in the heterozygote. Although diploid organisms can only have two alleles for any given

gene, it is common for more than two alleles for a gene to exist in a population. In humans, as in many animals and some plants, females have two X chromosomes and males have one X and one Y chromosome. Genes that are present on the X but not the Y chromosome are said to be X-linked, such that males only inherit one allele for the gene, and females inherit two.

According to Mendel's law of independent assortment, genes sort independently of each other into gametes during meiosis. This occurs because chromosomes, on which the genes reside, assort independently during meiosis and crossovers cause most genes on the same chromosomes to also behave independently. When genes are located in close proximity on the same chromosome, their alleles tend to be inherited together. This results in offspring ratios that violate Mendel's law of independent assortment. However, recombination serves to exchange genetic material on homologous chromosomes such that maternal and paternal alleles may be recombined on the same chromosome. This is why alleles on a given chromosome are not always inherited together. Recombination is a random event occurring anywhere on a chromosome. Therefore, genes that are far apart on the same chromosome are likely to still assort independently because of recombination events that occurred in the intervening chromosomal space.

Whether or not they are sorting independently, genes may interact at the level of gene products, such that the expression of an allele for one gene masks or modifies the expression of an allele for a different gene. This is called epistasis.

DNA Structure and Function

The model of the double-helix structure of DNA was proposed by Watson and Crick. The DNA molecule is a polymer of nucleotides. Each nucleotide is composed of a nitrogenous base, a five-carbon sugar (deoxyribose), and a phosphate group. There are four nitrogenous bases in DNA, two purines (adenine and guanine) and two pyrimidines (cytosine and thymine). A DNA molecule is composed of two strands. Each strand is composed of nucleotides bonded together covalently between the phosphate group of one and the deoxyribose sugar of the next. From this backbone extend the bases. The bases of one strand bond to the bases of the second strand with hydrogen bonds. Adenine always bonds with thymine, and cytosine always bonds with guanine. The bonding causes the two strands to spiral around each other in a shape called a double helix. Ribonucleic acid (RNA) is a second nucleic acid found in cells. RNA is a single-stranded polymer of nucleotides. It also differs from DNA in that it contains the sugar ribose, rather than deoxyribose, and the nucleotide uracil rather than thymine. Various RNA molecules function in the process of forming proteins from the genetic code in DNA.

Prokaryotes contain a single, double-stranded circular chromosome. Eukaryotes contain double-

stranded linear DNA molecules packaged into chromosomes. The DNA helix is wrapped around proteins to form nucleosomes. The protein coils are further coiled, and during mitosis and meiosis, the chromosomes become even more greatly coiled to facilitate their movement. Chromosomes have two distinct regions which can be distinguished by staining, reflecting different degrees of packaging and determined by whether the DNA in a region is being expressed (euchromatin) or not (heterochromatin).

DNA replicates by a semi-conservative method in which each of the two parental DNA strands act as a template for new DNA to be synthesized. After replication, each DNA has one parental or "old" strand, and one daughter or "new" strand.

Replication in eukaryotes starts at multiple origins of replication, while replication in prokaryotes starts from a single origin of replication. The DNA is opened with enzymes, resulting in the formation of the replication fork. Primase synthesizes an RNA primer to initiate synthesis by DNA polymerase, which can add nucleotides in only one direction. One strand is synthesized continuously in the direction of the replication fork; this is called the leading strand. The other strand is synthesized in a direction away from the replication fork, in short stretches of DNA known as Okazaki fragments. This strand is known as the lagging strand. Once replication is completed, the RNA primers are replaced by DNA nucleotides and the DNA is sealed with DNA ligase.

The ends of eukaryotic chromosomes pose a problem, as polymerase is unable to extend them without a primer. Telomerase, an enzyme with an inbuilt RNA template, extends the ends by copying the RNA template and extending one end of the chromosome. DNA polymerase can then extend the DNA using the primer. In this way, the ends of the chromosomes are protected. Cells have mechanisms for repairing DNA when it becomes damaged or errors are made in replication. These mechanisms include mismatch repair to replace nucleotides that are paired with a non-complementary base and nucleotide excision repair, which removes bases that are damaged such as thymine dimers.

In prokaryotes, mRNA synthesis is initiated at a promoter sequence on the DNA template. Elongation synthesizes new mRNA. Termination liberates the mRNA and occurs by mechanisms that stall the RNA polymerase and cause it to fall off the DNA template. Newly transcribed eukaryotic mRNAs are modified with a cap and a poly-A tail. These structures protect the mature mRNA from degradation and help export it from the nucleus. Eukaryotic mRNAs also undergo splicing, in which introns are removed and exons are reconnected with single-nucleotide accuracy. Only finished mRNAs are exported from the nucleus to the cytoplasm.

The central dogma describes the flow of genetic information in the cell from genes to mRNA to proteins. Genes are used to make mRNA by the process of transcription; mRNA is used to synthesize proteins by the process of translation. The genetic code is the correspondence between

the three-nucleotide mRNA codon and an amino acid. The genetic code is "translated" by the tRNA molecules, which associate a specific codon with a specific amino acid. The genetic code is degenerate because 64 triplet codons in mRNA specify only 20 amino acids and three stop codons. This means that more than one codon corresponds to an amino acid. Almost every species on the planet uses the same genetic code.

The players in translation include the mRNA template, ribosomes, tRNAs, and various enzymatic factors. The small ribosomal subunit binds to the mRNA template. Translation begins at the initiating AUG on the mRNA. The formation of bonds occurs between sequential amino acids specified by the mRNA template according to the genetic code. The ribosome accepts charged tRNAs, and as it steps along the mRNA, it catalyzes bonding between the new amino acid and the end of the growing polypeptide. The entire mRNA is translated in three-nucleotide "steps" of the ribosome. When a stop codon is encountered, a release factor binds and dissociates the components and frees the new protein.

While all somatic cells within an organism contain the same DNA, not all cells within that organism express the same proteins. Prokaryotic organisms express the entire DNA they encode in every cell, but not necessarily all at the same time. Proteins are expressed only when they are needed. Eukaryotic organisms express a subset of the DNA that is encoded in any given cell. In each cell type, the type and amount of protein is regulated by controlling gene expression. To express a protein, the DNA is first transcribed into RNA, which is then translated into proteins. In prokaryotic cells, these processes occur almost simultaneously. In eukaryotic cells, transcription occurs in the nucleus and is separate from the translation that occurs in the cytoplasm. Gene expression in prokaryotes is regulated only at the transcriptional level, whereas in eukaryotic cells, gene expression is regulated at the epigenetic, transcriptional, post-transcriptional, translational, and post-translational levels.

Additional Optional Reading:

1. Aiello, L. B., & Chiatti, B. D. (2017). Primer in Genetics and Genomics, Article 4-Inheritance Patterns. *Biological research for nursing*, *19*(4), 465–472. https://doi.org/10.1177/1099800417708616

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