Visualizing Cell Processes

A Series of Five Programs
produced by BioMEDIA ASSOCIATES

Content Guide for Program 2

DNA Replication and Cell Reproduction

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Each of the five programs in this series consists of a set of short, narrated, full-motion modules 1-3 minutes long. Each module conveys an essential process or concept of cellular biology. The modules are organized around national standards for teaching biology.

Many scientists will argue that single greatest scientific achievement of the last half of the 20th century was the discovery of the function of DNA. On these long molecules is written the blueprint for life and the specific instructions for each of the millions of species that make up the living world.

Understanding how DNA codes for the structural proteins that make up living things, and how it specifies the enzymes that govern biochemical processes requires a working knowledge of the structure of these information molecules and how they are replicated from one generation of cells to the next. Prokaryotic cells (bacteria) have all of their several thousand genes distributed along single long molecule of DNA. Eukaryotic cells (protists, plants and animals) have multiple DNA molecules (multiple chromosomes). When a cell divides each daughter cell receives a complete set of chromosomes. This is accomplished through a process of chromosome sorting and distribution known as mitosis.

1: Getting ready for Mitosis

In eukaryotic cells, like our own, the DNA is coiled around histone proteins forming units called nucleosomes. Nucleosomes are spaced along the DNA like beads on a string, a packaging strategy that shortens the total length of DNA to one-sixth of its uncoiled length.

At the onset of mitosis the nucleosomes become ever more tightly packed through looping and coiling to become part of a chromosome. At this stage, a chromosome is a double structure. Two identical DNA molecules produced through replication have condensed into two chromatids connected by a bridge called the "centromere." Coiling and supercoiling produces chromatids that are about a thousand times shorter than the total length of the DNA they contain.

2: Mitosis

Onion roots grow about five millimeters a day, requiring prodigious cell division. A longitudinal root section shows many cells in various stages of mitosis.

In interphase the stained chromatin is loosely distributed throughout the nucleus. This is the stage where genes are being transcribed and translated into proteins. The two dark-stained bodies seen in onion root cells are nucleoli, manufacturing centers for the special RNA molecules that make up ribosomes, the machines where proteins are

manufactured.

In prophase, chromosomes become clearly visible. During prophase, the nuclear envelope breaks down and disappears. The nucleoli vanish and a basket called the spindle forms around the chromosomes.

In metaphase, the chromosomes line up, pulled by the spindle fibers.

During anaphase, spindle fibers pull the chromatids to opposite sides of the cell.

In the final stage, telophase, a nuclear envelope forms around each set of chromosomes, and the nucleoli reappear. Mitosis has parceled out the identical sets of genetic material, and the cell can now divide. This describes mitosis in plant and animal cells. Fungi differ in some details, as do protists.

Cytokinesis refers to the division of one cell into two daughter cells. The process varies in different evolutionary lines of eukaryotes. In animal cells, a band of actin squeezes the cell in two. Plant cells are surrounded by a rigid cell wall, requiring a different strategy. When a plant cell divides, islands of membrane form across the middle of the cell (dividing the two nuclei that resulted from mitosis) creating a partition on which a new cell wall is laid down.

3: Meiosis Produces Genetic Variety

Meiosis is basically a process of converting the double sets of chromosomes in body cells to the single sets of chromosomes found in sex cells. At the beginning of meiosis, homologous chromosomes, one from each parent, pair up. During this process, parts of each chromatid may break off and exchange, a process called "crossing over." The next stage of meiosis reduces the chromosomes to a single set.

Following reduction, the chromatids separate creating four gametes. Crossing over, and the random shuffling of parental chromosomes during reduction, assures that each gamete will contain a unique mix of genetic information.

4: DNA, Nucleotide Structure and Bonding

DNA is an extremely long molecule composed of two strands wound in a double helix. Each strand is made up of a chain of nucleotides. The four nucleotides found in DNA have a common structure: a phosphate group and a sugar (common to all four), and a nitrogenous base unit, of which there are four kinds: thymine, guanine, cytosine and adenine.

Two kinds of bonds make the DNA molecule possible. The backbone of each strand is formed by strong covalent bonds between the phosphate and sugar groups. These phosphate/sugar units created the sides of the DNA ladder. The strands are held together by weak hydrogen bonds between the opposing nitrogenous bases (the rungs of the DNA ladder). In these cross-links, thymine bonds exclusively with adenine and guanine only with cytosine,"T" with "A" and "G" with "C."

The reason (as shown graphically in the programs) is that adenine and thymine have two hydrogen bonding sites so they bond only with each other. Cytosine and guanine have three, making them exclusive bonding partners. This bonding pattern allows DNA to be replicated with a high degree of precision.

5: DNA Replication
For life to have any continuity from one generation of cells to the next, the genetic blueprint must be duplicated with great precision. The beauty of the double helix is that the genetic instructions are encrypted on each strand. Therefore, each strand can serve as a template for creating its missing half so that two identical DNA molecules can be assembled from one. Essentially that is how genetic continuity is maintained through generations of cells, and through generations of individuals.

The process of DNA replication was first worked out in bacteria. Replication begins when an initiator protein chemically recognizes a particular string of nucleotides (the replication origin). In the next step, enzymes known as helicases break the bonds connecting the two strands. As the animation shows, replication will proceed in both directions away from the replication origin.

During this process, special proteins keep the two strands apart and prevent kinking. Another enzyme, primase, lays down a primer, which serves as the starting point for a new double helix.

With the DNA split, each strand can instruct the synthesis of its missing half, but to do so rapidly requires an enzyme that tracks along the strand, matching the appropriate nucleotides to create the complimentary strand. The enzyme is DNA polymerase.

6: Replicating the Leading and Lagging Strands
During replication, double-stranded DNA is opened in a loop called a replication bubble. At each end of the bubble is a replication fork where enzymes unravel the double helix exposing single strands of parent DNA.

In the DNA double helix the backbones of the strands run in opposite directions. DNA polymerase can only build a new complementary strand by adding nucleotides in one direction. Therefore, only one strand can be replicated in a continuous sweep. This strand is called the "leading strand."

The other strand, replicated in the opposite direction is called the "lagging strand." Replicating the lagging strand requires priming and a DNA polymerase that builds lagging strand moving away from the replication fork. This produces short segments of DNA called "Okazaki fragments." Finally, the enzyme ligase welds the Okazaki fragments into a continuous strand of DNA.

Replication occurs at many points simultaneously producing numerous replication bubbles that grow toward each other and merge replicating the cell's entire complement of DNA.

7: The Twisting Problem
As the DNA is opened at a replication fork a molecular twisting problem can be imagined. As the twisted molecule unwinds from the center, the twist tightens, preventing further opening of the helix.

During DNA replication a special enzyme, topoisomerase, temporarily breaks the DNA, making it possible for the helix to rotate removing the excess twist. Releasing the twist allows the replication fork to advance.

8: Proofreading and Repair
In the whir of DNA replication nucleotide-based pairs must be matched precisely. But about once in every 10,000 or so pairings a mismatched nucleotide gets jammed into the new strand. When an incorrect match occurs the DNA polymerase enzyme backs up and replaces it with the correct nucleotide.

Radiation can corrupt information molecules. For example, ultraviolet radiation can rearrange the chemical bonds in adjacent thymines causing them to join together producing a "thymine dimer." A specific repair enzyme monitors DNA for thymine dimers, cutting them out, allowing DNA polymerase to correct the damaged section.

In this way the genetic blueprint for each cell is passed on with very high accuracy. However, tiny errors creep in, and well they should. These mutations create the raw material for adaptation, and ultimately for the ongoing processes of evolution.