From DNA to Protein

Identifying DNA as the Genetic Material

Objectives: Describe Griffith's discovery of a transforming principle.
Explain how Avery identified DNA as the transforming principle.
Summarize the experiments of Hershey and Chase that confirmed DNA as the genetic material.

Warm Up: What do you think Mendel's observations have to do with the transforming principle mentioned in this section?

Words to know: bacteriophage

Griffith finds a "transforming principle."

- In 1928, Frederick Griffith was investigating two forms of bacteria that caused pneumonia.
- The two forms were Smooth (S) and Rough (R).
- When injected into mice, only the S type killed the mice.
- When the S bacteria were killed with heat, the mice were then unaffected.
- He then injected a mix of heat killed S and R bacteria into the mice and the mice died.
- He also found live S bacteria in the mice blood samples.
- Griffith concluded that there was some sort of "transforming principle" causing the bacteria to change.

What evidence suggested that there was a transforming principle?

Avery identifies DNA as the transforming principle.

- Oswald Avery and his group worked for 10 years to figure out Griffith's transforming principle.
- They developed a process to help them solve the riddle.
- **Qualitative Tests:** showed that no protein was present, but DNA was present.
- **Chemical Analysis:** the proportions of elements in the extract closely matched those found in DNA.
- **Enzyme Tests:** When the team added enzymes, the transformation still occurred. When the enzyme was added to breakdown DNA, the transformation did NOT occur.

List the key steps in the process that Avery's team used to identify the transforming principle.

Hershey and Chase confirm that DNA is the genetic material.

- Hershey and Chase were studying viruses that infect bacteria.
- This type of virus is called a **bacteriophage**.
- Hershey and Chase conducted two experiments:
    1. Bacteria were infected with phages that had radioactive sulfur atoms in the protein molecules.
        - When they separated the bacteria from the parts of the bacteriophage that remained outside, they found no radioactivity.
    2. They repeated the procedure with the DNA tagged with radioactive phosphorous. This time, the radioactivity was clearly present inside the bacteria.
- From their results, Hershey and Chase concluded that the phages' DNA had entered the bacteria, but the protein had not.
- Their finding FINALLY convinced scientists that the genetic material is **DNA** and NOT protein.

How did Hershey and Chase build upon Avery's chemical analysis results?

Structure of DNA

Objectives: Describe the interaction of the four necleotides that make up DNA.
Describe the three-dimensional structure of DNA.

Warm Up: What are some examples of simple units that can be used to produce great complexity?

Words to know: nucleotide, double helix, base pairing rule

DNA is Composed of Four Types of Nucleotides.

- The **DNA molecule** is a very long polymer, or chain of repeating units.
- The small units, or **MONOMERS**, that make up DNA are called **Nucleotides**.
- Each nucleotide is made of three parts:
    1. A **phosphate group**. (1 phosphorous with four oxygen)
    2. A ring-shaped sugar called **deoxyribose**.
    3. A **nitrogen base** (single or double ring built around carbon and nitrogen atoms).
- One molecule of DNA contains billions of nucleotides, but there are only four types of nucleotides in DNA.
- These nucleotides differ by their bases.
- Two are single ring structures called pyrimidines.
    1. Cytosine (C).
    2. Thymine (T).
- Two are double ring structures called purines.
    1. Adenine (A).
    2. Guanine (G).
- In the 1950's Erwin Chargaff figured out how the nitrogen bases paired up.
- He concluded that adenine always paired with thymine and guanine always paired with cytosine (A-T and C-G)

What is the only difference among the four DNA nucleotides?

Watson and Crick developed an accurate model of DNA's 3-D structure.

X-Ray Evidence

- Rosalind Franklin and Maurice Wilkins were studying DNA using x-ray crystallography.
- When DNA is bombarded with x-rays, the atoms in DNA diffract the x-rays in a pattern that can be captured on film.
- Franklin's data gave Watson and Crick what they needed to ultimately figure out the structure of DNA.

The Double Helix

- Watson and Crick made many models using metal and wood to figure out the structure of DNA.
- Their models put the sugar-phosphate backbones on the outside and the bases on the inside.
- They could not however figure out the base pairing because of the sizes of the bases.
- They finally figured out that by bonding a single-ring with a double-ring that everything fit.
- They created the double helix (twisted ladder) model in which two strands of DNA wind around each other.
- The strands are complementary – they fit together opposite of each other.
- Their pairing of the bases, finally explained Chargaff's Rule.

How did the Watson and Crick model explain Chargaff's Rule?

Nucleotides always pair in the same way.

- The Base Pairing Rule States: thymine (T) always pairs with adenine (A) and cytosine (C) always pairs with guanine (G).

What sequence of bases would pair with the sequence TGACTA?

DNA Replication

Objectives: Summarize the process of DNA replication.
Describe the role of enzymes in DNA replication.

Warm Up: What are some everyday uses of a template?

Words to know: replication, DNA polymerase

Replication copies the genetic information.

- One of the most powerful features of Watson and Crick's work is that they showed that DNA can be copied.
- Replication is the process in which DNA is copied during the cell cycle.
- This occurs during Interphase.
- Replication ensures that every cell has a complete set of identical genetic information.

How does replication ensure that cells have complete sets of DNA?

Proteins carry out the process of replication.

- DNA only stores information, enzymes and other proteins do the actual work of replication.
- DNA polymerase helps bond nucleotides together during replication.

The Replication Process

1. Enzymes unzip the double helix at various points.
2. Bases on each strand are exposed.
3. Free-floating nucleotides pair, one by one, with the bases on the template strands.
4. Two IDENTICAL molecules of DNA result. Each new molecule contains one new strand and one original strand of DNA.

How does step 4 of replication show that DNA acts as a template?

Replication is fast and accurate.

- In human cells, about 50 nucleotides are added every second to a new strand of DNA.
- Because it would take so long to replicate from one end of the DNA to the other, replication points occur at many different point at the same time and are joined together by enzymes.

What does a cell need to replicate its DNA so quickly?

Transcription

Objectives: Describe the relationship between RNA and DNA.
Identify the three kinds of RNA and their functions.
Compare transcription to replication.

Warm Up: How is the word transcription used in music?

Words to know: central dogma, RNA, transcription, RNA polymerase, messenger RNA (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA).

RNA carries out DNA's instructions.

- The central dogma for modern biology states that: information flows in one direction, from DNA to RNA to proteins.
- The central dogma involves three processes:
  - **Replication** – copies DNA.
  - **Transcription** – converts DNA message into RNA.
  - **Translation** – interprets the message from RNA into a string of amino acids (polypeptide) that forms proteins.
- In Prokaryotic cells, these three processes occur in the cytoplasm at about the same time.

- In eukaryotic cells, replication and transcription takes place in the nucleus and translation takes place in the cytoplasm and ribosomes.
- RNA works as an intermediate link between DNA and protein synthesis.
- RNA (ribonucleic acid) is a chain of nucleotides made of sugar, a phosphate and nitrogen base.
- RNA is single-stranded.
- Think of RNA as a temporary copy of DNA that is used then destroyed.

DNA	**RNA**
Sugar is Deoxyribose	Sugar is Ribose
Use the base pairs Adenine (A) and Thymine (T)	Uses the base pairs Adenine (A) and Uracil (U)
Double Stranded	Single Stranded

How do DNA and RNA differ?

Transcription makes three types of RNA.

- Transcription is the process of copying a sequence of DNA to produce a complimentary strand of RNA.
- During this process, a Gene, NOT the entire chromosome, is transferred into an RNA message.
- Transcription is catalyzed by RNA polymerase.
- Transcription has 3 basic steps:
    1. RNA polymerase recognizes the start site of a gene and the DNA strands separate.
    2. RNA polymerase uses one strand of DNA as a template to produce a complimentary strand of RNA (Remember A-U in RNA).
    3. RNA detaches from the DNA and transcription is complete.
- Transcription produces three types of RNA molecules:
    1. Messenger RNA (mRNA) – takes the DNA message for conversion to protein.
    2. Ribosomal RNA (rRNA) – forms part of ribosomes.
    3. Transfer RNA (tRNA) – brings amino acids from the cytoplasm to the ribosomes to help make proteins.

Explain why transcription only occurs in the nucleus of eukaryotes.

The transcription process is similar to replication.

Replication	**Transcription**
Occurs in the Nucleus	Occurs in the Nucleus
Requires DNA Polymerase	Requires RNA polymerase
Involves DNA	Involves DNA
Form two identical strands of DNA	Forms a single strand of RNA
Base pairs are A-T C-G	Base pairs are **A-T** C-G

How are the processes of transcription and replication similar?

Translation

Objectives: Describe how mRNA codons are translated into Amino Acids.
Summarize the process of protein synthesis.

Warm Up: How are computer codes the same as the codes for protein synthesis?

Words to know: translation, codon, stop codon, start codon, anticodon

Amino acids are coded by mRNA base sequences.

- Translation is the process that converts or translates an mRNA message into a polypeptide.
- One or more polypeptides form a protein.

- Base sequences can form 20 different amino acids, which can be arranged in numerous ways to form proteins.

Triplet Code

- A codon is a three-nucleotide sequence that codes for a amino acid.
- You can create a codon by divided your RNA sequence into groups of three.
- Codons that represent the same amino acid have at least the SAME first two letters.
- There are two special codons:
    1. Three stop codons that stop the chain of amino acids from joining (UGA, UAA, UAG)
    2. One start codon that begins all amino acid sequences (AUG, Methionine).

Common Language

- The genetic code is shared by almost all organisms – and even viruses.
- The common nature of the genetic code suggests that almost all organisms arose from a common ancestor.
- It also means that scientists can insert a gene from one organism into another organism to make a functional protein.

Suppose an mRNA molecule in the cytoplasm had 300 nucleotides. How many amino acids would be in the resulting protein?

Amino acids are linked to become a protein.

- mRNA carries the instructions from DNA to the cytoplasm from the nucleus.
- The cell then uses tRNA and ribosomes to complete translation.
- The mRNA strand fits through spaces in the ribosome.
- The tRNA acts as a sort of adaptor between mRNA and amino acids.
- The tRNA is called an anticodon because it is the go between for the amino acids and the mRNA.

Translation Steps

1. The exposed codon attracts an anticodon bearing an amino acid.
2. The tRNA pairs with the mRNA codon.
3. The ribosome helps form a peptide bond between the two amino acids.
4. The ribosome then breaks the bond between the codon and anticodon.
5. The ribosome shifts the mRNA to the next codon and creates the next amino acid.
6. This process continues until a STOP codon is read and the polypeptide chain is severed.

Explain the different roles of the large and small ribosomal subunits.

Mutations

Objectives: Distinguish between different types of mutations.
Explain why mutations may or may not affect phenotype.
List some factors that cause mutations.

Warm Up: What happens if, in recording your grade, a teacher transposes the numbers of your 91 average?

Words to know: mutation, point mutation, frameshift mutation, mutagen

Some mutations affect a single gene, while others affect an entire chromosome.

- A mutation is a change in an organism's DNA.
- Typically, mutations that affect a single gene happen during replication, whereas mutations that affect a group of genes or an entire chromosome happen during meiosis.

Gene Mutations

- A point mutation is a mutation in which one nucleotide is substituted for another.

- Usually, this type of mistake is caught and fixed by DNA polymerase; if not, the DNA may be permanently changed.
- Ex: THE CAT A**T**E THE RAT
  THE CAT A**P**E THE RAT

- A frameshift mutation involves the insertion or deletion of a nucleotide in the DNA sequence.
  - They can shift the entire sequence following them by one or more nucleotides.
  - Ex: TH**E** CAT ATE THE RAT
  - Deletion: THC ATA TET HER AT
  - Insertion: THE ECA TAT ETH ERA T

Chromosomal Mutations

- **Duplication** – Occurs when a sequence of the chromosome is repeated.
  - Ex: ABCDEFG
    ABCDECDEFG
- **Deletion** – Occurs when a sequence of the chromosome is removed.
  - Ex: ABCDEFG
    ABFG
- **Inversion** – Occurs when a sequence of the chromosome is backwards.
  - Ex: ABCDEFG
    ABEDCFG
- **Translocation** – Occurs when a piece of another chromosome is attached to a chromosome.
  - Ex: ABCDEFG
    ABCDEFGXYZ

How does a frameshift mutation affect reading frames?

Mutations may or may not affect phenotype.

Impact on Phenotype

- Chromosomal mutations affect a lot of genes and tend to have a big effect on an organism.
- A mutation can break up a gene, or it can make a new hybrid gene, with a new function.
- Gene mutations can cause the wrong amino acid to be made which can change an entire protein.

Impact on Offspring

- Mutations in sex cells can be passed on to offspring.
- They are the underlying source of genetic variation, which is the basis of natural selection.

Why aren't mutations in body cells passed on to offspring?

Mutations can be caused by several factors.

- Replication is a common place for mutations to occur.
- Many scientists believe these mutations are causes for aging.
- Mutagens are agents in the environment that can change DNA.
- Some mutagens are natural: UV rays.
- Some mutagens are man made: chemicals, x-rays, carcinogens.

Explain why mutagens can damage DNA in spite of repair enzymes.

Manipulating DNA

Objectives: Summarize how restriction enzymes cut DNA
Explain how restriction maps show the lengths of DNA fragments.

Warm Up: How many of you watch CSI? What does CSI stand for? How does DNA figure into that show?

Words to know: restriction enzyme, gel electrophoresis, restriction map

Scientists use several techniques to manipulate DNA.

- Chemicals, computers, and bacteria are just a few of the tools that have allowed advances in genetics research.
- Artificial nucleotides are used to sequence genes, and artificial copies of the gene are used to study gene expression.

Why might so many different methods be needed to study DNA and genes?

Restriction enzymes cut DNA.

- A whole chromosome is too large for scientists to study a particular gene easily, so they had to find a way to get much smaller pieces of DNA.
- In gel electrophoresis, an electrical current is used to separate a mixture of DNA fragments from each other.
- A sample of DNA is loaded into a gel, which is like a thin slab of hard gelatin.
- Restriction enzymes are enzymes that cut DNA molecules at specific nucleotide sequences.
- The sequence of nucleotides that is cut is called a restriction site.
- The ends at which the restriction sites are cut are called "Sticky Ends".

How are restriction enzymes used in making restriction maps?

Copying DNA

Objectives: Describe the role of polymerases in copying DNA segments.
Outline the three-step PRC process

Warm Up: How do you use the copy and past functions on Microsoft Word?

Words to know: polymerase chain reaction (PCR), primer

PCR uses polymerases to copy DNA segments.

- Polymerase chain reaction (PCR) is a technique that produces millions – or billions – of copies of a specific DNA sequence in just a few hours.
- DNA polymerase enzymes play a large role in this process.
- Under the right set of conditions, DNA polymerases copy DNA in a test tube just as they do inside cells.
- PCR was invented in 1985.

How are replication and PCR similar? Different? Explain.

PCR is a three-step process.

- PCR requires four materials: DNA, DNA polymerases, large amounts of each of the four DNA nucleotides (A,T,C,G) and two primers.
- A primer is a short segment of DNA that acts as the starting point for a new strand.
- PCR has three major steps:
    1. **Separating**: the container with al of the reactants is heated to separate the DNA into single strands.
    2. **Binding**: the container is cooled and the primers bind to their complementary DNA sequences.
    3. **Copying**: the container is heated again and the polymerases begin to build new strands of DNA.
- Each PCR cycle doubles the number of DNA copies.

Why is it necessary to keep changing the temperature in the PCR process?

DNA Fingerprinting

Objectives: Describe what a DNA fingerprint represents
Summarize how DNA fingerprints are used for identification.

Warm Up: What characteristics of a fingerprint make it useful for identification? What characteristics of DNA might make it useful for identification?

Words to know: DNA fingerprint

A DNA fingerprint is a type of restriction map.

- A DNA fingerprint is a representation of parts of an individual's DNA that can be used to identify a person at the molecular level.
- It is a specific type of restriction map.
- A DNA fingerprint can show relationships between family members or identify people at a crime scene who leave DNA behind.

Does a DNA Fingerprint show a person's genotype? Why or why not?

DNA fingerprinting is used for identification.

DNA Fingerprints and Probability

- Identification with DNA fingerprinting depends on probability.
- Usually DNA fingerprinting compares at least five regions of the genome.
- Because of this comparison, the probability of anyone else outside of a twin having the same sequence of 5 is less than .0001%.

How does identification by DNA fingerprinting depend on probability?

Genetic Engineering

Objectives: Describe how organisms are cloned.
Explain how new genes can be added to an organism's DNA.

Warm Up: Do you think it is ethical to manipulate the DNA of a human being?

Words to know: clone, genetic engineering, recombinant DNA, plasmid, transgenic, gen knockout

Entire organisms can be cloned.

- A clone is a genetically identical copy of a gene or of an organism.
    - Ex: Some plants clone themselves from their roots.
    - Bacteria produce identical genetic copes of themselves through binary fission.
    - Even identical twins are genetic clones of each other.
- To clone a mammal, scientists swap DNA between cells with a technique called nuclear transfer.
    1. An unfertilized egg is taken from an animal and the nucleus is removed.
    2. The nucleus from the animal to be cloned is inserted into the unfertilized egg.
    3. The egg is stimulated so that cell division begins.
    4. After a few days the embryo is implanted into a host mother.
    5. The host mother will eventually give birth to the clone baby.
- In 1997, a sheep named Dolly became the first clone of an adult mammal.
- The success led to the cloning of cows, pigs, and mice and now even household pets.
- The current excitement in cloning is that cloned organs can be used to save lives and can even help save endangered species.
- Cloning also brings controversy:
    1. The success rate in mammals is very low.
    2. Clones are not always as healthy as the original.
    3. Cloning reduces biodiversity.

4. Cloning touches on ethical issues as to whether scientists should play God.

Given the opportunity, would you have a pet cloned? Explain your answer based on your knowledge of genetics, biotechnology and cloning.

New genes can be added to an organism's DNA.

- The changing of an organism's DNA to give the organism new traits is called genetic engineering.
- Recombinant DNA is DNA that contains genes from more than organism.
- Scientists are using recombinant DNA in several different ways.
    1. Produce crop plants that can make medicine and vitamins.
    2. Vaccinations against viruses such as HIV.
- Bacteria are commonly used in genetic engineering because they have NO nucleus and a simple strand of DNA called a plasmid.
- A plasmid is a closed loop of DNA that is separate from the bacterial chromosome and that replicate on their own within the cell.
- The steps to creating recombinant DNA are:
    1. Scientists cut out the desired gene from a strand of DNA.
    2. The plasmids are cut with the same enzyme.
    3. The sticky ends of the DNA are then attached to the plasmid forming recombinant DNA.

How does gentic engineering rely on a shared genetic code?

Genetic engineering produces organisms with new traits.

- After a gene is added to a plasmid, the genetically engineered plasmids can be put into bacteria.
- The bacteria then reproduce that plasmid every time the divide.
- A transgenic organism has one or more genes from another organism into plasmids.
    - Ex: Transgenic bacteria produce insulin that is used by diabetics.

Genetic Engineering in Plants

- Recombinant plants contain traits such as:
    - Resistance to frost
    - Disease resistance
    - Insect resistance
    - Seedless fruits
    - Heartier corn and potatoes

Genetic Engineering in Animals

- These are harder to produce than plants.
- Transgenic traits in animals CAN be passed on to offspring from parents.
    - Transgenic mice are used for cancer research, diabetes and brain function and development.
- Transgenic mice are also used for research in turning off genes.
- Gene knockout mice are used to try to figure out ways to treat genetic diseases.

Concerns about Genetic Engineering

- There are concerns about possible effects of genetically engineered organisms on both human health and the environment.
- There are also basic questions of ethics in regards to genetic engineering.

Why is it important that a transgenic trait is passed on to the transgenic organism's offspring?

Genomics and Bioinformatics

Objectives: Describe genomics.
Identify how technology helps compare and study genes and proteins.

Warm Up: What could scientists do with the knowledge of the base sequence of an entire gene of chromosome?

Words to know: genomics, gene sequencing, Human Genome Project, bioinformatics, DNA microarray, proteomics

Genomics involves the study of genes, gene functions, and entire genomes.

- Genomics is the study of genomes, which can include the sequencing of all an organism's DNA.
- Scientists compare genomes both within and across species to find similarities and differences among DNA sequences.
- Biologists who study evolution can learn when closely related species diverged from each other.

DNA Sequencing

- Gene sequencing is the determining of DNA nucleotides in genes or in genomes.
- It is commonly done now through gel electrophoresis.
- Humans do NOT have the largest genome (most DNA) at 3000 million base pairs.
- Vanilla plants actually have 7672 million base pairs and lungfish 139,000 million base pairs.
- Gene sequencing helps scientists figure out how genes work.

The Human Genome Project

- The Human Genome Project had two major goals:
    1. To map and sequence all of the DNA base pairs of the human chromosomes and
    2. To identify all of the genes within the sequence.
- The first goal was accomplished in 2003.
- Now scientists are working on identifying genes, finding the locations of genes, and determining the functions of gene.
- By doing this, scientists are finding the causes of genetic disorders and, hopefully, cures.

How is genomics related to genes and DNA?

Technology allows the study and comparison of both genes and proteins.

Bioinformatics

- Bioinformatics is the use of computer databases to organize and analyze biological data.
- Powerful computer programs are needed to compare genomes that are billions of base pairs in length, especially if the genomes differ by only a small amount.
- This gives scientists a way to store, share and find data as well as predict future outcomes.

DNA Microarrays

- DNA microarrays are tools that allow scientists to study many genes, and that expression at once.
- A microarray is a small chip that is dotted with all of the genes being studied.
- The genes are laid out in a grid pattern.
- Microarrays help researchers find which genes are expressed in which tissues, and under what conditions.
    - Ex: Microarrays are used to compare gene expression in cancer cells vs. healthy cells.

Proteomics

- Proteomics is the study and comparison of all the proteins that result from an organism's genome.
- Proteomics can show shared evolutionary histories among organisms are studied by comparing proteins across species.

How is bioinformatics a form of data analysis?

Genetic Screening and Gene Therapy

Objectives: Explain how genetic screening can detect genetic disorders.
Describe how gene therapy research seeks to replace faulty genes.

Warm Up: Do you think some knowledge is not worth having?
Words to know: genetic screening, gene therapy

Genetic screening can detect genetic disorders.

- Genetic screening is the process of testing DNA to determine a person's risk of having or passing on a genetic disorder.
- Genetic screening often involves both pedigree analysis and DNA tests.
- It is still not possible to find every genetic defect but as the technology improves the testing gets better.
- Scientists can now detect: breast cancer, cystic fibrosis, and Duchenne's muscular dystrophy.

Why might genetic screening raise ethical concerns about privacy?

Gene therapy is the replacement of faulty genes.

- Gene therapy is the replacement of a defective or missing gene, or the addition of a new gene, into a person's genome to treat a disease.
- One method of gene therapy involves taking bone marrow cells and infecting them with a virus that has been genetically engineered with the new gene.
- That gene is then inserted into the patient and allowed to infect the patient's cells.

How does gene therapy rely on genetic screening?