Molecular Biology: Major Concepts and Learning Activities[1]

Students often do not understand the relationships between processes at the molecular level, genetics, and phenotypic characteristics.[2] This overview reviews Key Concepts and Learning Activities to help students understand how genes influence our traits by molecular processes. To help students understand the relevance of these molecular processes, the suggested Learning Activities discuss how alleles of specific genes influence human characteristics such as albinism, hemophilia, sickle cell anemia, and muscular dystrophy.[3]

Many of the activities presented here are part of a larger integrated sequence of learning activities for teaching genetics; see "Genetics – Major Concepts and Learning Activities", available at https://serendipstudio.org/exchange/bioactivities/GeneticsConcepts.

The overall approach and the recommended learning activities will help students to meet the Next Generation Science Standards (including Disciplinary Core Ideas, Scientific Practices, Crosscutting Concepts and Performance Expectations; http://www.nextgenscience.org/). Activities that are explicitly aligned with the Next Generation Science Standards are indicated by (NGSS) at the end of their descriptions.

Introduction to Proteins and DNA

Key Concepts

- Proteins are responsible for many important aspects of cell structure and function.
- Differences in the structure and function of proteins result in differences in the characteristics of biological organisms.
- Genes in the DNA provide the information necessary for making proteins.

Learning Activities

Introduction to the Functions of Proteins and DNA (available at https://serendipstudio.org/exchange/bioactivities/proteins)

These Teacher Notes present a sequence of discussion and analysis activities that will help students understand that proteins and DNA are not just abstract concepts in biology textbooks, but rather important molecules that have major effects on our bodies' characteristics. Students learn about the functions of proteins and how different versions of a protein can result in different characteristics. Then, students learn that genes in DNA determine which version of a protein is synthesized by a person's cells, and this is how genes influence our characteristics. These concepts are conveyed through a sequence of class discussions, videos, questions in the Student Handout, and an optional hands-on learning activity. This sequence can be used in an introductory unit on biological molecules or to introduce a unit on molecular biology. (NGSS)

[1] By Dr. Ingrid Waldron, Department of Biology, University of Pennsylvania, 2024; available at https://serendipstudio.org/exchange/bioactivities/MolBio

[2] A very useful discussion of key concepts, common misconceptions, and learning activities for molecular genetics is available in Chapter 6 of Hard to Teach Biology Concepts by Susan Koba with Ann Tweed, 2009, NSTA Press.

[3] The Student Handouts and Teacher Notes for the recommended Learning Activities provide background information on albinism, alcohol sensitivity, hemophilia, lactose intolerance, muscular dystrophy and sickle cell anemia.

DNA Structure and Replication

Key Concepts

- DNA is a nucleic acid made of two strands of nucleotides wound together in a spiral called a double helix.
- Each nucleotide is composed of a sugar molecule known as deoxyribose, a phosphate group, and one of four different nitrogenous bases: adenine (**A**), thymine (**T**), guanine (**G**), or cytosine (**C**).
- The phosphate and sugar parts of the nucleotides form the backbone of each strand in the DNA double helix.
- The bases extend toward the center of the double helix, and each base in one strand is matched with a complementary base in the other strand, in accord with the base-pairing rules: **A** pairs with **T** and **G** pairs with **C**.
- These characteristics are the same for the DNA of all organisms. The DNA of different organisms differs in the sequence of nucleotides, and these differences in nucleotide sequence are responsible for the genetic differences between different organisms.
- DNA replication produces two new DNA molecules that are identical to the original DNA molecule. Thus, each of the new DNA molecules has the same genetic information as the original DNA molecule.
- During DNA replication, the two strands of the original DNA double helix are separated and each old strand is used as a template to form a new DNA strand. The enzyme DNA polymerase adds nucleotides one-at-a-time, using the base-pairing rules to match each nucleotide in the old DNA strand with a complementary nucleotide in the new DNA strand. Thus, each new DNA double helix contains one strand from the original DNA molecule, together with a newly synthesized matching DNA strand.

Learning Activities

"**DNA Structure, Function and Replication**" is an analysis and discussion activity, available at https://serendipstudio.org/exchange/bioactivities/DNA. This analysis and discussion activity can be used to introduce your students to key concepts about the structure, function, and replication of DNA or to review these topics. Students learn how the genes in DNA give the instructions to make proteins, which influence our characteristics. They also learn how the double helix structure of DNA and the base-pairing rules provide the basis for DNA replication. This activity includes hands-on modeling of DNA replication. (NGSS)

or

"**DNA**" is a hands-on activity, available at https://serendipstudio.org/exchange/waldron/dna. In this activity, students extract DNA from Archaea or from their cheek cells. In addition, students learn or review key concepts about the structure, function, and replication of DNA. Students learn how the genes in DNA give the instructions to make proteins, which influence our characteristics. They also learn how the double helix structure of DNA and the base-pairing rules provide the basis for DNA replication. This activity includes multiple analysis and discussion questions and hands-on modeling of DNA replication. (NGSS)

The Molecular Biology of How Genes Influence Traits – Transcription and Translation

Key Concepts

A gene influences our phenotype by determining the sequence of amino acids in a protein which determines protein structure and function which in turn influences our characteristics. For example, different versions of the gene for hemoglobin (normal vs. sickle cell alleles) result in the production of normal vs. sickle cell hemoglobin, and sickle cell hemoglobin can result in sickle cell anemia. The nucleotide sequence in a gene specifies the amino acid sequence in a protein by the molecular processes of transcription and translation.

nucleotide sequence in the DNA of a **gene**

→ nucleotide sequence in messenger RNA (mRNA)
transcription

→ amino acid sequence in a protein
translation

→ structure and function of the protein
(e.g. normal hemoglobin vs. sickle cell hemoglobin)

→ person's **characteristics** or **traits**
(e.g. normal health vs. sickle cell anemia)

Transcription is the process that copies the message in a gene into a messenger RNA (mRNA) molecule that provides the instructions for making a protein molecule. The sequence of nucleotides in a gene in the DNA is copied into a corresponding sequence of nucleotides in the mRNA molecule. Each mRNA nucleotide is complementary to the corresponding DNA nucleotide (**C** pairs with **G** and **A** pairs with **T** (in DNA) or **U** (in RNA) in accord with the base-pairing rules). To make the mRNA molecule, the enzyme RNA polymerase adds the complementary nucleotides one-by-one to the growing mRNA molecule, using the base-pairing rules.

mRNA carries the genetic message from the nucleus to the ribosomes where polypeptides are synthesized. Each mRNA molecule codes for the sequence of amino acids in a polypeptide, and the polypeptide folds (and sometimes combines with one or more other polypeptides) to form a protein. The sequence of amino acids determines the structure and function of the protein.

Translation is the process that makes proteins. In the process of translation, the sequence of nucleotides in an mRNA molecule specifies the sequence of amino acids in a polypeptide. Each triplet codon in the mRNA codes for a specific amino acid in the polypeptide. The ribosome adds amino acids one-by-one to the growing polypeptide in accord with the instructions from the codons in the mRNA molecule.

During translation, each codon in the mRNA molecule is matched by the base-pairing rules to an anti-codon in a tRNA molecule. Different types of tRNA molecules with different anti-codons bring the right amino acids for each position in the polypeptide as the polypeptide is synthesized by the ribosome. For each type of tRNA, there is a specific enzyme that attaches the correct amino acid to match the anti-codon in that type of tRNA molecule. These processes are the

molecular embodiment of the genetic code which specifies which amino acid is inserted for each codon in the mRNA molecule.

Learning Activities

How Genes Can Cause Disease – Introduction to Transcription and Translation
https://serendipstudio.org/sci_edu/waldron/#trans
To begin this hands-on, minds-on activity, students learn about hemophilia. They learn that different versions of a gene give the instructions for making different versions of a protein, which result in hemophilia or normal health. Then, students learn how genes provide the instructions for making a protein via the processes of transcription and translation. They develop an understanding of the roles of RNA polymerase, the base-pairing rules, mRNA, tRNA and ribosomes. Then, students use their understanding of transcription and translation to explain how a change in a single nucleotide in the hemoglobin gene can result in sickle cell anemia. Finally, students use their understanding of translation to develop a partial explanation of how the coronavirus replicates inside our cells. Throughout, students use the information in brief explanations, videos and figures to answer analysis and discussion questions. In addition, students use simple paper models to simulate the processes of transcription and translation. (NGSS)

How Genes Can Cause Disease – Understanding Transcription and Translation is an analysis and discussion version of the above activity. (NGSS)

The Molecular Biology of Mutations and Cell Differentiation

Key Concepts

- A mutation is a permanent change in the DNA.
- DNA molecules experience frequent changes due to environmental factors (e.g. radiation) and intrinsic processes (e.g. errors in replicating DNA). DNA repair mechanisms reverse most of these DNA changes so the changes do not become permanent mutations and the accuracy of the genetic code is maintained.
- A change in a single nucleotide is a point mutation. Some point mutations result in a change in a single amino acid in the polypeptide produced by transcription and translation of the gene. Other point mutations change a codon to another codon for the same amino acid, resulting in no change in the amino acid sequence of the polypeptide. In other cases, a point mutation results in a stop codon which terminates translation and can result in a drastically shortened, nonfunctional protein.
- If a deletion mutation results in the deletion of any number of nucleotides that is not a multiple of 3, this causes a frameshift during translation of the mRNA. Every codon after this frameshift is changed, which usually results in the production of a nonfunctional protein. In contrast, a deletion mutation that results in the deletion of three nucleotides or a multiple of three nucleotides from the mRNA molecule will have less severe consequences since there is no frameshift and the subsequent codons will not be affected. This same frameshift rule applies to the effects of insertion mutations.
- During cell differentiation, cells acquire the specialized characteristics of each different type of cell. Transcription factors recruit RNA polymerase and induce epigenetic changes to activate transcription of the relevant genes to produce the proteins needed for the specialized structure and function of that type of cell.

Learning Activities:
As described above, both versions of our transcription and translation activity have a section about how the single nucleotide difference between sickle cell and normal hemoglobin alleles results in sickle cell vs. normal hemoglobin proteins and how sickle cell hemoglobin can result in sickle cell anemia:

- **How Genes Can Cause Disease – Introduction to Transcription and Translation** is a hands-on simulation activity (NGSS) or
- **How Genes Can Cause Disease – Understanding Transcription and Translation** is an analysis and discussion activity. (NGSS)

What types of mutations cause more vs. less severe muscular dystrophy?
https://serendipstudio.org/exchange/bioactivities/mutation
This analysis and discussion activity begins with a brief video about a teenager who has Duchenne muscular dystrophy. Then, students investigate the types of deletion mutation that cause the more severe Duchenne muscular dystrophy vs. the milder Becker muscular dystrophy. During this analysis, students review basic molecular biology, learn how to use a codon wheel, and analyze the molecular effects of different types of deletion and point mutations. Finally, students investigate X-linked recessive mutations to understand why almost all Duchenne muscular dystrophy patients are male. (NGSS)

UV, Mutations, and DNA Repair
https://serendipstudio.org/exchange/waldron/uvmutations
In this hands-on activity students learn about the effects of UV light, mutations and DNA repair on the survival of prokaryotes and the risk of skin cancer. In the first experiment, students evaluate the effects of different durations of UV exposure on survival and population growth of *Haloferax volcanii*. This experiment also tests for photorepair of DNA damage. Students design the second experiment, which evaluates the effectiveness of sunscreen. In addition, students answer analysis and discussion questions that promote their understanding of molecular biology, cancer, and the interpretation of experimental results. (NGSS)

Why and How Your Body Makes Millions of Red Blood Cells Every Minute
https://serendipstudio.org/exchange/bioactivities/RedBloodCells
In this activity, students learn about stem cells, cell differentiation, and how transcription factors contribute to cell differentiation. These concepts are introduced as students learn how the body makes red blood cells and answer multiple minds-on questions.

Genetic Engineering

Genetic engineering learning activities can be used to reinforce student understanding of molecular biology and to introduce students to practical applications of molecular biology.

Key Concepts covered in the two recommended Learning Activities

- Genes code for proteins (including enzymes). The genetic code is universal. Transcription of genes is the first step in producing proteins.
- (Almost) all the cells in an organism have the same genes in their DNA, but different types of cells have different amounts of specific proteins. These different proteins contribute to the different characteristics and functions of the different types of cells.
- Differences in the rate of transcription of specific genes are a major cause of the differing amounts of specific proteins in different types of cells.

- Promoters at the beginning of each gene play a crucial role in regulating the rate of transcription of each gene in different types of cells.
- Genetic engineering often makes use of bacterial molecular capabilities. For example, scientists have used the natural genetic engineering capabilities of a bacterium to insert genes that make pro-vitamin A in rice grains.
- Recent advances in genetic engineering make use of a bacterial defense against viruses. For example, gene editing by the CRISPR-Cas9 system has been used to treat severe sickle cell anemia.

Learning Activities

"Genetic Engineering Challenge – How can scientists develop a type of rice that could prevent vitamin A deficiency?" is an analysis and discussion activity, available at https://serendipstudio.org/exchange/bioactivities/geneticengineer. This analysis and discussion activity begins with an introduction to vitamin A deficiency and a review of transcription, translation, and the universal genetic code. Several questions challenge students to design a basic plan that could produce a genetically engineered rice plant that makes rice grains that contain pro-vitamin A. Subsequent information and questions guide students as they learn how scientists use bacteria to insert desired genes, together with an appropriate promoter, in the DNA of plant cells. In a final optional section, students evaluate the pro and con arguments in the controversy concerning Golden Rice. (NGSS)

Gene Editing with CRISPR-Cas – A Potential Cure for Severe Sickle Cell Anemia is available at https://serendipstudio.org/exchange/bioactivities/GeneEdit. This analysis and discussion activity introduces Victoria Gray whose severe sickle cell anemia was effectively treated by experimental gene editing with CRISPR-Cas. To begin, students review the molecular biology of sickle cell anemia. Next, they learn how bacteria use CRISPR-Cas to defend against viral infections. Then, students review the multiple research findings that scientists used to identify the target for gene editing, and they analyze the CRISPR-Cas gene editing treatment for sickle cell anemia. Finally, students consider ethical controversies related to the use of CRISPR-Cas. (NGSS)

Additional Molecular Biology Learning Activities

Learn Genetics (available at https://learn.genetics.utah.edu/content/basics/) offers a wide variety of learning resources relating to genetics, mutations, chromosomes, DNA, RNA, and transcription and translation.

Discovering the Genome (available at https://discoveringthegenome.org/resources-introduction-genomics) offers resources for learning about genomics, including DNA sequencing and bioinformatics.

A "Molecular Biology Vocabulary Review Game" is available at https://serendipstudio.org/exchange/bioactivities/molbiovocab. This game helps students to enjoy reviewing vocabulary related to DNA and RNA structure and function, transcription and translation.

Using Molecular and Evolutionary Biology to Understand HIV/AIDS and Treatment is available at https://serendipstudio.org/exchange/bioactivities/HIV. This analysis and discussion activity introduces students to the biology of HIV infection and treatment, including the molecular biology of the HIV virus lifecycle and the importance of understanding molecular biology and

natural selection for developing effective treatments. The questions in this activity challenge students to apply their understanding of basic molecular and cellular biology and natural selection and interpret information presented in prose and diagrams in order to understand multiple aspects of the biology of HIV/AIDS and treatment. (NGSS)

Additional Information

There are many important aspects of molecular biology that are ignored in the Key Concepts and Learning Activities presented above. Some important additional points are as follows.

In eukaryotic cells, transcription produces a primary RNA transcript or pre-mRNA molecule. This pre-mRNA molecule contains regions that code for the amino acid sequence in a polypeptide (exons) interspersed with regions that do not (introns). The pre-RNA must be spliced to remove introns in order to produce mRNA. Alternative splicing of different combinations of exons to form different mRNA molecules allows a single gene to code for several different polypeptides.

Proteins are formed when a polypeptide folds into a characteristic shape (and in some cases combines with other folded polypeptides). (Some proteins have a flexible shape with at least some regions that are often unfolded.)

The alleles discussed in the recommended Learning Activities on transcription and translation and mutation differ in the nucleotide sequence in the coding DNA. For example, the alleles for normal vs. sickle cell hemoglobin differ in a single nucleotide in the coding DNA. In contrast, some alleles differ in the nucleotide sequence in the regulatory DNA. For example, lactose intolerance is due to differences in the sequence of nucleotides in the regulatory DNA for the gene that codes for lactase; the lactose intolerance allele results in production of lactase by infants, but not adults, whereas the lactase persistence alleles result in production of lactase from infancy through adulthood.

The definition of a gene has changed over time. The classical definition of a gene was a discrete unit of inheritance that affects a phenotypic character. One molecular biology definition of a gene is a segment of DNA that codes for mRNA which in turn codes for a sequence of amino acids in a polypeptide. More recent molecular biology definitions of a gene take into account introns as well as exons, the importance of regulatory DNA, and also the fact that some genes code for ribosomal RNA, tRNA or other types of RNA that are not translated into a polypeptide. There is no single universally agreed-upon definition of a gene at this time. The changing definition of a gene illustrates the constantly evolving nature of science as scientists develop progressively more sophisticated understanding of concepts such as the gene. For additional information about the challenges and complexities of defining a gene, see http://www.biologyreference.com/Fo-Gr/Gene.html.

Help Me Understand Genetics (https://ghr.nlm.nih.gov/primer#howgeneswork) provides clear and accurate explanations of many aspects of molecular biology, genetics and health.