

Science Take-Out: From DNA to Protein Structure and Function

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Vocabulary:

Transcription: DNA → RNA; During transcription, a DNA sequence is read by an RNA polymerase, which produces a complementary, antiparallel RNA strand. The RNA complement includes uracil (U) in all instances where thymine (T) would have occurred in a DNA complement.

Translation: RNA → Protein; In translation, messenger RNA (mRNA) produced by transcription is decoded by the ribosome to produce a specific amino acid chain, or

polypeptide, that will later fold into an active protein.

RNA: Ribonucleic acid is one of the three major macromolecules (along with DNA and proteins) that are essential for all known forms of life. Like DNA, RNA is made up of a long chain of components called nucleotides. Each nucleotide consists of a nucleobase, a ribose sugar, and a phosphate group. RNA directs the synthesis of proteins.

Genotype: The genotype is the genetic makeup of

a cell, an organism, or an individual (i.e. the specific allele makeup of the individual). The genotype of an organism is the inherited instructions it carries within its genetic code.

Phenotype: A phenotype is the composite of an organism's observable characteristics or traits. Phenotypes result from the expression of an organism's genes as well as the influence of environmental factors and the interactions between the two.

? KEY QUESTION(S):

- How does a mutation at the DNA level affect the protein structure and function?

🕒 TIME ESTIMATE:

- Advanced Preparation: 30 minutes
- Student Procedure: 45 minutes

🎯 LEARNING STYLES:

- Visual and kinesthetic.

Lesson Summary:

With a commercially available kit from Science Take-Out, students step through the process of transcribing and translating a DNA sequence. Using the student worksheet provided here, students then consider how the acid phosphatase gene is affected by mutations and how the change in structure affects the function of the enzyme.

Student Learning Objectives:

The student will be able to...

1. Discuss observed inheritance patterns caused by recessive mode of inheritance
2. Describe the basic process of DNA replication and the transmission of genetic information
3. Explain how mutations in the GAA gene may or may not result in phenotypic change
4. Model the basic processes of transcription and translation and how they result in the expression of the GAA gene to produce a protein
5. Explain how and why the genetic code is universal and is common to almost all organisms



Genetic diseases are caused by negative mutations and can be passed along from one generation to the next. Pompe is an example of a genetic disease.

6. Describe the basic molecular structures and primary functions of DNA and proteins (biological macromolecules)
7. Construct proteins and amino acids structures. Explain the functions of proteins in living organisms. Relate the structure and function of enzymes.
8. Explain the role of enzymes.
9. Describe the function of models in science.

Standards:

See table on page 11-13.

SC.912.L.14.6	SC.912.L.16.4	SC.912.L.18.1	SC.912.N.1.6
SC.912.L.16.2	SC.912.L.16.5	SC.912.L.18.4	SC.912.N.3.5
SC.912.L.16.3	SC.912.L.16.9	SC.912.L.18.11	

Materials:

- Science Take-Out: *From DNA to Protein Structure and Function*, 1 kit per student group (recommend pairs)

Description	Source	Catalog #	Price
From DNA to Protein Structure and Function	Science Take-Out www.sciencetakeout.com	STO-106 (individual assembled kit)	1 assembled kit: \$8
		STO-106U (unassembled classroom sets)	1 pk of 10 unassembled kits: \$38 <i>(bulk discounts available)</i>

Background Information:

DNA is sometimes referred to as the blueprint of life. It holds the letters that code for almost all life on earth. Because DNA is so important, it has several proofreading and editing mechanisms in place to avoid errors as it replicates itself millions of times. However, occasionally there are mistakes. Those mistakes or mutations, changes in the DNA sequence, can lead to very different outcomes. Some are neutral. They occur in a region that does not affect the subsequent protein or the base change does not alter the amino acid codon. Some are beneficial. They cause a new protein to be made or alter the regulation of an existing protein, perhaps enabling the organism to gain an advantage in their environment. The ones we usually hear about however, are those that have a negative effect on the organism. Genetic diseases are caused by negative mutations and can be passed along from one generation to the next. Pompe is an example of a genetic disease.

In the case of Pompe disease, the acid alpha-glucosidase gene is damaged resulting in a protein that does not function correctly. There have been over 300 mutations identified to date, some with more devastating effects than others. A great deal of research is taking place to catalog the mutations and track potential correlations between genotype and phenotype. Some mutations are obviously deleterious, such as null mutations which prevent the amino

acids from being translated therefore no functioning protein is made. These mutations are predictive of early onset and the most severe form of Pompe disease.

In this lesson, students will practice the process of transcribing a sequence of DNA. Using complementary base pairing rules, substituting the RNA version of thymine, uracil, they will create the new single stranded RNA sequence. Since this RNA actually codes for a protein, it is mRNA and referred to as a transcript. Using the universal genetic code, three letter mRNA codons are translated into an amino acid chain. Amino acids have different chemical properties; they are hydrophobic or hydrophilic, acidic or basic. As the amino acid chain is folded into secondary, tertiary, and then a quaternary structure, the chemical properties of each amino acid affects the confirmation. Correct folding is crucial for enzymatic function.

Implementation Note: As written, the Science Take-Out Kit uses sickle cell disease and mutant hemoglobin as the protein example in part C to demonstrate a change in DNA can result in a change in protein structure and therefore function. This part has been modified in this curriculum to fit Pompe disease and GAA protein.

Advance Preparation:

- Use preparation guide in the Science Take-Out kit.
- Copy student pages from Science Take-Out for each student, substituting Section C with the pages below.

Procedure:

- Have students work in pairs.
- Follow procedure for part A of Science Take-Out kit. Optional: Part B can be completed for homework or as time allows in class. Substitute Part C below, which is adapted for Pompe.

Assessment Suggestions:

- Student worksheet can be used for assessment.

RESOURCES/REFERENCES:

Science Take-Out: *From DNA to Protein Structure and Function* Catalog# STO-106 (individual assembled kit) and STO-106U (unassembled classroom sets)

Transcription video: <http://www.youtube.com/watch?v=WsofH466lqk>

Transcription video: <http://www.youtube.com/watch?v=5MfSYnltYvg&feature=related> (DNA Learning Center) also at <http://www.dnalc.org/resources/3d/index.html>

Translation video: <http://www.youtube.com/watch?v=8dsTvBaUMvw&feature=relmfu> (DNA Learning Center) also at <http://www.dnalc.org/resources/3d/index.html>

Transcription/translation video from PBS: http://youtu.be/41_Ne5mS2ls



EXTENSIONS:

Activities

MSOE lending library – <http://cbm.msoe.edu/> has an amino acid starter kit that allows students to look closer at each amino acid <http://cbm.msoe.edu/teachRes/library/ak.html>

Transcription/translation 3D animations from DNA Learning Center: <http://www.dnalc.org/search?q=transcription>

Transcription/translation interactive animation from Utah (Learn Genetics) <http://learn.genetics.utah.edu/content/begin/dna/transcribe/> and

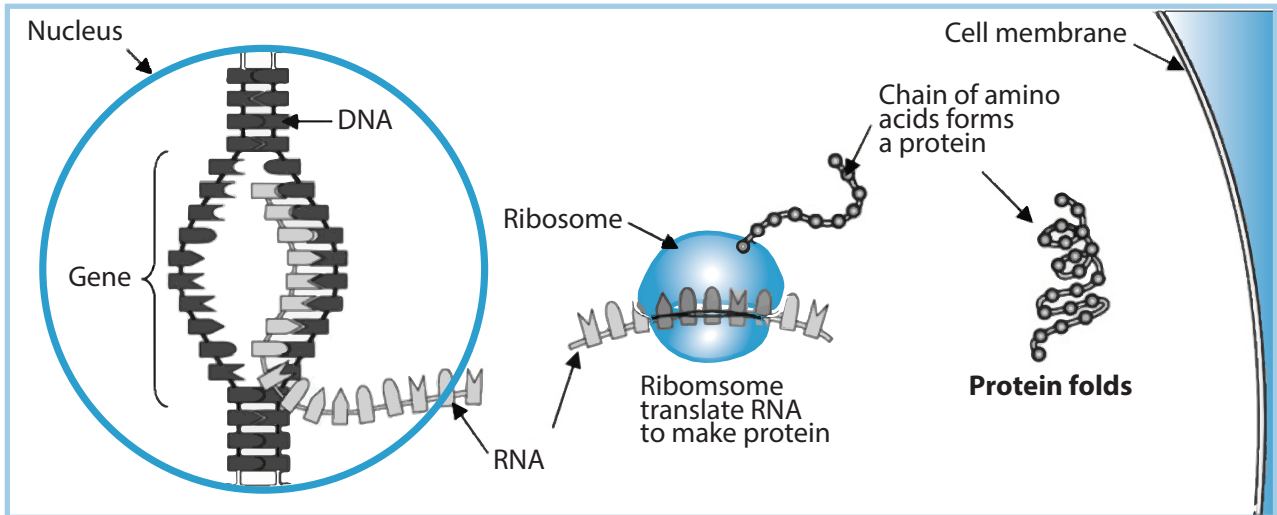
DNA to Protein: <http://learn.genetics.utah.edu/content/begin/dna/>

Literature

The National Institutes of Health *Structures of Life*, available in html, pdf, or print provides good background information about the role and importance of proteins. Chapter One is particularly relevant to this lesson. <http://publications.nigms.nih.gov/structlife/index.html>. May want to consider giving as reading homework prior to starting Lesson Four or as a review after the assignment.



Science Take-Out: From DNA to Protein Structure and Function



The nucleus of every cell contains chromosomes. These chromosomes are made of DNA molecules. Each DNA molecule consists of many genes. Each gene carries coded information for how to make one type of protein.

Your body makes many different kinds of proteins. Every protein in your body has a specific shape. It is this specific shape that allows each protein to perform a specific job. The combination of specific proteins that your body makes gives you your traits.

During protein synthesis, DNA is copied in the nucleus to make RNA. The RNA then moves to the cytoplasm where it attaches to a ribosome. The ribosome translates the coded information from the RNA to create a protein molecule with a specific sequence of amino acids. The protein folds into a particular shape that enables it to perform a specific function.

To help you understand how proteins are produced and how they function, you will model the processes of protein synthesis and protein folding.

YOUR TASKS:

- Model the processes of protein synthesis and protein folding.
- Relate the three dimensional (3-D) shape of proteins to their functions.

A. Modeling Protein Synthesis and Protein Folding

1. Use the **From DNA to Protein – Record Sheet** in your lab kit. The illustration in Step A of this worksheet represents a small part of the DNA code in a gene that carries instructions for making one kind of protein.
2. DNA molecules and genes cannot leave the nucleus. To carry the instructions to the ribosomes (protein factories) in the cytoplasm, the coded information in a gene (DNA) base sequence is transcribed (copied) to make messenger RNA (mRNA) molecules with complementary (opposite) base sequences.
3. Use the base pairing chart below to determine the base sequence code on the mRNA that would be produced when the DNA molecule is transcribed to make mRNA. The first few mRNA bases have been provided as samples. Write your answer on the mRNA line on the diagram (**Step B of your worksheet**).

Base on DNA	Complementary Base on mRNA
A	U
T	A
G	C
C	G



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4. The mRNA then leaves the nucleus and attaches to a ribosome in the cytoplasm. In the ribosome, the mRNA base sequence is translated to determine the sequence (order) of amino acid building blocks in a protein.
5. Use the mRNA base sequence on your diagram and the genetic code chart provided to translate the mRNA code into a sequence of amino acid building blocks in a protein (also called a polypeptide). Each amino acid will be represented by a circle. The colors for the amino acids (yellow, blue, red or white) are indicated on the genetic code chart.
 - Write the name of the amino acids in the protein in the box above the circle (Step C of your Record Sheet).
 - Color each circle with the appropriate color as shown in the example. If you do not have colored pencils, you may write the color in the space below each of the circles.
6. Proteins are made of amino acids hooked end-to-end like beads on a necklace. To simulate a protein, you will make a model of your protein using a long chenille stem (the fuzzy covered wire) and colored beads. Refer to the sequence of 15 amino acids (the colored circles on Step C of your Record Sheet) and arrange beads of the appropriate colors on the chenille stem. The beads should be approximately evenly spaced the along the chenille stem.
7. The model that you have created represents the unfolded, primary structure of a protein –which is the sequence of amino acids in a protein.
8. Proteins do not remain straight and orderly. They twist and buckle, folding in upon themselves to form 3-dimensional (3-D) shapes. Twist one half of your protein model around a pencil to make a spiral. This spiral region is called an “alpha-helix.”
9. Bend the other half of your protein molecule into a zig-zag shape by making a bend in the opposite direction at each bead. This zig-zag region is called a “beta-pleated sheet.”
10. The alpha-helix and beta-pleated sheet represent the secondary structure of a protein. Make a drawing to show the secondary structure of your protein model (Step D of your Record Sheet). Label the alpha helix region and the beta-pleated sheet region on your drawing.
11. Twist your protein into a 3-D shape according to these protein folding rules:
12. The resulting twisted structure is called the tertiary structure of a protein. Make a drawing to show the tertiary structure of your protein model (Step D of your Record Sheet). Note: Do the best you can to make your 2-dimensional drawing look like your 3D model.
13. Some protein chains are attracted to other protein chains. Work with a partner group and try putting your protein model next to their protein model in a way that still follows the rules of protein folding. This represents the quaternary structure of a protein.
14. Make a drawing to show the quaternary structure of your protein model (Step D of your Record Sheet).

Amino Acid (Bead) Color (based on chemical properties)	Protein Folding Rules
Yellow	These are fatty <u>hydrophobic</u> (water fearing) amino acids that should be clustered on the inside of the protein.
Blue	These are <u>negatively charged</u> basic amino acids that are attracted to red (positively charged) amino acids on the protein.
Red	These are <u>positively charged</u> acidic amino acids that are attracted to blue (negatively charged) amino acids on the protein.
White	These are <u>hydrophilic</u> (water loving) amino acids that should be clustered on the outside of the protein.



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B. From DNA to Protein – Record Sheet

Step A. Here is the sequence of bases in the DNA code for part of a gene DNA molecule

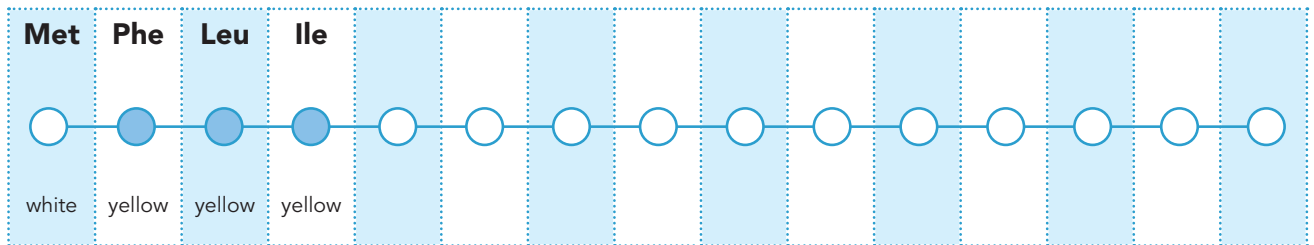
TAC	AAA	GAA	TAA	TGC	ATA	ACA	TTT	CAA	ACC	TCA	TCG	TTA	CTC	CCT
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Step B. Transcribe the DNA and write the sequence of bases in the mRNA code RNA molecule

AUG	UUU	CUU	AUU											
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Step C. Translate the mRNA and write the sequence of amino acids in the protein. Indicate the color associated with each of the amino acids in the circle below.

Sequence of amino acids in protein – the primary structure of your protein model



Step D. Fold your protein model into a 3-D shape.

Draw the secondary structure of your protein model	Draw the tertiary structure of your protein model	Draw the quaternary structure of your protein model



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C. From DNA to Protein – Application To GAA

Acid alpha-glucosidase (GAA) is a protein molecule found in lysosomes. GAA processes excess glycogen being stored in the lysosome and converts it to smaller components of glucose. Pompe disease is a primarily a muscular disease caused by a build-up of glycogen in the lysosomes. If lysosomes cannot break glycogen down, they swell, displacing surrounding muscle cells. Additionally, the lysosomes can burst, releasing acidic components to the surrounding area and destroying muscle tissue. People with Pompe disease inherit a mutation in the DNA base code that carries the information for how to make the GAA protein. This DNA mutation leads to a change in the sequence of the amino acids for GAA. In Pompe disease, one amino acid in the GAA protein is incorrect.

1. To model the effect of a change in the amino acid sequence of a protein, replace one of the yellow beads on your protein molecule with a red bead. Follow the “protein folding rules” on page 2 to refold your protein model.
2. How does changing the amino acid sequence on your model affect the protein model?

The change in the shape in the GAA protein compromises the enzymatic function of the protein. Since enzymes have a particular shape and fit together with specific compounds, if the shape of the enzyme is altered, it will not be able to function properly.

3. Explain how the change in enzyme function affects the structure and function of lysosomes.
4. Explain how the change in lysosome structure and function results in the symptoms of Pompe disease.
5. Arrange the following phrases in order to indicate the sequence of events that would occur as a result of a gene mutation in the gene that codes for the protein acid alpha-glucosidase (GAA).
 - ___ Gene mutation (change in the DNA code in the gene for GAA)
 - ___ Change in the mRNA code
 - ___ Change in the amino acid sequence of the GAA protein
 - ___ Change in the structure or function of body cells or tissues
 - ___ Change in the shape of a GAA protein
 - ___ Change in the ability of the GAA protein to function properly
 - ___ Change in characteristics and symptoms of a genetic disease



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1. To model the effect of a change in the amino acid sequence of a protein, replace one of the yellow beads on your protein molecule with a red bead. Follow the "protein folding rules" on page 2 to refold your protein model.

2. How does changing the amino acid sequence on your model affect the protein model?

Changes folding since different amino acids have different properties (i.e., attracted vs repelled) which then alters the shape or 3D structure of the protein

The change in the shape in the GAA protein compromises the enzymatic function of the protein. Since enzymes have a particular shape and fit together with specific compounds, if the shape of the enzyme is altered, it will not be able to function properly.

3. Explain how the change in enzyme function affects the structure and function of lysosomes.

The GAA enzyme is unable to break down glycogen in the lysosomes, causing glycogen to build up in the lysosome. As lysosomes become large and filled w/glycogen, the function of the entire cell is compromised.

4. Explain how the change in lysosome structure and function results in the symptoms of Pompe disease.

The growing lysosome displaces muscle cells. As the number of healthy muscle cells decreases, the integrity of the muscle tissue deteriorates, resulting in reduced muscle function. The compromised skeletal and cardiac muscles result in cardiac, diaphragm, and large motor movement difficulties.

5. Arrange the following phrases in order to indicate the sequence of events that would occur as a result of a gene mutation in the gene that codes for the protein acid alpha-glucosidase (GAA).

1 Gene mutation (change in the DNA code in the gene for GAA)

2 Change in the mRNA code

3 Change in the amino acid sequence of the GAA protein

6 Change in the structure or function of body cells or tissues

4 Change in the shape of a GAA protein

5 Change in the ability of the GAA protein to function properly

7 Change in characteristics and symptoms of a genetic disease