Genes, Mutations and Diseases: Understanding the Origins of Genetic Disorders through Experiential Learning

A five week series of lessons and experiments designed for cohesiveness as unit, but can be done invidually.

Unit Product of ASBMB HOPES 2013 Grant by:
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Unit Table of Contents

www.asbmb.org/912activity/

ASBMB American Society for Biochemistry and Molecular Biology

SJU

Genes, Mutations and Diseases: Understanding the Origins of Genetic Disorders through Experiential Learning

Lesson 2

Transcription, Translation and Mutations

Overview

The last lesson explained that genes are segments of DNA. This activity continues looking at DNA to answer, how are genes expressed? DNA is first transcribed into RNA then translated into proteins. Mutations in DNA may alter the protein, which can have large impacts on structure and function, evidenced here by red blood cells in sickle cell anemia.

Quick Guide and Materials:

- **Age Range:** High School
- **Preparation Time:** ~ 2 hours
- **In Class Time:** ~ 1.5 hours
- **Duration:** 1 week
- **Materials List:** Nucleotide molecule kits, microscopes and slides of normal and sickle cell blood smears

www.asbmb.org/912activity/lffj/lesson2

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Activity Outline

Sequence	Activity	Timing
A.	Lecture Slides 1-8	10 min
B.	Transcription (Slide 9)	10 min
C.	Lecture Slides 10-14	10 min
D.	Translation (Slide 15)	10 min
E.	Lecture Slide 16-20	10 min
F.	Microscopy (Slide 21)	25 min

Activity Breakdown Below

Materials

Nucleotide Molecule Kit

Laboratory Preparation for 6 kits - 3 Normal sequences (N-kits) and 3 Mutant/Sickle sequences (S-kits). If doing as a whole unit, only need enough to make RNA

- 18 strands of 4 ft pom-pom garland (michaels.com cat#10241838) (to represent backbone – sugar and phosphate)
- 306 1.5 in (38 mm) styrofoam balls (to represent nitrogenous base)
- 204 magnets (carolina.com cat# 955013))
- 408 safety Pins (to represent phosphodiester bonds)
- Green paint (to indicate phosphate group)
- Sharpie to label Styrofoam balls.

Microscopy Activity

- Microscopes
- Slides of normal blood smear (carolina.com cat# 313158)
- Slides of sickle cell anemia blood smear (carolina.com cat# 317374)

Microscopes- Compound microscopes can be purchased new, but you can also find much cheaper, used microscopes on websites like ebay.

Lecture Slides and Handouts

Lecture Material

Lecture- How are genes expressed?

The first step in protein synthesis is the synthesis of ribonucleic acid (RNA) using the gene's DNA sequence as a template. This process of DNA -> RNA is known as transcription. Translation is the process by which a polypeptide (a subunit of a protein) is formed. The genetic code in the mRNA's codons determines the placement of amino acids (the building blocks of proteins). A mutation is any change, no matter how minor, to a DNA sequence. Example found at: www.asbmb.org/912activity/

Handouts

Printable handouts contain protocols, pictures, questions for student during the experiment and further explanation of the science behind certain steps.

Instructor manual found at:
www.asbmb.org/912activity/
(contains answer key and reference pictures)
Printable student lab instructions/notebook is found at: www.asbmb.org/912activity/

Sickle Cell Anemia is a genetic disorder that results in the abnormally shaped red blood cells. In sickle cell patients, a mutation is found in the DNA that results in improperly produced hemoglobin protein in the red blood cells.

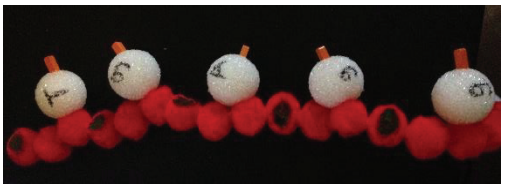
Transcription and Translation

Preparation of Nucleotide Molecule Kits

Each kit contains: 1 DNA Template Strand, 17 DNA nucleotides, 17 RNA nucleotides in a container. Entire kit should be "N" or "S." ***Note, if doing entire unit, only need to make RNA nucleotides now as DNA Template and nucleotides were made in the last activity*

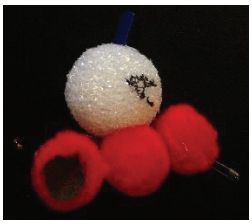
DNA Template strand

1. Take a strand of pom-pom garland and lay it out on a table.
2. At every third pom-pom in the garland, glue on a Styrofoam ball (need to get 17 balls onto the garland).
3. Glue one magnet onto each styrofoam ball
4. Paint the first pom-pom green. Then repeat at every third pom-pom.
5. Once everything is dried, write in the following sequence in order:
   - For N-kit strands: T-G-A-G-G-A-C-T-C-C-T-C-T-T-C-A-G
   - For S-kit strands: T-G-A-G-G-A-C-A-C-C-T-C-T-T-C-A-G
6. When you finish, should have the following (picture is showing a portion of the template sequence).



DNA Nucleotides (17 nucleotides per kit)

1. Take a strand of pom-pom garland and cut it after every third pom-pom.
2. Glue a styrofoam ball onto the middle pom-pom
3. Glue one magnet onto each styrofoam ball
4. Paint the first pom-pom green.
5. Add a safety pin to the pom-poms on each end.
6. Once everything is dried, write on the styrofoam ball one of the four nitrogenous bases as needed:
   - For N-kit strands: A, C, T, C, C, T, G, A, G, G, A, G, A, A, G, T, C
   - For S-kit strands: A, C, T, C, C, T, G, T, G, G, A, G, A, A, G, T, C
7. When you finish, you should have the following (picture is showing one nucleotide)



RNA Nucleotides (17 nucleotides per kit)

1. Follow same procedure as you did with DNA nucleotides, except, do not add a magnet to the stytrofoam ball.
2. Once everything is dried, write on the styrofoam ball one of the four nitrogenous bases as needed:
   - For N-kit strands: A, C, U, C, C, U, G, A, G, G, A, G, A, A, G, U, C
   - For S-kit strands: A, C, U, C, C, U, G, U, G, G, A, G, A, A, G, U, C

Transcription

Models in science are used to describe ideas, understand biological processes and make predictions.
Objective: Build a model to learn about transcription

In groups, work to build a model of transcription. The magnets and safety pins will serve as the hydrogen and phosphodiester bonds, respectively.

1. Build a model of DNA based on the DNA template. The magnets and safety pins will serve as the hydrogen and phosphodiester bonds, respectively.
2. Unwind the DNA molecule.
2. Looking at the DNA template strand, build the RNA that corresponds to your DNA molecule. The safety pins will serve as the phosphodiester bonds of the RNA backbone.

Translation

Translate the mRNA just synthesized using the genetic code.

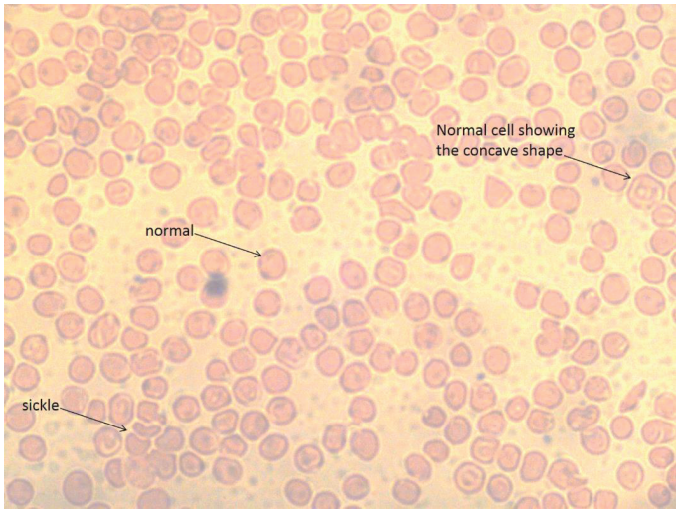
Using mRNA as a template, translate the mRNA into the proper polypeptide chain.

1. Write out the polypeptide (amino acid sequence).
2. Examine the other group's polypeptides. Does each group have the same polypeptide?
3. If a group does not have the same polypeptide, write down the polypeptide they constructed.
4. Examine the differences in DNA and RNA to see why the polypeptides are different between groups.

Microscopy

Using sickle cell anemia as an example, how do genetic mutations affect the structure and function of the proteins they encode?

1. Examine the blood smears of a normal and sickle cell patient. Record observations of the shape of normal blood cells and sickle cells.
2. Describe the type of mutation that causes sickle cell, ie substitution, insertion, deletion.



Contact Information

Regarding the lessons or curriculum, please contact Dr. Edwin Li (eli@sju.edu)
Regarding the lab exercises, troubleshooting or technical issues, please contact Dr. Brian Forster (bforster@sju.edu)

For additional lessons in this unit and others, please visit www.asbmb.org/9l2activity/